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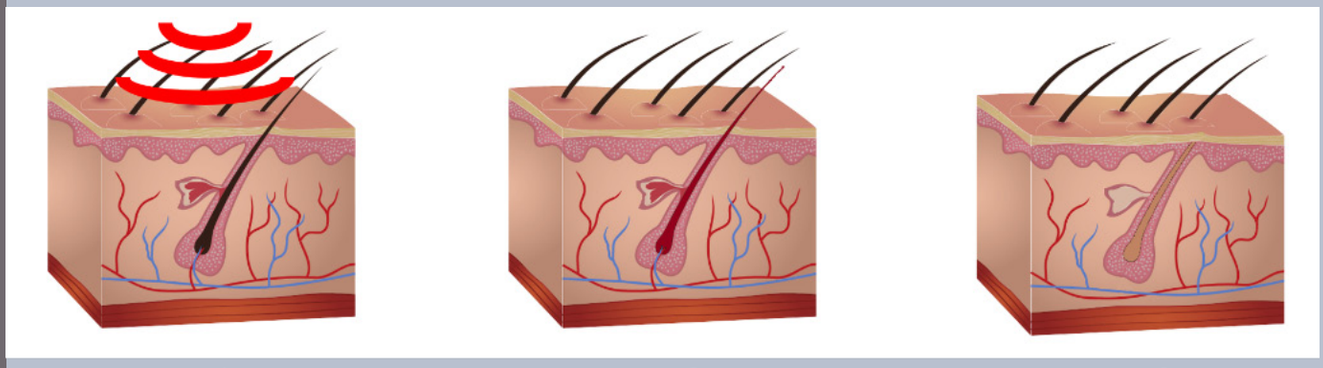

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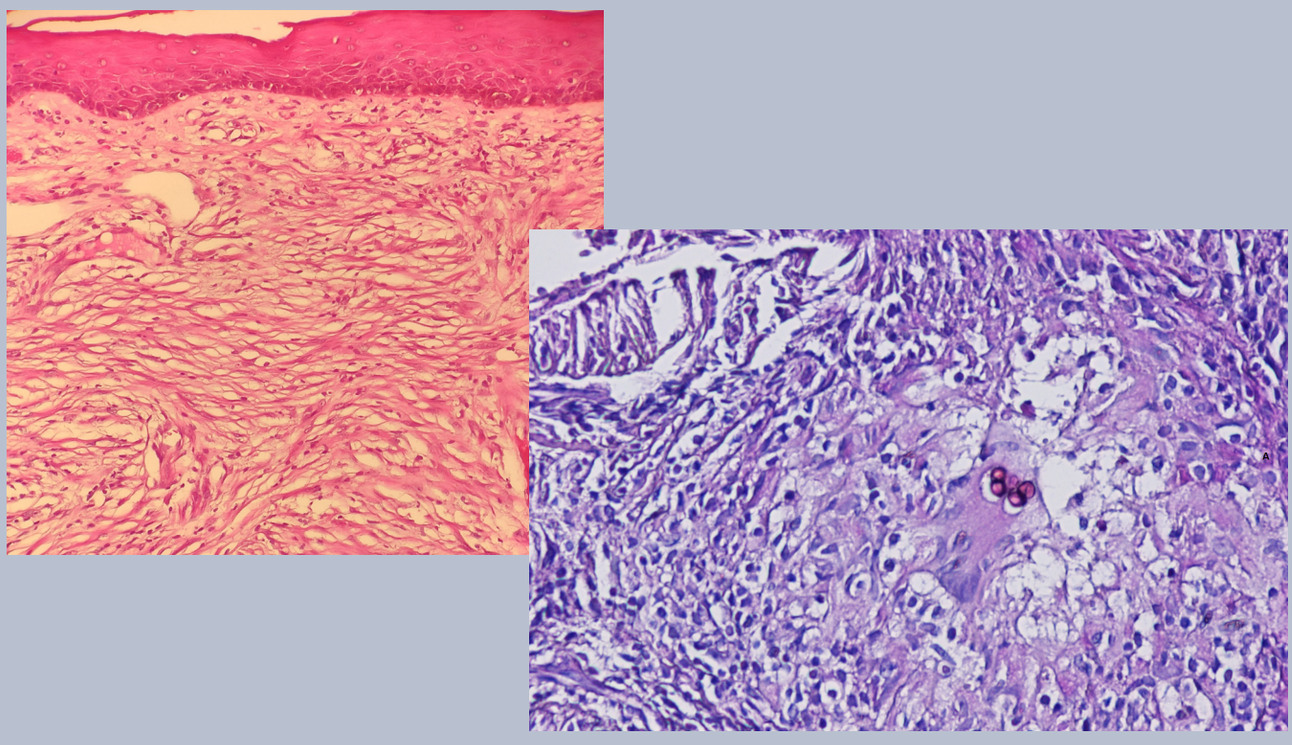

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Original Article

A pilot study assessing the various dermatoses associated with the use of a face mask during the COVID-19 pandemic

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ABSTRACT

Background: An occupational disease is any disease developing primarily as a result of exposure to risk factors arising from work activity and contributing to a significant portion of work-related diseases. Although COVID-19 is not dermatotropic, prolonged contact with personal protective equipment—that is, goggles, face shields, N95 respirators, double-layered gloves, etc.—may cause various dermatoses. Several dermatoses due to PPE have been well documented, but facial dermatoses specifically due to the use of face masks remain a relatively uncharted entity. In this study, we report preliminary data on individuals experiencing various facial dermatoses due to the use of face masks. **Objective:** The aim was to study the various facial dermatoses associated with the use of a face mask. **Materials and Methods:** After obtaining informed consent, individuals using a face mask were enrolled in this single-institution, questionnaire-based, cross-sectional study. **Results:** A total of 364 participants were enrolled for the study, among which 59.3% revealed to have worn a face mask for more than six months. A majority used ear-looped N95 masks. Nine problem areas were identified in the study. Among the facial dermatoses observed, acne was the most frequently reported, followed by redness. **Conclusion:** In spite of contact dermatitis arising due to masks, it is recommended to use well-fitted and comfortable masks for sufficient periods of time to reduce the risk of transmission, ensure safety, and reduce mask-related side effects.

Key words: Dermatitis; Mask-induced; Facial dermatoses; COVID-19; Mask dermatitis

INTRODUCTION

SARS-CoV-2, the COVID-19 virus, or the novel coronavirus are the various names given to the virus that originated in December 2019 in a small town in China called Wuhan [1]. Being highly infectious, it affected hundreds of thousands of people within a short amount of time worldwide, causing the World Health Organization to announce it as an infectious disease pandemic on January 30, 2020 [2].

The COVID-19 virus is spread by droplets or via fomites, creating the necessity to wear personal protective equipment, even if not directly in contact with patients affected by COVID-19 [1].

The mucosal membrane is the most common portal of entry for infection, including the conjunctiva and the optic canal—although with the lowest risk of transmission. Therefore, specific skin changes due to the COVID -19 virus are because of the secondary iatrogenic involvement of the skin [3].

An occupational disease is any disease that develops primarily due to work-related exposure to risk factors. Among all conditions coming under the wide umbrella of occupational dermatoses, the most common is occupational contact dermatitis, accounting for the majority of cases (79–95%), followed by contact urticaria, occupational marks, infectious dermatoses, and neoplasia, observed only in some [4].

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PPE includes gowns, gloves, masks, shoe covers, head covers, eye gear, and face shields [5]. Apart from the major shortage of PPE for healthcare professionals on the front lines and for the general public, the adverse effects from the long use of PPE are another major cause of concern [6].

According to the CDC and the WHO, wearing a face mask is mandatory if the patient is suffering from highly transmissible diseases such as tuberculosis, SARS, and COVID-19. The mask recommended for use is the N95 mask, with the N standing for NIOSH (National Institute for Occupational Safety and Health of the United States) and 95 indicating the filter efficiency of the particles. This, in simpler terms, means that an N95 mask is capable of effectively filtering 95% of airborne particles, including very small [7]. This is in comparison to the widely used surgical masks, which provide a barrier against large respiratory particles, but are ineffective in providing protection against smaller particles. Also, surgical masks are inefficient in preventing leakage around the mask during inhalation. Therefore, the reason why N95 masks are recommended is that surgical masks are ineffective and do not provide enough protection to people involved in direct care of patients with COVID-19 [2].

Among all measures taken to prevent the spread of COVID-19, the most important is social distancing, proper sanitization of the hands, and the use of face masks in and around the hospitals, and even inside the house.

Long hours of wearing a face mask and PPE come with a plethora of problems of their own, ranging from physiological to psychological burdens, and may also decrease the user's work efficiency. Prolonged use of N95 and surgical masks causes adverse effects such as difficulty in breathing, headaches, acne, rashes, skin breakdowns, and impaired cognition, to name a few [2]. Sensitivity to components in masks and PPE may cause urticarial and contact dermatitis. The most common chemical used in PPE is formaldehyde, which causes sensitivity and allergy to a significant portion of the population. Several others may also react with thiuram, found in the ear loops of surgical masks [8].

The COVID-19 pandemic has forged an exponential use of face masks of various kinds as PPE, not only by health workers but also by the general population [9].

Although contact dermatitis due to PPE has been well reported, mask-induced dermatitis is a relatively unexplored phenomenon, which is why this study was conducted, namely, to report preliminary data on individuals experiencing various facial dermatoses due to face masks.

MATERIALS AND METHODS

This anonymous, single-center, cross-sectional, questionnaire-based survey was distributed electronically at the beginning of November 2020 to healthcare professionals, patients, and their attenders. The majority of the survey respondents were males (51.1%, n = 186). The respondents' age ranged from less than 20 to more than 60 years. 3.6% (n = 13) were less than 20 years old. 69.2% (n = 252) were aged between 20 and 40 years, 26.4% (n = 96) between 40 and 60, and 0.80% (n = 3) were 60 years old and older.

Ethics Statement

The questionnaire and methodology of this study were approved by the Institutional Ethical Committee (ethics approval number: No. DMC/KLR/IEC/412/2020-21).

RESULTS

Among the 364 participants of this survey, all consented to participate in the study. 361 respondents (99.2%) agreed to wearing a mask (Fig. 1), with 59.3% (n = 216) having worn a mask for more than six months, 35.2% (n = 128) claiming to have worn a mask for 3–6 months, and about 5.5% (n = 20) having worn a mask for less than three months (Fig. 2). Most (53.02%, n = 193) of the interviewees have worn a mask for 6–12 hours daily, whereas 40.4% (n = 147) did so for less than six hours, and 6.6% (n = 24) for more than twelve hours (Fig. 3). A majority (69.8%, n = 254) of the mask users have worn an N95 mask, followed by 38.7% (n = 141) of those wearing surgical masks, 34.6% (n = 126) fabric masks, 8.5% (n = 31) FFP, and 7.1% (n = 26) something yet different (Fig. 4). Most of the mask users used ear-looped masks (77.5%, n = 282) and 49.7% (n = 181) used head-looped masks. The study revealed that 76.4% (n = 278) of the respondents who used masks had regularly experienced facial dermatitis in one or other form, while 23.6% (n = 86) reported none of these side effects (Fig. 5). In the study, pimples were one of the most prevalent skin reactions related to the use of a face mask. Other reported side effects included breathlessness (28.8%, n = 105), redness (28.8%, n = 105), rashes (25.5%, n = 93), itching (23.6%,

n = 86), oily skin (21.7%, n = 79), bad breath (17.6%, n = 64), blocked nose (15.1%, n = 55), and raw skin (10.4%, n = 38), to name a few (Fig. 5). Among 31.9% of the survey respondents (n = 116) reporting pimples as an adverse effect, 73.7% (n = 140) complained of papules while 36.3% (n = 69) complained of pustules. For those who had had adverse skin effects, the most common area was the bridge of the nose (31.6%, n = 115) and the cheeks (26.9%, n = 98). Other areas of skin breakdown were the chin (19.8%, n = 72), the area behind the ears (17%, n = 62), the jawline (17.7%, n = 41), and the nape of the neck (4.1%, n = 15) (Fig. 6).

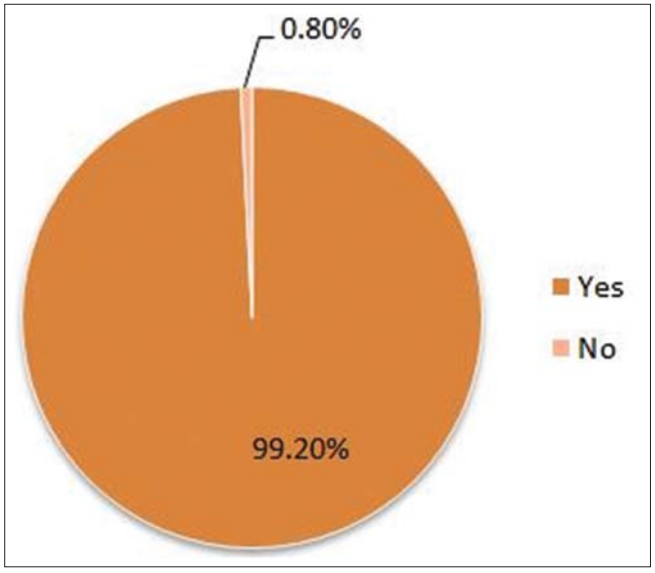

Figure 1: Do you wear a mask?.

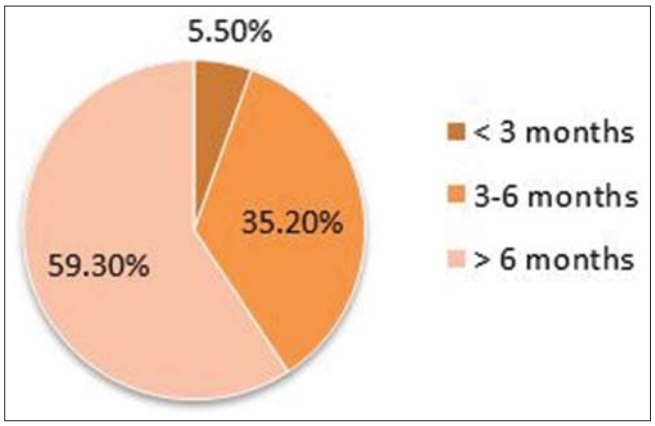

Figure 2: Duration (From when the mask is being used).

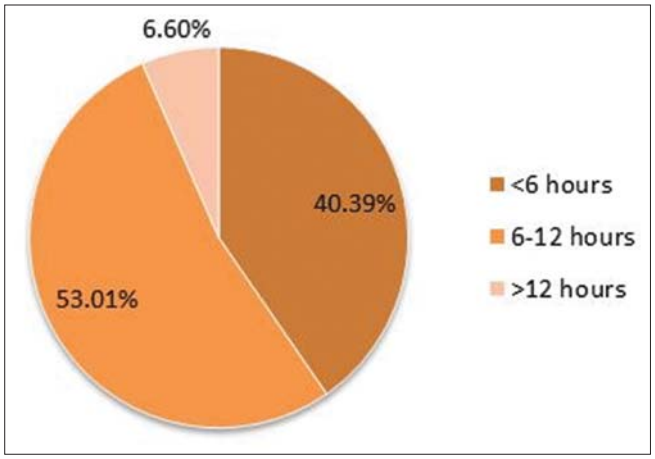

Figure 3: Number of hours of using mask daily

DISCUSSION

The COVID-19 pandemic has spread rapidly across the globe, greatly affecting how people as a whole interact,

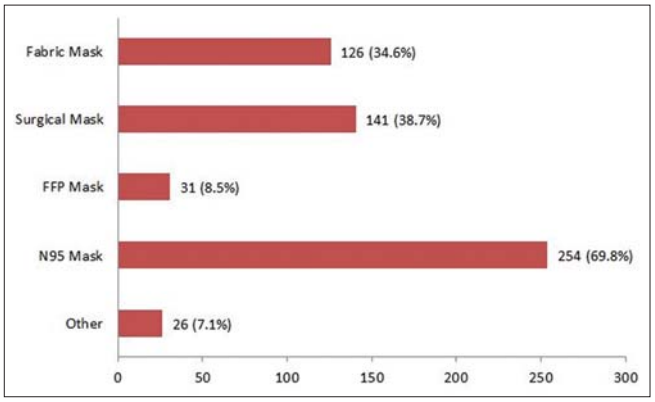

Figure 4: Type of mask used.

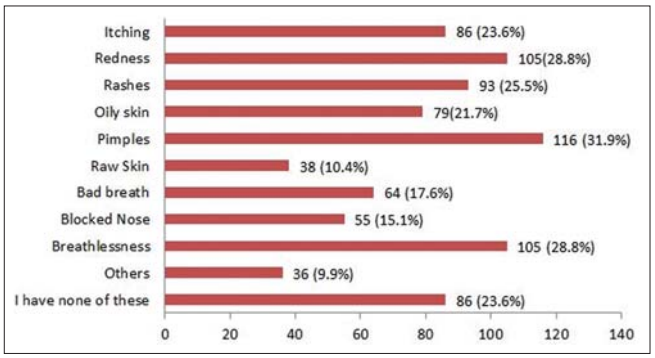

Figure 5: Main issue faced by the mask user.

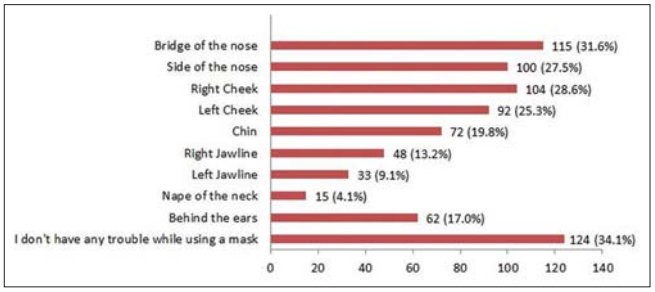

Figure 6: Areas of trouble.

work, and go about their daily life [1]. We are still in the very middle of the pandemic, and it does not seem to be ending any time soon. In fact, the cases are again on the rise, pointing toward a second wave [2].

Appropriate personal protective equipment (PPE) and frequent hand hygiene are suggested to prevent transmission of the virus [10]. However, there is evidence suggesting that these practices have a negative impact on skin health [11].

A great number of subjects who participated in this study reported adverse reactions to prolonged mask use during COVID-19. Pimples, breathlessness, rashes, and redness were all recognized as common adverse effects, which was in accordance with a study by Rosner [2]. A former study indicated that more than one-third of health care workers complained of acne, facial itching, and even dermatitis from wearing an N95 mask [12].

The skin complications are due to the hyperhydration effect of personal protective equipment (PPE), friction, epidermal barrier breakdown, and contact reactions, all of which may aggravate an existing skin disease [12].

Wearing properly fitted masks, avoiding latex straps, using soft materials, frequently changing one's masks, taking regular breaks to remove one's mask, wiping the skin to remove sweat, and frequently washing the face may help to alleviate these dermatoses [13].

Preventive measures such as removing one's mask for 10–15 minutes every two hours, provided it is safe to do so, using a gentle, non-comedogenic, fragrance-free cleanser twice a day, ensuring that the area is free of makeup, wearing straps on the crown of the head instead of straps sitting on top of the ears, and applying an alcohol-free barrier film on the areas of direct contact with PPE—for instance, the nose, cheeks, and the area behind the ears—to protect the skin from unnecessary friction may tackle most of the problems. Applying petrolatum to open areas 3–4 times a day if skin damage is present will be beneficial. For open areas of skin damage, a hydrocolloid dressing may help in faster healing; however, using these dressings under an N95 mask requires refit testing to ensure adequate seal [13].

The authors suggest using homemade cotton-cloth face masks by the general population while at home. Those with preexisting dermatoses such as chronic urticaria, seborrheic dermatitis, or atopic dermatitis should take special precautions, and the use of disposable surgical masks should be encouraged [8].

CONCLUSION

At present, there is widespread use of facial masks due to the COVID-19 pandemic, which has led to an increase in the incidence of allergies and contact dermatitis caused by contact with face masks [14]. Improved hydration and rest, skincare, frequent breaks, and properly fitted, comfortable masks are recommendations for future management of the adverse effects related to prolonged mask use [2].

Limitations

While this survey captured the experiences of the general population, including many health care professionals or those associated with the healthcare facility working on the front lines during COVID-19, there are some limitations to this study. First, preexisting conditions such as a high BMI, asthma, and other conditions were not assessed in this survey, and these could be impacting or increasing the adverse effects addressed in this survey. Second, issues such as high stress levels and the quality of sleep were also not included in this survey, and these important factors may also contribute to the adverse effects reported by the survey's respondents.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Original Article

Feasibility of learning dermatology among undergraduates through online means: the impact of COVID-19

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ABSTRACT

Background: The outbreak of the deadly disease COVID-19 has shaken the entire world. The pandemic has resulted in a global lockdown affecting all areas of life, including medical education. This has impeded the traditional way of teaching and learning activities and forced educational institutions such as medical universities to shift rapidly to distance and online learning. **Aims and Objectives:** The aim was to find out the impact of COVID-19 and the perception of undergraduate students of B.P. Koirala Institute of Health Sciences (BPKIHS) of learning dermatology through online means. **Methods:** A cross-sectional study was conducted with a self-administered online questionnaire. The inclusion criteria were all MBBS third and fourth years students of BPKIHS willing to participate in the study. **Result:** A total of 151 participants agreed to complete the online survey questionnaire. The overall attitude toward online education was positive. The majority of students agreed that online learning material should be of high quality for online education (66.2%) and that online learning will bring new opportunities for organizing teaching and learning (62.3%). Zoom and Dudal were the most common online tools used by students. The geographic location, lack of past experience in using online tools, and communication barriers such as a poor Internet connection and frequent electricity cutoffs were identified by students as the main barriers to online education. **Conclusion:** Although the COVID-19 pandemic culminated in the lockdown of medical universities, it provided opportunities for bringing innovations into effect. Such large-scale studies are missing in developing countries such as Nepal, thus further research is needed to explore these possibilities nationwide.

Key words: COVID-19; feasibility; online learning

INTRODUCTION

The COVID-19 pandemic, which began in December 2019 in Wuhan, China, has affected all areas of life, including education. As the situation worsened, the global lockdown culminated in a lockdown of educational institutions, which affected over 1.5 billion students as per a report by UNESCO [1,2]. The pandemic has challenged the well-established traditional structure of undergraduate medical education, whose backbone has been in-person teaching, as social distancing measures impeded students from assembling in learning labs, lecture halls, and small-group rooms [3,4]. The pandemic has forced educational institutions to shift rapidly to distance and online learning, and hence novel methods of delivering education to medical students have been introduced [5]. Lectures have rapidly been developed to be delivered online as webinars using various platforms, such as Zoom [6]. Using a similar web portal for online teaching by medical undergraduates would be an innovative step in Nepalese medical education. However, digital medical education is in its infancy in the geographically challenging and mountainous country of Nepal [7].

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Online learning systems, which may be synchronous or asynchronous, are web-based software for distributing, tracking, and managing courses over the Internet. It involves the implementation of advancement in technology to direct, design, and deliver learning content and to facilitate two-way communication between students and faculties [8].

Undergraduate dermatology exposure is variable, limited, and often suboptimal due to a restricted time schedule, which has been further compromised by the pandemic [9,10]. Previous studies have shown postgraduate students' perspective on these online classes, yet undergraduate students' perception is missing and it is even more important as this group is entirely dependent on online teaching during the pandemic [11]. It remains unclear whether students are ready and willing to make use of online education to obtain quality learning opportunities, which could change students' attitudes and impressions completely, and consequently the general theme of online education [12].

In developed countries, resources for online learning that have made online education feasible are easily available. However, there are limitations in developing countries such as Nepal that hinder online teaching and learning. So far, there has been a paucity of research regarding this aspect. Hence, this study was designed to assess the individual's perspective regarding the tools and methods in terms of acceptability and the impact and the barriers being encountered, which would help to plan the future implementation of online education tools accordingly. Further, the study was designed to determine the impact of COVID-19 on undergraduate medical education, which would help policymakers in taking possible steps to lessen this impact nationwide.

The objectives of this study were to determine the impact of COVID-19 and the perception of undergraduate students of B.P. Koirala Institute of Health Sciences (BPKIHS) of learning dermatology through online means.

MATERIALS AND METHODOLOGY

This cross-sectional study was conducted after obtaining ethical clearance from the Undergraduate Medical Research Protocol Review Board (UM-RPRB) of BPKIHS (code: 06/2020, date of approval: Sep. 15, 2020). The study was conducted with a self-administered online questionnaire among third- and fourth-year MBBS students of BPKIHS from October 1 through November 30, 2020. After taking well-informed consent, data was collected from the 151 students. Non-probability consecutive sampling was used. The questionnaire was comprised of a sociodemographic profile of the subject, a contextual matter that comprised basic questions on the impact of COVID-19 and specific questions that regarded online education tools that the students have been using, perceptions and attitudes of the students toward online learning and barriers/challenges of online education faced by the students.

The variables were entered with Microsoft Excel and statistical analysis was performed with the IBM SPSS software, version 23. Continuous variables were expressed as means (+/- SD) or as medians, whereas categorical variables were expressed as numbers (%). A chi-square test was employed to analyze the data statistically. P values of < 0.05 were considered statistically significant.

RESULTS

A total of 151 students agreed to participate in the study. The vast majority of the participants were male (68.2%). Most of the participants were between 21- and 25-year-old (96.7%). Among these, 20.5% were from rural areas and 79.5% were from urban areas. The pandemic had affected the students in various aspects. Many were forced to leave colleges and return home, which had created undue stress regarding their study and career (Table 1).

The various devices used, the sources of Internet connection, the preferred online learning platforms, and the monthly expenditure of the students for the purpose of online learning systems are summarized in Table 2.

As for assessing the perceptions and attitude of the students toward online teaching, a majority agreed with easy access to the Internet (91, 60.3%), possessing satisfactory computer skills (96, 63.6%), the necessity of high-quality online learning materials (100, 66.2%), online learning bringing new opportunities (94, 62.3%). Similarly, a majority disagreed with online education replacing the traditional approach (98, 64.9%), feeling comfortable to communicate (50, 33.1%), and medical universities adopting online learning more extensively (66, 43.7%) (Table 3).

Table 1: Impact of COVID-19 on the students.

Characteristics	Categories		
	Agreed n (%)	Disagree n (%)	Neutra n (%)
Ability to carry out clinical learning in wards	6 (4)	137 (90.7)	8 (5.3)
Forced to return home	98 (64.9)	24 (15.9)	29 (19.2)
More concerned about the future	117 (77.5)	5 (3.3)	29 (19.2)
Worried of not being able to afford college after the pandemic	16 (10.6)	73 (48.3)	62 (41.1)
Mental stress and anxiety increasing among medical students	114 (75.5)	7 (4.6)	30 (19.9)
Medical education system challenged worldwide, especially in resource-poor countries	143 (94.7)	1 (0.7)	7 (4.6)

Table 2: Various parameters related to online teaching.

Characteristics	Category	Frequency n (%)
Device used	Mobile	42(27.8)
	Laptop	24(15.9)
	Other	5(3.3)
	Combined	80(53.0)
Source of the Internet	Cellular data	36 (23.8)
	Wi-Fi	82(54.3)
	Combined	33(21.9)
Frequency of Internet use	Daily	101(66.9)
	Several times a week	39 (25.8)
	Several times a month	6 (4)
	Less often	5 (3.3)
Monthly expenditure (NRS)	< 500	21 (13.9)
	500 – 1000	65 (43.0)
	1000 – 1500	47 (31.1)
	> 1500	18 (11.9)
Preferred tool	Dudal	46 (30.5)
	Zoom	72 (47.7)
	YouTube	24 (15.9)
	Google Classroom	8 (5.3)
	Facebook	1 (0.7)

A majority of the students noted poor Internet connection quality, frequent power cutoffs, difficulties in maintaining focus as the major challenges and barriers of online teaching. However, they did not consider the lack of availability of gadgets and lack of knowledge regarding the utility of online software as barriers to online learning (Table 4).

DISCUSSION

The COVID-19 pandemic has had a tremendous effect on medical education. It is also challenging for medical educationists' ability to adapt to this unique situation [13]. The situation has forced medical educationists to think 'out of the box' and act innovatively with digital technologies [4].

Thus, this study was done to assess the feasibility of online learning: the impact of COVID-19 on

Table 3: Perceptions and attitudes of the students toward online teaching.

Characteristics	Categories		
	Agreed n (%)	Disagreed n (%)	Neutral n (%)
Online education enables students to continue their education similarly to the traditional approach.	18 (11.9)	98 (64.9)	35 (22.2)
I am able to easily access the Internet for my studies.	91 (60.3)	21 (13.9)	39 (25.8)
With the existence of online education, the pandemic does not disrupt my future plans.	14 (9.3)	96 (63.6)	41 (27.2)
I feel comfortable to actively communicate with my classmates and instructors online.	37 (24.5)	50 (33.1)	64 (42.4)
I have satisfactory computer skills for dealing with online courses and assignments.	96 (63.6)	21 (13.9)	34 (22.2)
Online learning saves time and effort for both teachers and students.	58 (38.4)	58 (38.4)	35 (23.2)
It is essential that online learning materials be of high quality for online education.	100 (66.2)	18 (11.9)	33 (21.9)
Online learning will bring new opportunities for organizing teaching and learning.	94 (62.3)	17 (11.3)	40 (26.5)
Medical universities should adopt online learning more extensively.	28 (18.5)	66 (43.7)	57 (37.7)
Online learning increases the quality of learning as it integrates all forms of media, that is, print, audio, video, and animation.	53 (35.1)	42 (27.8)	56 (37.1)

Table 4: Challenges and barriers to online class.

Characteristics	Categories		
	Agreed n (%)	Disagreed n (%)	Neutral n (%)
Online education makes me uncomfortable because I don't have the knowledge about the technology.	12 (7.9)	105 (69.5)	34 (22.5)
I don't have an adequate availability of hardware and software for online education.	23 (15.2)	94 (62.3)	34 (22.5)
Poor Internet as a barrier to online education.	133 (88.1)	5 (3.3)	13 (8.6)
Frequent electricity cutoffs as a barrier to online education.	90 (59.6)	29 (19.2)	32 (21.2)
Feeling a difficulty in maintaining focus during online classes.	110 (72.8)	13 (8.6)	28 (18.5)
Spending more time on the Internet causes stress and anxiety.	103 (68.2)	10 (6.6)	38 (25.2)
Unable to convince my parents to online education.	7 (4.6)	115 (76.2)	29 (19.2)
Unable to maintain privacy for my online classes.	29 (19.2)	64 (42.4)	58 (38.4)

undergraduate dermatology education. The results revealed that a majority of the students had positive attitudes toward online learning despite various challenges and barriers. The pandemic has affected all areas of life, including education. Educational institutions were shut down, both for the safety of the students and the communities. Social distancing measures have impeded students in assembling in learning labs, lecture halls, and small-group rooms [4]. In a similar way, our study revealed that, due to the COVID-19 pandemic, students were forced to return to their homes, due to which they were unable to continue their clinical learning in wards, which had led to an increase in mental stress and anxiety among medical students, making them more concerned about their future.

According to our study, Zoom and Dudal were the most commonly used tools for online learning. Also, the students preferred the Zoom application for their future studies. These results correspond to those obtained by Atreya et al. and Sandhu et al. [6,7].

Perception/Attitudes toward Online Learning

According to our study, the students had a positive attitude toward online learning. 38.4% of the students revealed a positive response toward the statement "online learning saves time and effort for both teachers and students," which corresponds with the findings by Panda et al. A significant percentage of the students (66.2%) agreed with the statement "it is essential that online learning material be of high quality for online education," which corresponds with the findings by Panda et al. [14]. Likewise, 35.1% of the students revealed a positive response toward the statement "online learning increases the quality of learning as it integrates all forms of media, that is, print, audio, video, and animation," which corresponds to the study by Panda et al. [14].

Similarly, a majority of the students (63.6%) in our study agreed with the statement "I have satisfactory computer skills for dealing with online courses/assignments." This was not consistent with a study by Muflih et al. In a similar way, a majority (60.3%) of the students agreed with the statement "I am able to easily access the Internet for my studies," which is opposite to the findings by Muflih et al. [12].

Based on our study, the significant challenges and barriers to online education were lack of past experience in using online tools for learning, communication barriers such as a poor Internet connection, frequent electricity cutoffs, and difficulty in maintaining focus during online classes and stress and anxiety in using the Internet.

According to Muflih et al., the barriers to online education according to students were "lack of past experience in using online tools" (74.3%), which is consistent with our study [12]. According to the findings of our study, the students agreed that, in resource-poor countries such as Nepal, a poor network (86.8%), a poor Internet connection (88.1%), and frequent electricity cutoffs (59.6%) were the communication barriers for online learning, which is in accordance with Atreya et al. and Panda et al. [7,14]. Regarding the statement "spending more time on the Internet causes stress/anxiety," a majority of the students (68.2%) agreed, which is consistent with a study carried out by Rajab et al. and Kapasia et al. [15,16].

The study was limited by a small sample size. Similarly, the study was conducted in a single institution and hence may not be representative of the scenario throughout the country.

CONCLUSION

The study was conducted to determine the feasibility of online learning due to the emergence of COVID-19 among medical undergraduate students representing dermatology education. According to our study, online learning is feasible in resource-poor countries such as Nepal, yet various factors impose challenges on its success. Although the COVID-19 pandemic has culminated in the lockdown of medical universities, it provided opportunities for bringing innovations into effect. Such studies are missing in developing countries such as Nepal, thus further research is needed to explore these possibilities nationwide.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in the study was obtained from all patients.

Ethical approval

Undergraduate Medical Research Protocol Review Board (UM-RPRB) of BPKIHS (code: 06/2020, date of approval: Sep. 15, 2020).

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Our Dermatology Online

Original Article

Onychomycosis in patients with diabetes mellitus: Etiology, clinical features, and treatment response

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ABSTRACT

Background: Onychomycosis accounts for 30% of all superficial mycoses and 50% of all nail diseases. One of the most studied predisposing factors is diabetes mellitus, with a frequency of onychomycosis of 31.5% in these patients. Many show resistance to standard therapeutics and have "polypharmacy", which represents a risk for pharmacological interactions. **Objective:** The objective was to assess the clinical response to therapy, evaluate with histopathology, direct examination with KOH and white-calcofluor, and culture the most frequent etiologic agents associated with the development of onychomycosis in patients with diabetes mellitus. **Materials and Methods:** A non-randomized, uncontrolled, open-ended, prospective cohort study was conducted on 46 patients with onychomycosis and diabetes mellitus. Treatment was assigned according to clinical findings and specific indications for treatment. **Results:** From the samples taken for direct examination with KOH and calcofluor-white, culture, and histopathological study, positive results were: 39 (84.1%) patients to the direct examination, 32 (69.6%) to the culture, 27 (65.2%) with a positive histopathological study, and 17 (54.86%) to the calcofluor-white. On clinical evaluation, we found no treatment response in 8 patients (20%), a partial response in 14 patients (25%), and a complete response in 18 patients (45%). Out of the 46 patients evaluated initially, 25 persisted with onychomycosis after six months of follow-up. **Conclusion:** The prevalence of onychomycosis is increasing and requires correct diagnosis since there are other non-fungal diseases of the nails that resemble onychomycosis. Presumably, the immunosuppression of diabetes, its systemic affection, and the foot abnormalities of a diabetic patient cause more nail dystrophy, an increased fungal load, and treatment resistance.

Key words: onychomycosis; diabetes mellitus; mycoses; dermatophytes; non-dermatophytes molds; nails; immunosuppression; fungi; polypharmacy

INTRODUCTION

Onychomycosis affects 5.5% of the general population [1] and accounts for 30% of all superficial mycoses and 50% of all nail diseases [2,3]. The estimated prevalence is over 10% in the general population and about 40% in older adults [2]. The main causative agents of onychomycosis are dermatophytes; however, in those that do not respond to standard therapeutics, non-dermatophyte molds should be considered associated or causal agents [2].

One of the most studied predisposing factors is diabetes mellitus, with a frequency of onychomycosis of 31.5% in these patients [2,4]. It is now accepted that diabetes increases the relative risk of developing onychomycosis (from 1.5 to 2.8 times) compared to non-diabetic patients [2]. In a study on 400 patients in India, the prevalence of onychomycosis in diabetics was found to be 17%, being 6.8% in the control group [4]. Other factors related to an increased incidence of onychomycosis include old age, male sex, repeated nail traumas, genetic predisposition and underlying diseases

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such as immunodeficiency, and peripheral vascular disease [4]. Nail thickness has been positively associated with higher HbA1C levels [5], accelerating the typical subungual keratinization induced by fungal infection. Fungal infections exceed 50% of all types of infections among diabetic patients [6]. Diabetic patients with onychomycosis exhibit a higher percentage of gangrene and foot ulcers (12.2%) compared to those without onychomycosis (3.8%) [7,8].

Onychomycosis represents a risk for the development of the diabetic foot due its association with difficulty in nail clipping, causing the patient to injure themselves, producing an access route for bacterial agents [9]. Many of these patients show resistance to standard therapeutics (in some cases associated with incomplete previous treatments); they also have "polypharmacy," which represents a risk of pharmacological interactions in systemic management, or have contraindications for systemic management, hence they are candidates for topical treatment, after culture.

This study aimed to assess the clinical response to therapy and to evaluate with histopathology, direct examination with KOH and white-calcofluor, and culture the most frequent etiologic agents associated with the development of onychomycosis in patients with diabetes mellitus, both susceptible and resistant to standard treatment.

MATERIALS AND METHODS

A non-randomized, uncontrolled, open-ended, prospective cohort study was conducted on 46 patients with onychomycosis and diabetes mellitus treated at the Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán," regardless of the time of evolution. Treatment was assigned according to clinical findings and specific indications for treatment, according to the type of onychomycosis and the number of affected nails (Table 1).

All patients were treated after their first dermatology evaluation with a follow-up at three months (in the case of systemic treatment) and at six months (in the case of topical treatment). Nails were photographed for follow-up and the samples were taken for direct examination with KOH 10% and calcofluor-white, and for mycological culture with agar for dermatophytes, SDA and potato dextrose agar. Furthermore, the distal edge of one of the affected nails was cut for histopathological study. Treatment adherence evaluation was conducted by interrogation during patient evaluations.

Table 1: Treatment assigned according to clinical findings and specific indications according to the type of onychomycosis and the number of affected nails

Terbinafine 250 mg every 24 hours for 3 months	Patients with the indication of systemic treatment without liver failure, creatinine clearance greater than 50 ml/min or those who had no interacting drugs.
Itraconazole 200 mg every 24 hours for 3 months	Patients with the indication of systemic treatment, without liver failure, with or without renal failure, or those who had no interacting drugs.
Fluconazole 150 mg every 7 days, for 3 months	Patients with the indication of systemic treatment, with superficial white onychomycosis.
Urea 40% and bifonazole 2% topical	Patients with the indication of topical treatment, who presented subungual hyperkeratosis or those who had contraindications for systemic treatment.
Amorolfine lacquer	Patients with the indication of topical treatment, without subungual hyperkeratosis.

Ethics Statement

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, were adhered to and the appropriate ethical review committee approval was received.

RESULTS

46 patients with diabetes and a clinical suspicion of onychomycosis were evaluated, 24 males (52.2%) and 22 females (47.8%), with an age ranging from 30 to 90 years, with a median of 57. Two patients were eliminated from the final analysis for death, and no sample was obtained for study from four other patients as they were lost on the last consultation.

Among the patients evaluated, a total of 25 (54.3%) were clinically found with distal subungual onychomycosis, 29 (63%) with total dystrophic onychomycosis, 2 (4.3%) with superficial white onychomycosis, 4 (8.7%) with lateral subungual onychomycosis, among whom the most affected finger was the first left toe, with 41.3%.

Among the treatments indicated, 2 received itraconazole 200 mg daily (4.3%), 7 received itraconazole in pulses, 13 received oral terbinafine daily (30.4%), 2 applied amorolfine lacquer, and 15 were treated with topical bifonazole at 2% plus urea 40% (37.5%). We found global healing of 73%, with topical management with urea 40% + bifonazole, and a response of 9% with

systemic terbinafine, 17% with itraconazole in pulses, and 50% with itraconazole daily (Table 2).

All nails at follow-up were photographed. Samples were taken for direct examination with KOH and calcofluor-white, culture and histopathological study. The positive results were: 39 (84.1%) patients to direct examination, 32 (69.6%) to culture, 27 (65.2%) with positive histopathological study, and 17 (54.86%) with calcofluor-white. At the end of the study, the patients underwent a new clinical evaluation and new samples were taken for direct examination with KOH and calcofluor-white, culture, and histopathological study. Positive results were found in 10 patients (25%) with direct examination, 18 (45%) patients with positive culture, and 20 patients (54.28%) with positive histopathology.

Table 2: Treatment and mycological cure in patients with onychomycosis and diabetes mellitus

Treatment	Mycological Cure				Total	
	Yes		No			
	No.	%	No.	%	No.	%
Terbinafine	1	9	10	91	11	100
Terbinafine + urea and bifonazole	0	0	2	100	2	100
Itraconazole pulses	1	17	5	83	6	100
Itraconazole pulses + urea and bifonazole	1	100	0	0	1	100
Itraconazole 200 mg daily	1	50	1	50	2	100
Urea + Bifonazol	11	73	4	27	15	100
Cyclopyrroxolamine lacquer	1	100	0	0	1	100
Amorolfine lacquer	0	0	2	100	2	100
Total	16	40	24	60	40	100

The most frequent histopathological findings before treatment were as follows: compact keratin (93%), parakeratosis (88%), septate short filaments (63%), and bacterial colonies (45%). In biopsies after treatment with positive results, parakeratosis was found in 95%, other frequent findings were septate short filaments (18%), serum (48%), and bacterial colonies (60%) (Table 3) (Fig. 1).

In 40 patients evaluated at the end of the study, 2 showed no treatment adherence (5%), 9 patients (22.5%) showed 50% adherence, and 29 patients (72.5%) showed 100% adherence. It was considered 100% adherence in those who applied their treatment from the beginning, 50% in those who began the treatment late and 0% in those who failed to begin the treatment. Greater adherence was found in patients with systemic treatment (17 of the 29; 58.62%), compared to 13 patients with topical treatment (13 of the 29; 44.82).

Four patients received systemic treatment, with a minimum of one month of treatment (late onset) and a maximum of five months (prolonged treatment to clinical cure), with a median of 3; and among the 18 patients with topical treatment, the minimum treatment duration observed was two months and the maximum was six months, with a median of four; with a patient with indicated topical treatment which was not initiated. On clinical evaluation, we found no response in 8 patients (20%), a partial response in 14 patients (25%), and a complete response in 18 patients (45%) out

Table 3: Histopathological findings at the beginning and end of the study in nail biopsies of patients with onychomycosis and diabetes mellitus

Before Treatment	N	%	Histopathological Finding	Before Treatment			After Treatment	
				N	%		N	%
Positive	28	70	Compact keratin	37	93	Positive	38	95
			Melanic pigment			17 (42%)	1	3
			Hematoma in the stratum corneum				1	3
			Parakeratosis	35	88		37	93
			Septate short filaments	25	63		7	18
			Non-septate short filaments				1	3
			Gram-positive cocci bacteria	18	45		24	60
			Serum	13	33		19	48
			Microabscesses of neutrophils	4	10		8	20
			Arthrospores	3	8		2	5
			Pseudohyphae	2	5			
			Laminar keratin	2	5			
			Septate filaments, thick or long	2	5		3	8
			Yeast	1	3		4	10
			Branched and angled septate filaments at 15–40°				8	20
			Septate short filaments with vesicular dilatations				4	10
Negative	12	30				23 (58%)		
Total	40	100				40 (100%)		

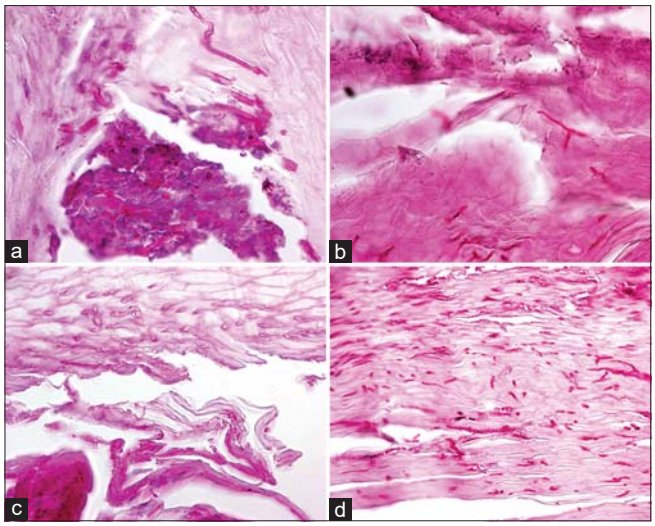

Figure 1: (a) Compact keratin sheets associated with bacterial colonies, septate filaments. (b) Compact keratin sheets associated with bacterial colonies, septate and angled filaments. (c) Compact keratin sheets and thick filaments. (d) Compact keratin sheets associated with bacterial colonies, spores, hyphae, and pseudohyphae.

of the total of 40 patients evaluated. Finally, considering the clinic, and the control studies by histopathological study, direct examination, and culture, it was found that, out of the 46 patients evaluated initially, 25 persisted with onychomycosis. Among these, a late onset of treatment was found in 13 patients, and among the causes evaluated, 11 patients reported economic causes, 1 apathy, and 1 gastrointestinal alterations, such as heartburn, after the beginning of systemic treatment.

Considering the patients who completed their treatment in a consistent manner, completing the minimum treatment required for systemic (three months) or topical (six months) treatment and who, with or without clinical resolution, continued with positive diagnostic studies (direct examination, culture, or histopathological study), 4 (10%) were considered resistant to conventional treatment, without being able to consider the remaining 21 within this group, since they had not completed the indicated treatment by the late onset of the same.

DISCUSSION

Onychomycosis in diabetics is more than just a cosmetic problem and may be a limb-threatening infection if managed inappropriately [7]. A prospective study of 1285 diabetic patients found that the presence of onychomycosis is a significant predictor for the development of foot ulcers [8]. Onychomycosis in diabetic patients is more frequently observed in the presence of poor glycemic control and peripheral vascular disease [10]. A study found that the presence of onychomycosis in patients with diabetes is associated with subclinical atherosclerosis, which in diabetic patients represents the leading cause of death. [11]. The thickened, brittle nails typical of this infection are capable of causing damage to the surrounding skin that may go unnoticed due to coexistent neuropathy. Enlarged, dystrophic toenails may also put increased pressure on the underlying toe, compromising its tenuous vascular supply and causing pressure ulcers [11,12]. The pressure required to clip thickened toenails may cause inadvertent damage to the surrounding skin. If the patient is unable to perform appropriate foot hygiene, overgrowth of thickened toenails may cause damage to the surrounding skin as well. The subungual debris typical of distal subungual onychomycosis may become a reservoir for molds and bacteria [11,13], which may represent potential invaders of the compromised skin barrier. According to the Achilles Foot Screening Project, the most commonly clinically diagnosed foot diseases in the total population of patients who visited a dermatologist were fungal infections (35%), especially onychomycosis (23%) and tinea pedis (22%) [14]. Its etiology includes dermatophytes, yeasts, and fungi, in order of frequency. Regarding this, in a retrospective study lasting for 14 years on onychomycosis by molds, conducted at the Hospital General de Mexico by Bonifaz et al. [15], it was found that the most frequent clinical presentation was lateral and distal subungual in 69% of the cases, with *Scopulariopsis brevicaulis* in 34/78 patients and *Aspergillus niger* in 13/78 (16.6%) of the patients studied [15] Mixed infections and those caused by non-dermatophyte molds are more prevalent than previously thought, especially in warmer climates [16].

The results found in this study are consistent with the rest of the literature, since most of the patients presented total dystrophic onychomycosis, followed by distal subungual onychomycosis, and the most affected finger was the first of the left foot, with 41.3%.

Dermatophytic onychomycosis, predominates in male patients in a relation of 2:1. The global prevalence falls between 2–15% in adults and represents 50% of all ungual conditions [12].

Indications for systemic treatment include having three or more affected nail plates or having the condition on one nail at the level of the nail matrix [15]. The main difference in treatment is due to the fact that

some of the patients have chronic renal disease with creatinine clearance less than 50 ml/min, which contraindicates the use of terbinafine. Although it is the safest drug with the fewest drug interactions, there are no controlled studies in patients with creatinine clearance below 50 ml/min. For these, itraconazole may be used safely, although most of our population has polypharmacy, which sometimes makes management difficult because of drug interactions. It also requires greater vigilance with baseline and follow-up liver function tests.

Direct examination is performed after adding potassium hydroxide (KOH). KOH preparations have been reported to have a false-negativity rate of 5–15% [15]. Direct examination with KOH, although operator-dependent, correlates with culture results and with the number of positive histopathological studies, the latter being the gold standard in the diagnosis of onychomycosis, and further supports the positivity of cultures and rules out their contamination. Fungi may be better visualized by adding chlorazol black, periodic acid–Schiff (PAS), or calcofluor-white stain [17]. The use of the latter significantly increases the sensitivity and specificity of this technique for the detection of dermatophytes, yeasts, and non-dermatophyte fungi [18].

Among the main limitations of the study was the lack of confirmation through molecular biology studies, due to the lack of equipment in the institute. One of the key difficulties in interpreting this study is that the majority of fungi identified by culture are either not known to be nail pathogens or are highly rare pathogens. Despite diminution of immunity in some diabetics, the pathogens cited, such as *Fusarium*, cause onychomycosis in the face of profound neutropenia, which is rather different from that in diabetics. Another explanation might be that a dermatophyte in the nail has not grown due to the presence of contaminating fungi. Another is that the fungi found are secondary to some other cause of onychodystrophy.

The presence of bacterial clusters is interesting. It might be due to space under the nail, and the growth of bacteria such as *S. aureus*, which is key to the development of diabetic ulcers, is favored.

The increase in the number of histopathological findings in the control biopsies is thought to have been due to the fact that, initially, some of the patients were managed by "podiatrists," and, in addition to having been treated with bad nail cutting, they were given excessive filing of the nails, which made it difficult for some patients to take samples from their nails. When taking control samples, filing and cutting were intentionally suspended for a week prior to the evaluation for facilitation.

Diagnosis of onychomycosis is difficult because of the difficulty in isolating fungi from infected nails. The classical technique is performed with a curette. However, Shemer et al. showed in a study on 194 patients that, with a technique in which a channel 1–2 mm in size is perforated with an ungual drill, a medial, distal, and proximal sample can be taken, being effective for culture and therefore for diagnosis [19] (Fig. 2). Nail sampling is, in fact, a delicate procedure that requires the mycelium front to be reached by the instrument in order to provide positive cultures [20,21]. Histopathology of nail clippings stained with PAS also referred to as histomycology with PAS is the most sensitive method of diagnosing onychomycosis [22], while others point out that it is not more effective than direct examination [23,24]. Confocal laser-scanning microscopy is an emerging diagnostic technique. The aspect of dermatophytes appears as a network of lengthy structures with high reflection and the typical shape of hyphae [25,26]. Other interesting new tools in the diagnosis of onychomycosis are the dermatophyte test strip and Raman spectroscopy [22].

Immunosuppressed patients show variation in clinical presentation, as well as in causative agents. Additionally, fungi traditionally considered as non-pathogenic may be found as pathogens, often associated with high mortality, as in the case of *Fusarium* species that cause perionyxis and may provide a gateway for a disseminated infection [27]. As for the isolated agents in the cultures for this study, a large number of opportunistic fungi was found (*Acremonium* sp. *Candida* sp. (Fig. 3), *Alternaria* sp. *Aureobasidium* sp., *Aspergillus* sp., *Candida guilliermondi*, *Candida albicans*, *Rhodotorula* sp., *Cryptococcus albidus*

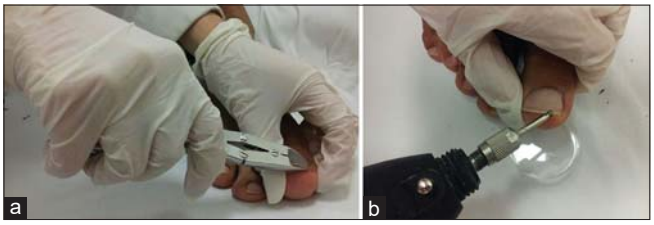

Figure 2: (a) Nail cutting technique for histopathological study. (b) The technique to obtain the sample with a drill for direct examination with KOH, calcofluor white, and culture.

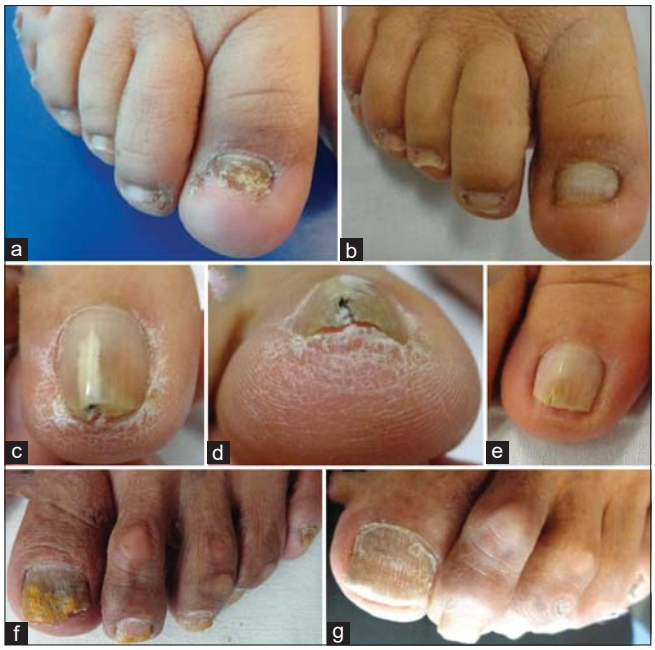

Figure 3: (a-b) *Candida parapsilopsis*. Positive on direct examination and culture. (a) Initial photograph with total dystrophic onychomycosis. (b) Final photograph after six months of topical treatment with 40% urea and bifonazole. Clinical and mycological cure. (c-e) *Acremonium sp., Candida sp.* Positive direct examination and histopathological study. (c-d) Initial photograph. (e) Final photograph after six months of topical treatment with 40% urea and bifonazole. Clinical and mycological cure. (f-g) *Cladosporium sp., Candida parapsilopsis*. Negative initial direct and histopathological examination. (f) Photograph after two months of systemic treatment (total dystrophic onychomycosis). (g) Final photograph after five months of systemic treatment. Clinical cure.

(Fig. 4), *Fusarium* sp. (Fig. 5), among others), which is probably associated with diabetes-associated immunosuppression (Table 4) [28,29].

In general, greater therapeutic failure was seen in onychomycosis caused by non-dermatophytes molds, followed by yeasts. Although the clinical improvement in these patients, both partial and total, was highly evident and larger than expected, the mycological and histological cure was far below from what was expected, hence we consider that a longer treatment time is required, either with the same medication or with topical and systemic combination therapy, and wait for a new culture and histological study. Approximately 20–25% of patients do not respond to the initial therapy and often switch to different treatments. An undetermined percentage of patients do not respond to any of the therapies [30]. The non-dermatophyte molds such as *Fusarium* spp., are the most resistant fungi to standard treatment for onychomycosis either topical or systemic [31], non-responders are defined as those patients who received treatment for six and three months without improvement in more than 50% of the nail unit [32,33].

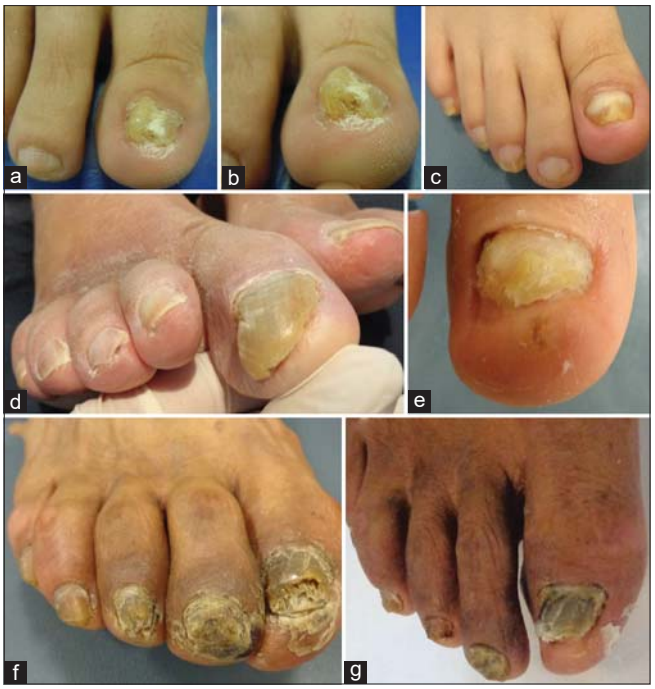

Figure 4: (a-c) *Cryptococcus albidus*. Positive direct and histopathological examination. (a-b) Photograph at the onset of topical treatment (total dystrophic onychomycosis). (c) After six months of topical treatment. Clinical and mycological cure. (d-e) *Fusarium sp.* Positive direct examination and histopathological study. (d) Initial photograph (total dystrophic onychomycosis). (e) After five months of systemic treatment with itraconazole 200 mg per day and 40% topical urea. Clinical and mycological cure. (f-g) *Cryptococcus albidus, Cladosporium sp.* Positive direct examination. (f) Initial photograph (total dystrophic onychomycosis). (g) Final photograph (one month of systemic treatment with itraconazole in pulses of 400 mg). 10% improvement.

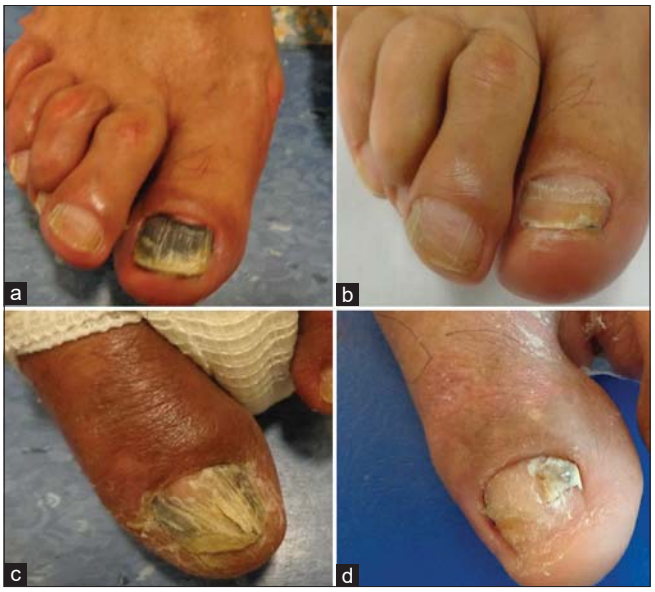

Figure 5: (a-d) *Fusarium sp.* Negative direct examination. Positive histopathological study. (a) Initial photograph (total dystrophic onychomycosis). (b) After three months of systemic treatment with itraconazole pulses of 400 mg per day and topical urea at 40%). Clinical cure without mycological cure. (c) Left foot. (d) Left foot control.

Table 4: Comparison of culture isolates before and after treatment.

	Isolates Before Treatment (*n* = 26)	Mycological Cure (*n* = 15)	Mycological Failure After Treatment (*n* = 11)
Onychomycosis by yeasts	9 (34.6%)	7 (46.6%)	2 (18%)
Candida sp.	1 (3.8%)		
C. albicans			
C. parapsilopsis	5 (19.2%)		2 (18%)
C guilliermondi	3 (11.5%)		
Other yeasts	4 (15.3%)	1 (6.66%)	3 (27%)
Rhodotorula sp.			
Rhodotorula glutini	1 (3.8%)		
Rhodotorula mucilagi			1 (9%)
Cryptococcus albidus	3 (11.5%)		
Cryptococcus neoformans.			1 (9%)
Cryptococcus unigutt.			1 (9%)
Filamentous fungi			
Dermatophytes	1 (3.8%)		1(9%)
Trichophyton sp.	1 (3.8%)		1 (9%)
Non-dermatophytes	12 (46.15%)	7 (46.6%)	5 (45.4%)
Filamentous hyaline fungi:			
Acremonium			
Fusarium sp.	1 (3.8%)		1 (9%)
Aspergillus sp.	3 (11.5%)		2 (18%)
Dematiaceous	2 (7.6%)		
Alternaria sp.			
Cladosporium sp.	2 (7.6%)		
Mucorales (zigomycetous).	1 (3.8%)		1 (9%)
Absidia sp.			
Epicoccum sp.			
Penicillium sp.			
Aerobasidium sp.			
Trichoderma sp.	2 (7.6%)		1 (9%)
	1 (3.8%)		

It would be worth conducting a study on patients without diabetes mellitus to compare whether it is the immunosuppression of diabetes and its systemic affection as well as the foot abnormalities of the diabetic patient that cause more nail dystrophy, an increased fungal load, and treatment resistance.

Recently, a reproducible and objective system called the Onychomycosis Severity Index (OSI) was created to describe the extent and involvement of distal subungual onychomycosis, with points are given based on the area (%) of nail involvement, the proximity of the disease to the matrix, and the presence of dermatophytoma or subungual hyperkeratosis [16].

In conclusion, onychomycosis is a common ungual disease that affects a large part of the global population. Its prevalence is increasing, influenced in part by its association with older age, lifestyle, and concomitant diseases. It may cause disability and lead to mild to severe complications, among which the most important is the diabetic foot, which may condition osteomyelitis and sepsis, which justifies its early treatment. In addition, it requires a correct diagnosis, which includes clinical evaluation, direct examination, culture, and a histopathological study, since there are other non-fungal diseases of the nails that resemble onychomycosis and are over-treated, generating expensive treatments with potential adverse effects, which makes it mandatory to confirm the clinical diagnosis with direct examination, culture, and, if possible, histopathological study. The treatment of onychomycosis is one additional facet of diabetic care that promises to further improve outcomes in these patients.

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Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Original Article

Prevalence of dermatoses among hairdressers and beauticians in Srinagar, the capital city of Kashmir, India

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ABSTRACT

Background: Skin disorders among hairdressers and beauticians have been recognized as a common problem, owing to the prolonged exposure to a variety of irritants and allergens. **Objectives:** The aim was to study the prevalence of dermatoses among hairdressers and beauticians in Srinagar, the capital city of Kashmir, India. **Methods:** The study was conducted on 100 respondents from 57 salons and parlors located within the borders of the city. Detailed history taking and complete examination were performed during personal visits. Patch tests were performed with the Indian standard series on all participants. **Results:** The mean age of the study sample was 24.3 ± 6.3 years. 54% of the studied cases were found to suffer from one or more skin disorders. Hand eczema was the most commonly encountered dermatosis, observed in 32% of the cases. Three patterns of hand eczema were recognized: classic (14%), interdigital (6%), and threading (8%). Callosities were seen in 19% of the cases. We employed the term *scissor nodule* for the typical pattern of a callosity caused by the finger rings of scissors. Nail staining was encountered in 19%. The most common allergens leading to a positive patch test were found to be paraphenylenediamine (PPD) in thirteen cases, followed by a fragrance mix in nine, nickel sulfate in nine, thiuram in three, and formaldehyde in one. **Conclusion:** Skin disorders are common among hairdressers and beauticians. Raising awareness of these disorders and methods of their prevention among this group is imperative.

Key words: Beauticians; Hairdressers; Dermatoses; Prevalence; Kashmir, India

INTRODUCTION

The history of hairdressing and beauty salons dates back thousands of years. Ancient Egyptians were well versed in the art of hair dyeing with vegetable dyes as early as 5000 BC [1]. Hairdressers were held in great esteem in some cultures of Africa, owing to the belief that a person's spirit occupies their hair. The word *hairdresser* is used for the first time in Europe during the 17th century. While influential and wealthy families had personal barbers in their homes, community barbershops sprouted for the less privileged. Beauty salons became popular during the 20th century. Focused on women, these places provided services such as facials and hairstyling, additionally serving as social spaces, allowing women to socialize. The role of hairdressers and beauticians in the 21st century has expanded from traditional hairdressing and cleaning to a myriad of cosmetic procedures such as conditioning, bleaching, dyeing, waving, straightening, waxing, cleansing, and providing spa treatments.

Hairdressers and beauticians bear the increased risk of developing occupational dermatoses due to exposure to a variety of irritants and sensitizers, such as shampoos, conditioners, dyes, bleaches, waxes, nail

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polishes, massage oils, and skin care products. Contact dermatitis is the dominant occupational dermatosis encountered and includes both irritant and allergic contact dermatitis [2]. Irritant dermatitis is attributed to wet work and exposure to irritants such as shampoos, conditioners, and styling products [3]. This results in delipidation of the skin leading to dry, flaked, split, and cracked skin. Ammonium persulfate in bleaches, *para*-phenylenediamine and *para*-aminoazobenzene in hair dyes, nickel sulfate and cobalt chloride in metals, balsam of Peru in fragrances, formaldehyde in preservatives, and glyceryl thioglycolate in wave components are the common allergens [4].

In India, hairdressers and beauticians work for long hours, take fewer precautions, and are less likely to be certified in their field of expertise when compared to those in Western countries. The licensing procedure is also less rigorous and the possibility of untrained professionals performing this sort of work is a valid concern. The distinction between hairdressers and beauticians is not clear-cut in India and both services are often provided by same person at a salon or parlor and, thus, the terms may be used interchangeably. The statistics regarding the prevalence of dermatoses among hairdressers and beauticians in the subcontinent are not plentiful. In this study, we attempted to determine the prevalence, clinical features, and pattern of dermatoses in hairdressers and beauticians in Srinagar, the capital city of Kashmir, India. We also aimed to educate and raise awareness among the study group regarding potential skin problems and relevant preventive measures.

MATERIALS AND METHODS

The study was an observational cross-sectional study conducted in the district Srinagar, the summer capital of Jammu and Kashmir. One hundred hairdressers and beauticians working in 57 salons and parlors located in Srinagar were included in the study. Institutional ethical committee clearance was acquired before recruiting the participants for the study. The sample size was decided after consultation with a statistician. The selection of salons for the study was performed randomly by multistage cluster sampling. The subjects were recruited during personal visits at randomly selected salons and parlors after explaining the purview of the study and obtaining a valid consent.

Inclusion Criteria

All hairdressers and beauticians working full-time for at least one year and willing to participate in the study were enrolled in the study.

Exclusion Criteria

Trainees and apprentices and those who did not consent to take part in the study were excluded.

The study participants were interviewed regarding their job description, work exposure, medical history, occupational history, and use of protective equipment such as gloves and aprons. Skin examination was performed in search of dermatoses. All the relevant data was recorded on predesigned proformas. Patch tests were performed with the Indian standard series on all participants, which consists of twenty antigens commonly implicated in the causation of allergic contact dermatitis (Table 1).

The antigens were placed on twenty patch test chambers mounted on two adhesive tapes. The adhesive tape along with the patch test chambers constituted a patch test unit. The two patch test units thus formed were stuck on the back of each participant (Fig. 1). The sites of application of the antigens were marked on the back with skin markers. The patch test units were removed after 48 hours and readings were taken at that time and again at 96 hours. The grading of the patch test results based on the morphology of the lesions as per the guidelines of The International Contact Dermatitis Research Group (ICDRG) (Table 2) [5].

Table 1: Antigens in the Indian standard series

No.	Name of antigen
1	Vaseline
2	Wood alcohol (lanolin)
3	Balsam of Peru
4	Formaldehyde
5	Mercaptobenzothiazole
6	Potassium bichromate
7	Nickel sulfate
8	Cobalt sulfate
9	Colophony
10	Epoxy resins
11	Paraben mix
12	Paraphenylenediamine
13	Parthenium
14	Neomycin sulfate
15	Benzocaine
16	Chlorocresol
17	Fragrance mix
18	Thiuram mix
19	Nitrofurazone
20	Black rubber mix

All the data was compiled in the form of a master chart and statistical analysis was done with the OpenEpi software. A p of less than 0.05 was defined as significant.

RESULTS

The study included a total of 100 participants—54 males and 46 females. Most of the hairdressers and beauticians were nonlocals, comprising 59% of the study sample. The average age was 14 to 48 years, with a mean age of 24.3 ± 6.3 years (Table 3).

Out of the 100 participants, 54 (54%) had one or more occupational dermatoses, while the remaining 46 were free of skin problems. The various dermatoses encountered during the course of the study are listed and described below.

Table 2: Grading of patch test results as per the guidelines of International Contact Dermatitis Research Group (ICDRG)

Morphological Symbol		Interpretation
-/	No reaction	Negative
?	Erythema only, no infiltration	Doubtful reaction
+	Erythema, infiltration, and/or papules	Weakly positive
++	Erythema, infiltration, papules, and vesicles	Strongly positive
+++	Erythema, infiltration, and confluent vesicles	Extremely positive
IR	Vesicles, blisters, and necrosis	Irritant reaction
NT		Not tested

Table 3: Demographic characteristics of our study sample

No.	Characteristic	Group	Number	Percentage
1	Age	10–20 years old	20	20%
		21–30 years old	68	68%
		31–40 years old	10	10%
		41–50 years old	2	2%
2	Gender	Male	54	54%
		Female	46	46%
3	Professional experience	< 1 year	0	0%
		1–5 years	68	68%
		5–10 years	24	24%
		> 10 years	8	8%

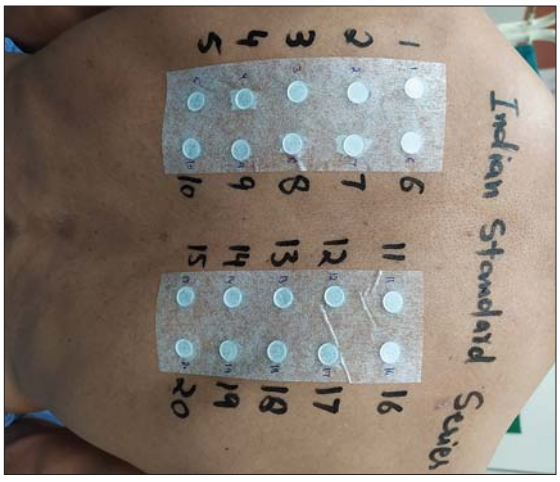

Figure 1: Patch test units applied on the back of a respondent.

Hand Eczema

Hand eczema was the most commonly encountered occupational dermatosis, observed in 41% of the cases. We found three common patterns of hand eczema: classic, interdigital, and threading. Classic eczema mostly involved the palmar and dorsal surface of the hands, while interdigital eczema involved the web spaces of the fingers, as the name suggests (Figs. 2 and 3). Threading eczema involved friction occurring as a result of a thread wound around the fingers during hair removal procedures (Fig. 4). Isolated classic hand eczema was seen in 20% of the cases, interdigital eczema in 9%, and threading eczema in 8%. A combination of classic with interdigital or threading eczema was seen each in 2% of the cases. Out of the 41 cases with hand eczema, only 13 cases (31.7%; n = 13/41) used gloves

Figure 2: Classical hand eczema – Scaling and fissuring on the palms.

Figure 3: Interdigital eczema – Scaling involving the interdigital spaces predominantly.

as a protective measure. However, none of the cases reported consistent and proper use of protective gloves. The use of gloves was, at best, sporadic and as needed. Among the 59 cases without hand eczema, 40 (67.8%; n = 40/59) reported proper and consistent use of gloves. The difference between the two groups was found to be statistically significant ($p = 0.0003$).

Callosities

Friction-induced callosities involving the hands were noted in 19 cases (19%). The callosities were observed on the palmar surface of the hands in 2 cases (2%) (Fig. 5). These might be attributed to the regular use of foot files for pedicure. However, the more common variety of callosities encountered was on the dorsal surface of the middle phalanx of the ring finger and, less commonly, on the thumb of the right hand, in 17 cases (17%) (Fig. 6). We colloquially used the term *scissor nodules* to refer to these lesions due to their typical location and nodular morphology.

Nail Staining

Staining of the distal portion of the nails was an occupation-related dermatosis encountered in 19 (19%) participants involved in hair dying professionally, but only in cases in which the hairdresser or beautician preferred bare hands for the application of dyes (Fig. 7). The color of the nail stains varied from brownish-black to blue and could generally subside with time off work.

PATCH TEST RESULTS

Patch testing was performed in all cases, regardless of the presence or absence of a dermatosis reported. Out of the 100 cases, positive results were obtained in 35 (35%), including 22 suffering from hand eczema and 13 without evidence of contact dermatitis. Out of the

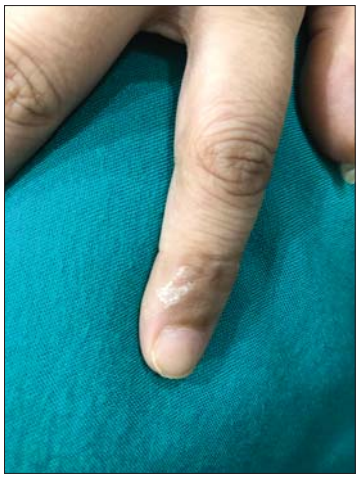

Figure 4: Threading eczema – Fissures with scaling on the lateral aspect of the index finger.

Figure 5: Callosities involving the palmar surface of hands.

Figure 6: Scissor nodule – Nodular callosity on the dorsum of middle phalanx of ring finger.

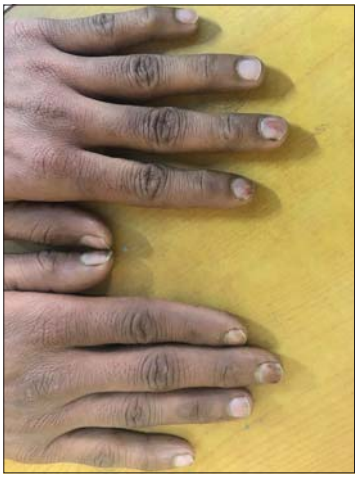

Figure 7: Nail staining – Bluish black staining of distal end of nails.

41 cases with hand eczema, 22 (53.7%; n = 22/41) gave a positive patch test, while, among the remaining 59, only 13 (22%; n = 13/59). The difference between the two groups was found to be statistically significant, pointing toward a strong possibility of allergic contact dermatitis in the former group ($p = 0.001$). A positive reaction in the group with hand eczema was observed in 16 (80%; n = 16/20) cases with classic eczema, 3 (75%; n = 3/4) with combination eczema, 2 with interdigital eczema (22.2%; n = 2/9), 1 with threading eczema (12.5%; n = 1/8). Patch testing was found to be the most relevant in the setting of classic hand eczema with the chi-squared test ($p = 0.001$). The most common allergens leading to a positive patch test were found to be paraphenylenediamine (PPD) in thirteen cases (13%; n = 13/100), followed by a fragrance mix in nine (9%; n = 9/100), nickel sulfate in nine (9%; n = 9/100), thiuram in three (3%; n = 3/100), and formaldehyde in one (1%; n = 1/100). All the 22 cases who tested positive for PPD or a fragrance mix (Figs. 8 and 9) were suffering from hand eczema, while the 13 cases who tested positive for nickel sulfate or thiuram had no clinical evidence of eczema. Thus, a causal relationship between hypersensitivity and eczema might be established in the case of PPD and a fragrance mix but, in the case of nickel sulfate, thiuram, and formaldehyde, there was hypersensitivity but no causal association with eczema.

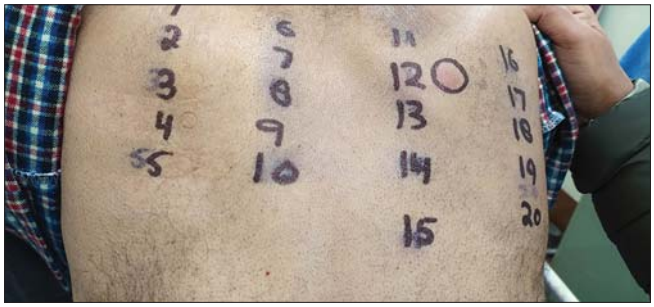

Figure 8: Patch test positive with erythema and induration at site 12 (Paraphenylene diamine).

Figure 9: Patch test positive with erythema and induration at site 17 (Fragrance mix).

DISCUSSION

Skin disorders are a common problem among hairdressers and beauticians, owing to the nature of their work and the regular exposure to chemicals. Out of the studied cases, 59% were found to suffer from one or more dermatoses. This was similar to a study from Dhaka, reporting the frequency of dermatoses among hairdressers to be 76.7%, and to another study by Caroe et al., reporting the prevalence to be 46.7% [6,7].

Hand eczema was the most commonly encountered dermatosis and this was consistent with previous studies [6,8,9]. Three patterns of hand eczema were encountered: classic hand eczema, presenting with scaly plaques on the palmar surfaces of the hands, occurring due to exposure to a myriad of allergens; interdigital eczema, involving the web spaces of the fingers, seen in cases frequently involved in wet work such as shampooing clients and spa treatments, occurring typically due to the passage of hair between the hairdresser's fingers during these procedures, increasing exposure to irritants; and threading eczema, most commonly seen in the form of linear fissures with scaling and involving the lateral aspect of the distal phalanx of the index finger, occurring due to constant friction caused by a thread twisted around the index finger in threading procedures such as hair removal. The role of mechanical friction in the development and aggravation of eczema is a well-known fact, documented in a number of studies [10,11]. We also witnessed a similar pattern. Based on history taking, work patterns, and the clinical presentation, it may likely be presumed that interdigital eczema is irritant in nature, classic hand eczema is allergic in nature, while threading eczema is frictional in nature.

Proper and consistent use of gloves during all procedures offered good protection against the development of eczema, as documented by a statistically significant difference observed in our study. Although sensitivity to thiuram was documented by patch testing in some cases, no clinical significance could be assigned to this finding.

Callosities were commonly encountered among the study subjects and occurred due to constant friction.

Callosities involving the palmar surfaces of the hands were seen in a minority of the cases (Fig. 5), while the more commonly encountered pattern involved the dorsum of the distal phalanx of the ring finger and thumb, colloquially termed *scissor nodules* (Fig. 6). These occurred on the dominant hand due to hairdressers' typical habit of holding the scissors by the thumb and ring finger and occurred classically in cases in the habit of using scissors with iron finger rings. Scissors with plastic finger rings were less likely to cause *scissor nodules*.

Staining of the distal portion of the nails was another problem encountered among the hairdressers and beauticians (Fig. 7). It was associated with the use of coloring agents and was found exclusively in cases lacking consistency in the use of gloves during hair dying. Most were uncomfortable with the use of gloves and believed that applying dyes directly with bare hands resulted in a better final result and more customer satisfaction. The staining was of a semipermanent nature as it was resistant to washing, even repeatedly, but would improve over a couple of months off work.

Patch testing was done in all cases, regardless of the presence or absence of eczema. Among the studied participants, 35% (n = 35/100) tested positive. This was comparable with the findings reported by a Polish and a Danish study, reporting positive patch test results in 38.1% and 55.1% of cases, respectively. [12,13] Although Gupta et al. reported a much higher positivity of patch test results in their study (73.3%), this might be attributed to the fact that they did patch testing only in cases with suspected contact dermatitis [14]. Classic hand eczema showed a statistically significant relation with patch test positivity. Out of the three patterns of hand eczema noted in our study, classic hand eczema was the most likely to be allergic in nature. This was consistent with the clinical assessment that interdigital eczema is related to excessive wet work with shampoos and chemicals while threading eczema is related to friction. Out of all 41 cases of eczema, 53.7% (n = 22/41) were confirmed as allergic in nature, based on history taking, clinical examination, and patch testing, while 21.9% (n = 9/41) were cases of irritant dermatitis. This finding was in consonance with a previous study by Lyons et al. [15], who reported the prevalence of allergic and irritant contact dermatitis to be 71% and 20%, respectively.

The most common allergens of occupational relevance determined by patch testing were paraphenylenediamine (13%), followed by a fragrance mix (9%), and thiuram (3%). Although thiuram sensitization might be attributed to the use of gloves, no clinical relevance could be attributed to this finding. Antigens such as nickel sulfate (9%) and formaldehyde (1%) also showed a positive reaction in certain cases but these were unlikely to bear clinical relevance. Our findings were similar to those reported by Gupta and Minamoto, who found the most common allergens to be paraphenylenediamine, followed by a fragrance mix [15,16]. A study by Krecisz et al. documented nickel sulfate to be the most common sensitizer (29.3%) [12]. While it was much less so, their study included more than 90% of females, while ours had a more balanced distribution, with approx. 50% of females.

Skin disorders are a prevalent health problem among hairdressers and beauticians in the region of India, affecting more than 50% of respondents. Proper and consistent use of protective equipment such as gloves and the avoidance of prolonged exposure to irritants and allergens should be promoted in this group. With proper education and institution of protective measures, the prevalence of dermatoses in this vulnerable group may be reduced greatly.

Limitations

We used no cosmetic series when patch testing our study sample, which could have been more informative, and the sample size in our study was small.

CONCLUSION

The incidence of cosmetic dermatitis is high among beauticians and hairdressers. Hair dyes, creams, and shampoos are the commonly implicated agents in the causation of eczema, whereas paraphenylenediamine and a fragrance mix are the most common causative allergens. Callosities and nail staining are also encountered commonly, although these are not especially bothersome to the patient. Recommendation regarding the proper precautions and protective equipment for this group of professionals is needed.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Original Article

A clinicomycological study on chronic dermatophytosis in a tertiary care hospital in North India: An observational study

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ABSTRACT

Background: Chronic dermatophytosis is a considerable challenge in routine clinical practice. There is, however, scarce information available in the literature on its extent and characteristics. **Aim:** The aim of this study was to evaluate the host-related factors of chronic dermatophytosis and to identify the common fungal isolates. **Methods:** The study enrolled a total of 145 cases of chronic dermatophytosis attending the out-patient department of a tertiary care hospital in Jammu from November 2017 through October 2018. A detailed history was taken, followed by a clinical examination and investigations such as routine baseline investigations, an absolute eosinophil count, a wet mount for direct microscopy, and a fungal culture. **Results:** The most common presentation was tinea corporis with tinea cruris (33.1%), followed by tinea corporis alone. The majority of the patients (54.5%) had more than 20% of the body surface area involved. Most of the patients were manual workers (n = 44; 30.3%). The number of hours of sun exposure varied between 1 to 8.5 hours (mean ± SD: 3.53 ± 1.75 h). The fungal culture was positive in 65 (44.8%) patients. The most frequent isolates were *Trichophyton mentagrophytes* (53.8%), followed by *Trichophyton rubrum* (38.5%). **Conclusion:** We found *Trichophyton mentagrophytes* the predominant pathogen in chronic dermatophytosis, followed by *Trichophyton rubrum*, which demonstrates a changing trend as far as the causative organism is considered. Besides, various risk factors for chronicity such as prolonged sun exposure, lack of proper hygiene, wearing tight-fitting synthetic clothes, the use of topical steroids, and non-compliance to treatment were identified.

Key words: Chronic dermatophytosis; *Trichophyton mentagrophytes*; Topical steroids

INTRODUCTION

The dermatophytes are a group of closely related fungi with the capacity to invade keratinized tissue to produce infection: dermatophytosis. The etiologic agents of dermatophytosis include three anamorphic (asexual) genera: *Epidermophyton*, *Microsporum*, and *Trichophyton* [1].

We are witnessing, nowadays, a tremendous increase in the number of cases of chronic and recurrent dermatophytosis [2]. This pattern of dermatophytosis is also reported in other parts of the world, especially the tropics [3]. Although there is no standard definition of *chronic dermatophytosis*, the term refers to patients who have been suffering from the disease for more than six months to one year, with or without recurrence, in spite of being treated [2]. In view of the lack of recent studies on the various host and pathogen related factors contributing to chronic dermatophytosis, this observational study was conducted.

METHODS

Study Design and Setting

This was an observational study conducted at the Postgraduate Department of Dermatology of a tertiary

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care hospital in North India from November 2017 through October 2018. After obtaining approval from the institutional ethical committee, patients reporting to the Dermatology OPD were deemed eligible. The diagnosis of dermatophytosis was clinical. A written informed consent was taken from all the patients.

Inclusion Criteria

Included were clinically diagnosed cases of dermatophytosis with the duration of the disease of at least six months, with or without recurrence.

Exclusion Criteria

Excluded were:
1. Patients suffering from dermatophytosis for less than six months.
2. Patients suffering from onychomycosis without lesions of tinea on other body sites.
3. Pregnant and lactating women.

Patient Characteristics

A detailed history was taken on the following variables and was recorded in a predesigned proforma: age, gender, duration of disease, treatment history, family history, personal history, personal hygiene, type of clothing, fomite sharing, overcrowding, socioeconomic status, occupational history particularly regarding working in hot and humid conditions, other systemic or cutaneous diseases such as immunodeficiency states or atopy, and any concomitant drug intake known to cause interactions with antifungals.

A detailed general, physical, systemic, and cutaneous examination was performed. The assessment of lesions of dermatophytosis included the site of involvement and the percentage of body surface involvement. Accordingly, the disease was classified as tinea capitis, tinea corporis, tinea cruris, tinea barbae, tinea faciei, tinea manuum, tinea pedis, and tinea unguium.

Investigations such as complete blood count (CBC), a kidney function test (KFT), a liver function test (LFT), absolute eosinophil count, and blood sugar fasting were performed. HIV serology was performed only for high-risk patients after proper counseling.

Sample Collection for Mycological Study

After properly cleaning the lesion with a spirit swab, samples were collected by scraping the active edges with a sterile scalpel blade. Hairs were taken in case of tinea capitis. The samples obtained were taken to the laboratory in clean black paper envelopes. KOH wet mount preparations were made and examined under the microscope against the presence of fungal hyphae. The specimens were inoculated into test tubes with Sabouraud dextrose agar with cycloheximide (0.05 g/L) and chloramphenicol (0.005 g/L) and incubated at 28°C for at least four weeks before labeling as negative. Species identification was performed by gross morphology of the fungal colonies, pigmentation, and microscopy with a Lactophenol cotton blue mount.

Statistical Analysis

Initially, the data was entered in a predesigned proforma and, subsequently, a database was created with Microsoft Excel for the purpose of data analysis. The data was reported as mean values and percentages as was appropriate for the quantitative and qualitative variables, respectively.

RESULTS

The mean age of the study subjects was 34.7 ± 12.9 years, ranging between 9 to 70 years. The most cases were in the age group 30–49 years (n = 70; 48.3%). The male-to-female ratio was 1.26:1. The mean duration of the disease was 13.4 ± 6.18 months, ranging from 7 to 36 months. With most patients, the duration of the disease ranged from 10 to 19 months (n = 80; 55.2%).

Most of the patients were manual workers (n = 44; 30.3%). The number of hours of sun exposure varied between 1 to 8.5 hours (3.53 ± 1.75 hours). Around 99 (68.3%) patients were exposed to more than 2.5 hours of sunlight a day.

Personal hygiene was average in most of the patients (n = 81; 55.9%). The most preferred type of cloth fabric was synthetic, which was used by more than half of the patients (50.4%). A history of fomite sharing was present in the majority of the patients (74.5%).

A majority of the patients (55.2%) lived in overcrowded conditions. Almost all socioeconomic classes were affected, with the upper middle class (n = 40; 27.6%), upper lower class (n = 38; 26.2%), and lower middle class (n = 37; 25.5%) almost equally affected, followed by the lower class (n = 24; 16.5%) and upper class (n = 6; 4.1%).

Comorbidities were present in 34 patients. Diabetes was present in 12 (8.3%) patients, followed by hypertension in 11 (5.5%) patients, atopic dermatitis and bronchial asthma in 3 (2.1%) patients each, and anemia in 2 (1.4%) patients. Osteoarthritis, palmoplantar psoriasis, and pemphigus vulgaris were present in 1 (0.7%) patient each.

A family history of dermatophytosis was present in 63 (43.5%) patients. Only some patients had a family history of atopy (n = 16; 11.0%).

All patients had used topical antifungals. A majority (n = 114; 78.6%) had used steroid-containing antifungal creams, and most (n = 106; 73.1%) had used systemic antifungals, such as itraconazole, terbinafine, fluconazole, and griseofulvin. However, adequate antifungal use was noted only in 56 (38.6%) patients. Additionally, the use of systemic corticosteroids was noted in 9 (6.21%) patients.

More than half of the patients (54.5%) had more than 20% of the body surface area involvement, and a majority (n = 105; 72.4%) had multiple-site involvement, followed by tinea corporis alone (n = 23; 15.9%) and tinea cruris alone (n = 17; 11.7%) (Fig. 1). The most common presentation was tinea corporis with tinea cruris (33.1%), followed by tinea corporis alone. Among those with multiple-site involvement, a significant number had tinea faciei (14.48%) and tinea unguium (13.10%) (Figs. 2 – 3). Various atypical presentations such as eczematous, pustular, pseudoimbricata, etc., were also seen in several patients (Fig. 4).

The absolute eosinophil count was raised (> 450 cells/μL) in 32 (26.1%) patients. Out of the 145 patients, 20 (13.79%) were tested for an HIV infection but were all negative.

KOH scraping was positive for fungal hyphae in 91.3% of the patients.

A fungal culture was positive in 65 (44.8%) patients. The most frequent isolate was *Trichophyton mentagrophytes* (n = 35; 53.9%) (Figs. 5 – 6), followed by *Trichophyton rubrum* (n = 25; 38.5%), *Trichophyton tonsurans* (n = 3; 4.6%), *Microsporum canis* (n = 1; 1.5%), and *Trichophyton verrucosum* (n = 1; 1.5%).

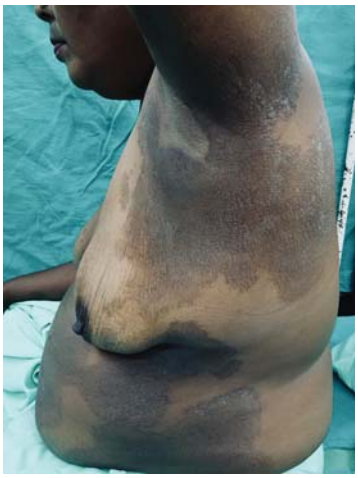

Figure 1: Extensive tinea corporis and tinea axillaris caused by *T. mentagrophytes* in a patient with bronchial asthma on oral steroids.

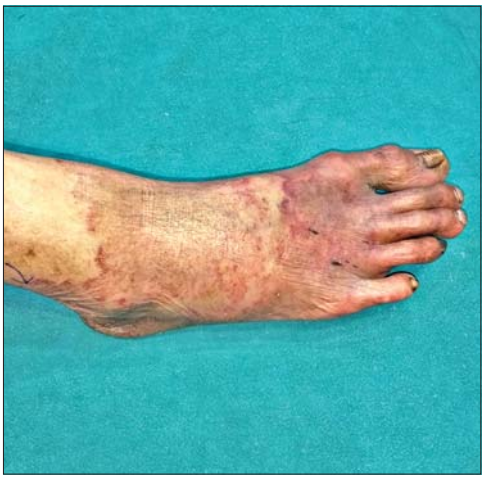

Figure 2: Tinea pedis extending to the dorsum with onychomycosis in a diabetic patient.

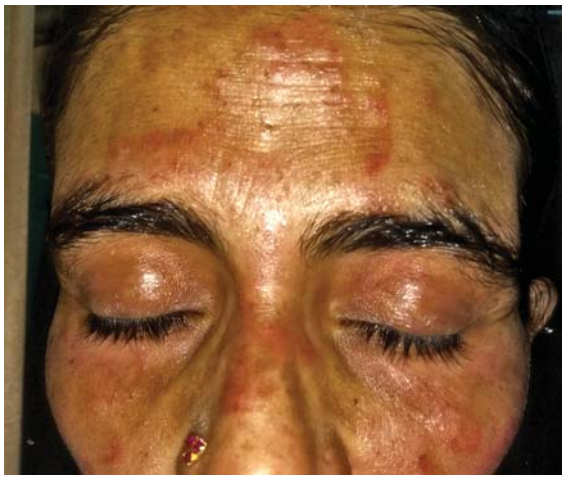

Figure 3: Tinea faciei in an adult.

DISCUSSION

We studied a total of 145 patients with chronic dermatophytosis. The most commonly affected age group was 30–49 years old. These results are in accordance with a study by Sivaprakasam and Govindan [4]. Also, in a study by Vineetha et al. [5],

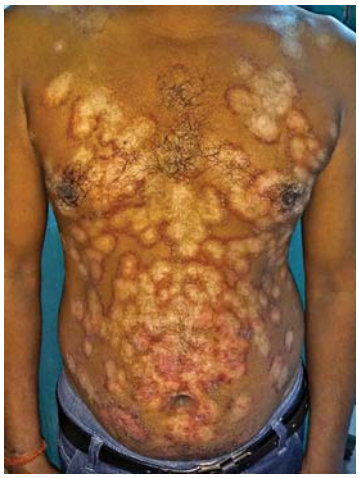

Figure 4: Atypical presentation of tinea corporis in a patient with steroid abuse: multiple coalescent annular lesions with central hypopigmentation.

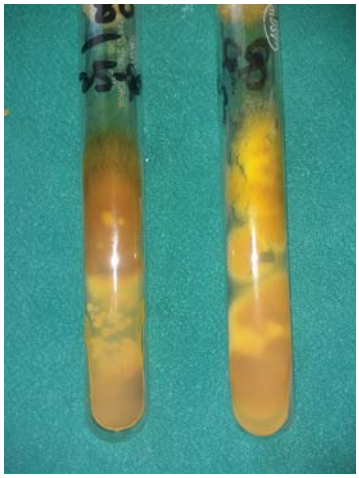

Figure 5: Obverse and reverse of macroscopic colony morphology of *T. mentagrophytes*.

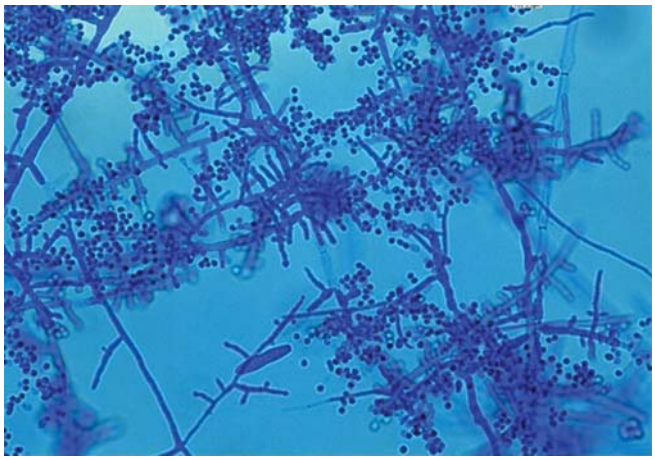

Figure 6: Lactophenol cotton blue mount of *T. mentagrophytes* viewed under the magnification 40×.

the most common age group affected by chronic dermatophytosis was 40–50 years old, and, in those with the first episode of the infection, the most commonly affected age group was in their second decade of life. Thus, chronic dermatophytosis is more common in the middle-age group and this may be due to the more vigorous physical activity associated with their occupation and the waning level of immunity and other comorbidities prevalent in this age group.

Chronic dermatophytosis was more common in males, with a male-to-female ratio of 1.26:1. Similar findings were obtained in other studies [5,6]. The generally increased prevalence in males may be correlated with their involvement in heavy physical work, more frequent outdoor activities, and thus an increased risk of exposure to infections.

In our study, more than half of the cases (54.5%) had large body surface area involvement, and some presented themselves with an erythroderma-like condition. Ohashi et al. reported a case of erythroderma caused by dermatophytosis [7]. The larger body surface area involvement may be correlated with the chronicity of the disease.

Also, a majority of the cases (72.4%) had experienced the involvement of more than one body site. This is in accordance with a similar study by Pathania et al. [6] The most common presentation in our study was tinea corporis with tinea cruris, followed by tinea corporis alone. Thus, multiple-site involvement may be a risk factor for the chronicity of dermatophytosis. Also, the involvement of groins may be related to the wearing of tight-fitting clothes and an increased sweating rate, both of which create a moist environment, which is favorable to the persistence and growth of dermatophytes. Also, tinea unguium was present in 13.1% of the patients, and most of them were diabetic. Thus, the persistence of the fungus in these areas may be a source of a spreading action to other body sites.

In our study, we found a relatively high number of cases with tinea faciei (14.5%), in comparison with previous studies, and most of these patients were adults. Tinea faciei used to be rare in adults. Vineetha et al., in a similar study, found only 4.3% cases of tinea faciei in chronic dermatophytosis patients [5]. Sivaprakasam and Govindan found 6.7% of their cases affected by tinea faciei [4]. Thus, there is a changing trend as far as the pattern of involvement of dermatophytes is considered.

Most of the cases (30.34%) were manual workers. Other commonly affected groups were students, followed by

housewives and army/police personnel. All these groups are engaged in heavy outdoor work and/or household activities and/or wearing tight-fitting clothes for long periods of time, which predisposes to perspiration. In a study by Sharma R et al., students and army personnel were most commonly affected, but they included both new and chronic cases [8].

The mean of the hours of sun exposure was 3.5, and a majority of the cases (68.35%) were exposed to more than 2.5 hours of sunlight. Prolonged sun exposure precipitates sweating, which may predispose to the chronicity of the disease.

Around half (50.35%) of the patients in our study preferred wearing tight-fitting synthetic clothing, such as jeans, leggings, etc., and these were infrequently washed. Such clothing are, once again, a predisposing factor for excessive sweating, and their infrequent washing creates a damp environment favorable to the proliferation of fungus.

The most common socioeconomic class in our study was upper middle, with 27.59% of the patients in this group. Another commonly affected class was upper lower (26.21%), followed by lower middle, lower, and upper. Hosthota et al. reported that 57.3% of their cases belonged to low socioeconomic strata, but their study included both new and chronic cases [9]. The occurrence of a chronic disease in the higher socioeconomic group in our study might have been associated with a different lifestyle, as in wearing synthetic clothing, such as jeans and leggings, the use of modern toilet seats, the use of washing machines for washing clothes, when the chances of mixing clothes belonging to different family members is increased and, thus, the spread of infection is faster.

Although most of the patients had average personal hygiene, poor personal hygiene, with infrequent washing of clothes and taking baths less often, was present in 20% of the cases. A history of fomite sharing with other family members was present in 74.48% of the cases, and a majority (55.17%) lived in overcrowded conditions. All these factors were reported to be responsible for the chronicity and recurrence of dermatophytosis in previous studies [6].

A history of similar complaints in other family members was present in 43.45% of the cases, which may be due to fomite sharing, sharing of footwear, and mixing of clothes in washing machines. Untreated family members are, in turn, a source of reinfection, which may be a cause of the chronicity.

The most common comorbidity in our study was diabetes, present in 8.3% of the cases. This is in accordance with a study by Vineetha et al., in which diabetes was present in 11% of the chronic cases [5], and a much higher prevalence (30%) was reported by Sivaprakasam and Govindan [4]. Other associated comorbidities included hypertension, hypothyroidism, atopic dermatitis, bronchial asthma, and anemia. Osteoarthritis, palmoplantar psoriasis, and pemphigus vulgaris were present each in 1 (0.69%) patient. Patients with bronchial asthma were on oral and inhalational steroids, the patient with palmoplantar psoriasis was on methotrexate, and the patient with pemphigus vulgaris was on high-dose steroid pulse therapy and cyclophosphamide.

We know that atopics have a defective tilt of immunity toward TH2 cytokines and predispose to chronic dermatophytosis. In our study, atopy was present in 4.14% of the patients while 11.03% had atopic diathesis among family members. The absolute eosinophil count was high (> 450 cells/μL) in 26.07% of the patients.

There is a general lack of awareness regarding the use and side effects of topical steroids among various non-dermatologists and medical practitioners, as demonstrated in a study by Abrol and Sharma [10]. A considerable number of patients (78.62%) in our study had been applying topical antifungals that contained corticosteroids. Vineetha et al. also reported the use of topical steroid/antifungal creams by their patients, but the percentage was lower (63%) when compared with our study [5]. Some of the patients had been applying plain topical potent corticosteroids as well. Corticosteroids suppress the signs and symptoms of inflammation, but dermatophytes continue to grow, leading to the subsequent flare of the disease [11]. Some of the patients (6.21%) had also used oral steroids during the course of the disease. Thus, the use of corticosteroids may be the cause of the chronicity in these patients.

73.10% of the patients in our study had been using oral antifungals in the form of fluconazole, itraconazole, terbinafine, or griseofulvin. However, in most cases (61.38%), the dose and the duration of therapy were inadequate. The patients discontinued the medicine without medical advice as soon as they felt better. Non-compliance is a major cause of

concern for a dermatologist as far as the treatment of dermatophytosis is concerned. Thus, proper education of the patients on the dose and duration of therapy may prove helpful.

In our study, KOH scraping was positive for fungal hyphae in 91.03% of the patients. A high positivity rate may be attributed to a high organism load in chronic cases, while the KOH negativity in some may be attributed to the minimal scaling present in the lesions.

The fungal culture was positive in 44.83% of the cases. However, Pathania et al. were able to grow dermatophytes in 60% of the cases [6]. A lower culture positivity rate in our study might have been due to more frequent antifungal use by chronic cases. Vineetha et al. were able to isolate dermatophytes in only 12% of cases of chronic dermatophytosis [5].

The most frequent isolate in our present study was *Trichophyton mentagrophytes* (53.85%), followed by *Trichophyton rubrum* (38.46%), *Trichophyton tonsurans* (4.61%), and *Microsporum canis* and *Trichophyton verrucosum* (1.54% each). Most of the previous studies conducted in India have found *Trichophyton rubrum* the most common isolate [4,12,13]. Recently, however, several researchers have reported *Trichophyton mentagrophytes* to be the predominant isolate [8,14,15]. Thus, there is a changing trend as far as the pathogenic organism of dermatophytosis is considered. *Trichophyton mentagrophytes* is associated with more widespread and inflammatory lesions. Also, some researchers have demonstrated its ability to survive longer on skin scales as compared to *Trichophyton rubrum* [16].

Table 1: Distribution of the patients according to the pattern of involvement

Pattern of involvement	No. of patients	Percentage
Multiple-site involvement	105	72.4
Tinea corporis alone	23	15.9
Tinea cruris alone	17	11.7

Table 2: Distribution of the patients according to the fungal isolates

Fungus isolate	No. of patients	Percentage
Trichophyton mentagrophytes	35	53.8
Trichophyton rubrum	25	38.4
Trichophyton tonsurans	3	4.6
Microsporum canis	1	1.5
Trichophyton verrucosum	1	1.5
Total	65	100

Table 3: Risk factors

Risk factors assessed	Percentage of patients
Manual workers	30.3
More than 2.5 hours of sun exposure	68.3
Synthetic clothing	50.4
Fomite sharing	74.5
Family history of dermatophytosis	43.5
Comorbidities	23.4
Extensive body area involvement (> 20%)	54.5
Multiple-site involvement	72.4
Steroid application	78.6
Inadequate treatment	61.4
Absolute eosinophil count above 450	26.2

CONCLUSION

Our study recognized *Trichophyton mentagrophytes* as the predominant organism and tinea corporis with tinea cruris as the most common clinical presentation. Several risk factors that may contribute to the chronicity of dermatophytosis were identified in the majority of the patients. These included lack of proper hygiene, fomite sharing, wearing tight-fitting synthetic clothes, the presence of an infective focus in the family, prolonged sun exposure, the involvement of a larger body surface area, atopic diathesis, comorbidities, the use of topical steroids, and non-compliance to treatment. Thus, identifying and modifying the modifiable risk factors may be helpful in routine clinical practice.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Original Article

Psoriasis is a systemic disease: A proposed approach for inflammation scale calculation

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ABSTRACT

Background: Psoriasis is a skin disease affecting 2.3% of the Iraqi population and begins as a local disease with subsequent systemic comorbidities. **Aim:** The aim was to clarify whether psoriasis is a local or systemic disease. **Materials and Methods:** A total of 211 subjects with psoriasis and 163 sex- and age-matched controls were included in the study. Serum adiponectin, interleukin-6, interleukin-8, interleukin-10 (IL-10), interleukin-23 (IL-23), interleukin-18 (IL-18), paraoxonase, lipoprotein (a), osteopontin, chemerin, tumor necrosis factor-α (TNF-α), high-sensitivity C- reactive protein (hs-CRP), bilirubin, D-dimer, and creatinine were determined using commercial kits. **Results:** There was no significant difference in the mean age and BMI between psoriasis and the control groups. However, there was significantly higher mean serum values of IL-6, IL-8, IL-10, IL-23, lipoprotein (a), chemerin, TNF-α, hs-CRP, osteopontin, D-dimer, troponin I, creatinine, bilirubin, and platelet counts in psoriatic patients than in the controls. Meanwhile, the serum mean values of adiponectin, paraoxonase, and cortisol were significantly lower in psoriasis subjects than in the controls. The mathematical model was proposed to clarify whether psoriasis is a systemic or local disease. The application of the model to our data of biomarkers indicated the presence of systemic inflammation in psoriasis. **Conclusion:** The present study finding suggests that psoriasis is a systemic disease rather than a local skin disease. However, there is a need for the application of the model in a large-scale study.

Key words: Psoriasis; Interleukin 10; Interleukin 18; Interleukin 23; Paraoxonase; Lipoprotein (a); Osteopontin; chemerin

INTRODUCTION

Psoriasis is a skin disease affecting 2.3% of the Iraqi population [1] and 1–3% globally [2]. The disease is characterized by a chronic natural history characterized by remission, relapse, and acute exacerbation [3]. Although psoriasis has an obscure etiology, previous studies have suggested that genetic, infectious, immunological, and environmental factors play a role in the induction of the disease [4,5]. Psoriasis is induced as a local dermatological disease with subsequent immuno-inflammatory and metabolic changes [6,7].

In the literature, numerous studies have reported systemic changes, such as dyslipidemia, cytokines, and inflammatory and immunologic biomarker abnormalities [8-27]. Some researchers suggest that psoriasis is a systemic disease rather than a local skin disease [6,7,17,28-35]. An alternative explanation for the biomarker abnormalities is that the disease is a combined local and systemic syndrome or that the local skin changes are a dermatological manifestation of a systemic disease.

Suggestions that psoriasis is a systemic disease depend on findings of increased or decreased serum or plasma levels of immunological, inflammatory, and metabolic biomarkers [6,7,17,28-35]. However, there are conflicting variations in these biomarkers among different studies.

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The diagnosis of systemic inflammation with a mathematical model was previously reported for clinical conditions such as obstetric, acute multiple injuries, heart surgery, and sepsis [36,37]. Thus, this study proposed a mathematical model for the calculation of a scale that may be employed to diagnose the presence of systemic inflammation in psoriasis and to monitor treatment response of the disease.

MATERIALS AND METHODS

Study Population

The present study included 211 subjects with psoriasis attending a dermatology clinic during the period from January 2012 till the end of May 2014.

A total of 163 subjects, sex- and age-matched controls, were included in the study.

The mean age of the patients was 37.85 (±14.81) years, and that of the control group was 36.76 (±10.92) years with no significant difference between the two groups. Additionally, the mean BMI was 25.83 (±6.41) in the patients with psoriasis and 25.90 (±13.16) in the controls, with a non-significant difference. The gender frequency rate was not significantly different between the patients and controls (Table 1). The study was approved by the ethical committee of Tikrit University College of Medicine and informed consent was taken from each subject included in the study. Individuals with liver disease, a family history of hyperlipidemia, diabetes, cardiovascular disease, hypertension, smoking, hypothyroidism, renal disease, connective tissue disease, and those using lipid-lowering drugs were excluded from the study.

Table 1: Biomarkers in the subjects with psoriasis in comparison to the controls

Biomarker	Mean (SD)		t	P
	Psoriasis	Controls		
Adiponectin ng/ml	7.23 (3.42)	8.28 (5.14)		
IL- 6 pg/ml	41.85 (13.27)	4.31 (1.87)		
IL-8 pg/ml	47.61 (19.77)	7.68 (2.32)		
IL-10 pg/ml	8.78 (4.81)	5.31 (3.73)		
IL -18 pg/ml	601.7 (247.46)	45.8 (23.11)		
IL-23 pg/ml	73.48 (29.91)	5.98 (6.71)		
Paraoxonase mIU/ml	38.96 (4.15)	91.65 (16.73)		
Lipoprotein (a) mg/dl	376.60 (35.8)	21.85 (13.62)		
Chemerin ng/ml	214.88 (80.5)	34.31 (17.62)		
TNF-α pg/ml	277.93 (150.3)	146.60 (90.9)		
hs-CRP mg/dl	3.75 (0.74)	1.37 (0.39)		
D-dimer ng/ml	374.82 (261.9)	249.61 (217.80)		
Cortisol nmol/L	195.60 (37.8)	289.00 (53.11)		
Troponin I ng/ml	0.27 (0.31)	0.04 (0.09)		
Platelets 10^3 /mm^3	287 (99.7)	256 (113)		
Bilirubin mg/dl	1.91 (0.17)	0.78 (0.09)		
Creatinine mg/dl	1.23 (0.87)	0.71 (0.19)		
Osteopontin pg/ml	638.34 (225.80)	45.78 (18.95)		

Determination of Inflammation

Inflammatory responses were determined with an approach by Zotova et al. [37], with some modifications. Step 1 involved systemic cellular stress estimation performed using some cytokines and other inflammatory mediators as indicators of systemic inflammatory responses (SIR). In step 2, the systemic inflammation scale was determined by SIR systemic microthrombogenesis, organ dysfunction, systemic alterations, and distress reactions [38,39]. The calculation sequences are described below.

1. Calculation of the reactivity index scale (0–6) with the indices shown in Table 2 for IL-6, IL-8, IL-10, IL-18, IL-23, TNF-α, hs-CRP, chemerin, lipoprotein (a), paraoxonase, and adiponectin.
2. Calculation of the coefficient of reactivity (CR) [0-36] with the data extracted from Table 2. The sum of 7 (60%) largest RISs from the 11 factors used gave the CR scale.
3. Transformation of the CR scale (0–36) into the reactivity level scale (RLS) with 0–5 points (40) as shown in Table 3.
4. The Sequential Organ Failure Assessment (SOFA) scale was calculated with the serum level of bilirubin, creatinine, osteopontin, the platelet count, and the presence of sepsis and erythroderma. The SOFA scale was within the range of (0–4) (Table 4).
5. The last step was the calculation of the Systemic Inflammation (SI) scale using the phenomenon described in Table 5.

Investigations

Serum adiponectin, interleukin-6, interleukin-8, interleukin-10, interleukin-18, interleukin-23, paraoxonase enzyme, lipoprotein (a), TNF-α, osteopontin, chemerin, and high sensitivity CRP levels were measured by the enzyme-linked immunosorbent assay. The procedure was performed according to manufacturer instructions.

Statistical Analysis

Variable values were presented as a mean ± standard deviation [SD]. The Student's *t*-test was used to

Table 2: Indices for the calculation of the reactivity index scale (0–6)

Biomarker	UMN	Reactivity Index						
		0	1	2	3	4	5	6
IL-6	6.18 pg/ml	≤ 3	≤ 6	≤ 12	≤25	≤50	≤100	>100
IL-8	10 pg/ml	≤ 5	≤ 10	≤ 20	≤40	≤80	≤160	>160
IL-10	9.04 pg/ml	≤ 1	≤ 2	≤ 5	≤10	≤20	≤100	>100
IL-18	68.91 pg/ml	≤ 35	≤ 70	≤140	≤280	≤560	≤1120	>1120
IL-23	12.69 pg/ml	≤ 5	≤ 10	≤ 25	≤50	≤100	≤200	>200
TNF – α	8.01 pg/ml	≤ 5	≤ 25	≤ 50	≤100	≤200	≤400	>400
hs-CRP	2.76 mg/dl	≤ 1	≤ 2	≤ 3	≤4	≤5	≤10	>10
Chemerin	51.90 ng/ml	≤ 25	≤ 50	≤100	≤200	≤400	≤800	>800
Lipoprotein(a)	35.45 mg/dl	≤ 20	≤ 40	≤ 80	≤160	≤320	≤640	>640
Paraoxonase	108.4mIU/ml	> 200	≤ 200	≤100	≤50	≤25	≤10	≤5
Adiponectin	13.42 ng/ml	>32	≤ 32	≤ 16	≤8	≤4	≤2	≤1

Table 3: Transformation of CR into RL

RL Scale	CR Scale	Inflammation Level
0	0–6	Normal physiology.
1	7–12	Classical inflammation but no systemic inflammation.
2	13–18	Typical classical with the possibility of the depressive phase of systemic inflammation.
3	19–24	Zone of uncertainty.
4	25–30	Typical for the hyperergic option of systemic inflammation with a low possibility of classical inflammation.
5	31–36	Confirms the presence of systemic inflammation.

Table 4: Sequential Organ Failure Assessment (SOFA) scale calculation parameters

Biomarker	Scale (0–4)				
	0	1	2	3	4
Bilirubin mg/dl	< 1.2	1.2–1.9	2–5.9	6–11.9	≥ 12
Creatinine mg/dl	< 1.2	1.2–1.9	2–3.4	3.5–4.9	≥ 5
Platelets 10^3 /mm^3	> 150	< 150	< 100	< 50	< 20
Osteopontin pg/ml	≤ 65	≤ 130	≤ 260	≤ 520	> 520
Sepsis	Negative	Negative	Negative	Positive < 12 hrs.	Positive > 12 hrs.
Erythroderma	Negative	Negative	Negative	Positive < 24 hrs.	Positive > 24 hrs.

Table 5: Parameters for the calculation of the Systemic Inflammation (SI) scale

Phenomenon	Criteria	Points
Systemic Inflammatory Response (SIR)	Levels RL-scale (0–5)	2–5
Microthrombogenesis	D-dimer (≥ 500 ng/ml)	1
Distress Response	Cortisol (≥ 1380 or <100 nmol/L)	1
Systemic alteration	Troponin I (≥ 0.2 ng/mL) Myoglobulin (≥ 800 ng/ml)	1
Multiple Organ Dysfunction (MOD)	SOFA scale and/or other MOD criteria	1

determine the significant differences between the groups. A P value of less than 0.05 was regarded as significant.

RESULTS

There was no significant difference in the mean age and BMI between the psoriatic and control groups. However, there was a significantly higher mean serum value of IL-6, IL-8, IL-10, IL-23, lipoprotein (a), chemerin, TNF-α, hs-CRP, osteopontin, D-dimer, troponin I, creatinine, bilirubin, and the platelet count in the psoriatic patients than in the controls. Meanwhile, the serum mean values of adiponectin, paraoxonase, and cortisol were significantly lower in the psoriatic subjects than in the controls (Table 1).

DISCUSSION

The above biomarkers were selected to determine the levels of inflammation based on the reported association between psoriasis and these biomarkers [41]. Previous studies showed an increase in serum levels of IL-6, IL-8, IL-10, IL-23, lipoprotein (a), chemerin, TNF-α, hs-CRP, osteopontin, D-dimer, Troponin I, creatinine, bilirubin, creatinine, and the platelet count in patients with psoriasis, and a decrease in the serum levels of adiponectin, paraoxonase, and cortisol [21,32,41-64]. Serum osteopontin was selected as a biomarker for the calculation of the SOFA scale depending on its role as the bridging of adaptive and innate immunity in autoimmune diseases, including psoriasis [65].

Table 6 shows the data of the RI scale calculated as described in Table 2 with the information in Table 5. Then, CR was calculated by the sum of the 7 [60%] largest values of RIS and, thus, the CR value for the psoriatic patients was 32. According to the criteria presented in Table 3, the CR scale value was

Table 6: Coefficient Reactivity, the SOFA scale, and the SI scale in patients with psoriasis

A. Coefficient Reactivity (CR) calculation (–36)	
Biomarker	**CR points**
IL-6	4
IL-8	4
IL-10	3
IL-18	5
IL-23	4
TNF – α	5
hs-CRP	5
Chemerin	5
Lipoprotein(a)	4
Paraoxonase	3
Adiponectin	3
B. SOFA scale	
Biomarker	**Point s**
Bilirubin	1
Creatinine	1
Platelets	0
Osteopontin	4
Sepsis	0
Erythroderma	0
SUM	6
B. SI scale	
Phenomenon	**Points**
Systemic Inflammatory Response (SIR)	5
Microthrombogenesis	0
Distress Response	0
Systemic Alteration	1
Multiple Organ Dysfunction (MOD)	1
SUM	7
Scale value indicating systemic inflammation	≥ 5

transformed into the RL scale and, thus, for our study cohort, the RL scale was 5 (Table 3).

Table 6, shows the SOFA scale calculated according to the criteria presented in Table 4 and, thus, the SOFA scale value for the psoriatic patients was 6. The systemic inflammation scale (SI) was determined with the criteria presented in Table 5 and, for the psoriatic patients, the SI scale was 7. The scale cut-off value that indicated systemic inflammation was equal to or above 5 points.

The mathematical model for the diagnosis of systemic inflammation was used previously in other clinical conditions, such as in obstetric, acute multiple injuries, heart surgery, and sepsis [36,37].

CONCLUSION

The mathematic model presented here is of predictive value in the determination of systemic inflammation and the discrimination between local and systemic inflammation.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Brief Report

Challenges and impact of COVID-19 on teledermatology practice in providing continued care to patients in a time of disarray

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) pandemic has significantly affected all areas of life in most countries. Telehealth has gained importance during this era of social distancing, including teledermatology (TD). The purpose of this survey was to determine the challenges and impact of COVID-19 on TD practice in providing continued care to patients by dermatologists in Pakistan. **Methods:** A questionnaire comprised of fifteen questions was created with Google Forms and distributed to dermatologists practicing in various cities of Pakistan via WhatsApp or e-mail, then the data was collected. **Results:** A total of 81 dermatologists from various cities of Pakistan responded to the survey, among whom about two thirds reported a positive experience with TD, yet some had issues in communication gaps and breaches of confidentiality, and the majority considered it unequal to in-person visits. **Conclusion:** TD plays an important role during the COVID-19 pandemic as a simple, time-saving procedure allowing social distancing with good patient satisfaction.

Key words: impact; COVID-19; teledermatology

INTRODUCTION

Coronavirus disease 2019 (COVID-19) initially reported in Wuhan, China, in December 2019 was declared a pandemic by the WHO in March 2020 [1]. It has rapidly spread all over the world and now affects 214 countries worldwide, with over 103.2 million cases and 2.2 million deaths [2]. Pakistan has also suffered, with 547,648 confirmed cases and 11,746 deaths, and has entered the second peak phase [2].

COVID-19 has affected almost every aspect of life and has had huge social, economic, and healthcare impact [3]. One of the most effective measures for reducing the rapid spread of COVID-19 in the community is social distancing, as demonstrated by several researchers [4]. The minimal recommended distance for effective social distancing by the WHO is 1 m [5], whereas other researchers are in favor of even greater distances [6]. Healthcare workers are particularly at risk of exposure to COVID-19 during routine occupational activities and, in turn, may themselves become sources of viral dissemination in the community [7]. Therefore, hospitals and healthcare systems all over the world have postponed all non-urgent face-to-face consultations and elective surgery procedures to reduce healthcare related spread of the infection [8,9]. Similarly, in-person dermatological consultations have been significantly reduced worldwide, including in Pakistan [9,10].

The global decrease in clinical consultations has led to increasing dependence on telehealth procedures [11]. Telehealth utilizes modern communication technologies during medical consultations and teaching while maintaining distance [12]. Teledermatology (TD) is

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the application of telehealth services in dermatological practice [13]. Since diagnosis in dermatology is greatly dependent on visual examination, it is highly suitable for telemedicine practice [14]. TD is able to ensure continued provision of basic dermatological care for patients while decreasing COVID-19 risk for both healthcare practitioners and patients. Furthermore, TD helps triage patients who need in-patient visits for complete cutaneous examination and any relevant procedures such as skin biopsy [15].

Several researchers worldwide have reported the trend of shifting dermatology consultations to TD platforms with positive outcomes [16]. Some facilities have even transitioned completely to e-health during peak COVID-19 infection rates [17]. There have been numerous studies on the use of TD for providing dermatological care with the focus on dermatologists' experience and patient outcomes relevant to their skin disorder [13,18,19]. In Pakistan, since the imposition of countrywide lockdown in April 2020, which was partially lifted later, dermatology outpatient departments have not resumed full operation, especially in government sectors. Furthermore, private consultations have also been reduced significantly during the COVID-19 pandemic [10]. However, no study has been done on TD practice in Pakistan during COVID-19 according to our knowledge. The objective of our study was to assess the use of TD and the challenges faced by dermatologists from all over Pakistan during the COVID-19 pandemic.

METHODS

A questionnaire comprised of fifteen questions was created with Google Forms and distributed to dermatologists practicing in various cities of Pakistan via WhatsApp or e-mail, then the data was collected in July 2020. The last date of data collection was July 25, 2020.

RESULTS

The survey was distributed among Pakistan Association of Dermatologists (PAD)-registered dermatologists and 81 of them responded. Among these 50 were females and 31 males. These ranged from professors to postgraduate trainees and medical officers. The vast majority (75%) belonged to Punjab, followed by KPK, with only 3 from Islamabad, and 2 and 1 from Balochistan and Sindh, respectively. None belonged to Gilgit-Baltistan.

Only 4 respondents (5%) had never done TD till the date of the survey, while the majority had used it to varying degrees. WhatsApp was the medium used almost exclusively, with only rare instances of Facebook or audio calls.

Most participants had a positive experience with TD and reported an increase in TD consultations since the pre-COVID era. Many, however, considered TD visits unlike face-to-face consultations. The responses were divided over the level of communication comfort and many practitioners considered such communication insufficient compared to in-person visits. Technologic malfunction was highly uncommon.

DISCUSSION

COVID-19-related social distancing has led to a significant decrease in non-urgent face-to-face consultations worldwide, including in Pakistan [8-10]. Simultaneously, there has been a shift in favor of telehealth [10,11], and this is likely to continue till the pandemic either ends or a safe and effective vaccine is available for the general population.

Our survey assessed the experience of dermatologists in Pakistan and the drawbacks and difficulties that they had experienced while practicing TD during the COVID-19 pandemic. It was noted that almost two thirds of our respondents were females while males comprised one third. This ratio may be due to the fact that female doctors tend to prefer dermatology as a field of medicine in Pakistan. Most of the participants (77.8%) were professorial staff or consultant dermatologists. This may be due to private practice by consultants, which has shifted partly or wholly to online services during the pandemic. Punjab comprised the main chunk, probably due to the home territory of the surveyed.

It was noted that only a handful (5%) had never practiced TD till the date of the survey, while most (95%) had used it with varying frequencies. This is comparable to studies from the U.S., and India, where telehealth practice by dermatologists during COVID-19 comprised 86.5% and 88.5%, respectively [18,19]. However, a German survey revealed that only 38.8% of dermatology practices offered TD, although there

had been a four-fold increase since the pre-COVID times [9].

WhatsApp was the predominant platform used by practitioners in our survey (90%) and very rarely audio calls or Facebook were employed. This agrees with studies from all over the world, where the use of WhatsApp as a telehealth tool, including TD, during the pandemic has been advocated [20,21]. Similarly, researches even from before the appearance of COVID-19 had favored WhatsApp for teleconsultations [22], and this has become even more relevant in the present social distancing era. The widespread use of WhatsApp as a means of communication by the general population globally even prior to the pandemic [23] and the ease of video calling and image sharing and minimal data charges have made it the medium of choice for TD practice in Pakistan.

Most of our participants had a positive experience with TD. Two thirds considered it to improve access to healthcare, help to save time, and keep patients safe during the pandemic. Andrees et al. also consider TD as a time-effective platform that may supplement or replace traditional visits [24]. About three quarters found it easy and simple to use, although only a half reported their experience as pleasant. The discomfort felt by some of the surveyed may be attributed to the lack of routine use of TD before the COVID-19 pandemic. 60% of the practitioners felt that teleconsultations improved their productivity. More than two thirds reported an increase in TD consultations since the pre-COVID era. This agrees with international studies from Germany, the U.S., and India [9,18,19]. However, a majority (76%) considered TD visits unlike face-to-face consultations. Furthermore, the responses were divided over the level of communication comfort and many practitioners considered such communication insufficient compared to in-person visits. Whited, too, reviewed that, although clinicians found TD as comprehensive as physical visits, they had more confidence in clinical visits due to more effective communication [25]. A meta-analysis by Bastola also revealed that the diagnostic accuracy of TD is less than in-person checkups [15]. Similarly, a pre-COVID review found that traditional consultations were diagnostically more effective than TD [26]. Mehrtens et al., on the other hand, found fair diagnostic concordance (68%) between TD and in-person visits, as did Arzberger et al. [27,28]. Meanwhile, a review by Trettel et al. found variable results, with some studies in favor of TD diagnoses and other studies opposing [29].

The clinicians in our survey reported variable patient satisfaction. However, in a recent survey, Ruggerio et al. from Italy found more than 90% of their patients were satisfied with teleconsultations [30]. Similarly, Mehrtens et al. observed that 82% of the patients surveyed were satisfied with TD care [27]. The perception of moderate-to-low patient satisfaction by our dermatologists may be due to the novelty of this approach for both patients and caregivers in Pakistan, as well as the feeling of incomplete consultation by the patient when compared to traditional in-person visits.

Our respondents were divided over the perception of the patient's confidentiality breach. Bull et al. from the U.S. also observed that some patients and practitioners had privacy issues with online consultations [31]. This lack of a proper system to maintain patient confidentiality was also pointed out by Wang et al. in their review [32].

Most of our participants experienced uncommon technologic difficulties. The long-standing status of WhatsApp as a popular social media network even before the current pandemic probably accounts for the uncommon technologic malfunctions observed.

Limitations of our study include a relatively small sample size with a predominant representation of the Punjab province. Furthermore, since the relaxation of COVID-19 restrictions, the experiences of the respondents may have diverged from those expressed in our survey. Patient experience regarding the level of privacy and satisfaction may be surveyed independently of the clinician viewpoint. Further studies with larger sample sizes may help to outline the drawbacks and advantages of TD practice in Pakistan in more detail as we enter the second peak phase of COVID-19.

CONCLUSION

TD has emerged as a time-saving, effective, and easily accessible platform that may continue to provide good healthcare while ensuring the safety of patients and healthcare personnel. Overall, most participating dermatologists in our survey had a good experience regarding the use of TD during COVID-19 restrictions. There are some barriers, such as communication gaps, the patient's confidentiality, and the present lack of clinician confidence compared with a clinical setup. However, it will continue as an important strategy for the provision of outpatient and non-urgent medical

care to the dermatologically unwell patient in the near future. At the same time, there is a need for formulating and implementing universal guidelines and a structural framework that would safeguard the interests of patients being treated with telehealth as well as those of attending physicians.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Brief Report

Eosinopenia: An early diagnostic marker of COVID-19

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is a global pandemic that has affected over two hundred countries and led to the increasing challenge of identifying, diagnosing, and treating patients. An effective early diagnostic marker is necessary for the identification of affected individuals, which would further aid in helping the prognosis. **Objective:** The aim was to study the diagnostic role of the eosinophil count in COVID-19 infection. **Methodology:** Thirty-five COVID-19 cases, confirmed either by RT-PCR or HRCT (high-resolution CT scan) were included in this cross-sectional study. **Results:** Out of the 35 patients, 26 (74.3%) had an eosinophil count of 0, six (17.1%) had a count of 1–2 eosinophils, and one had a count of 4. **Conclusion:** The absence of eosinophils in the routine complete blood count examination may certainly help in the early identification of a COVID-19 infection. Early identification may help in early therapeutic management and hence prevent further deterioration of the patient's health.

Key words: COVID-19; biomarkers; eosinopenia; eosinophil count

INTRODUCTION

Coronaviruses have led to the outbreak of diseases in East Asia and the Middle East in the past decades. Lately, a new coronavirus virus has emerged in Wuhan, China, whose genome sequencing differs from previous strains and has been named *severe acute respiratory syndrome CoV-2* (SARS-CoV-2) [1]. This virus strain causes COVID-19 (coronavirus disease 2019), which emerged at the end of 2019 [1]. COVID-19 was declared a global pandemic by the WHO on March 11, 2020 [2]. As of February 8, a total of 106,765,682 cases and 2,328,912 deaths have been reported by the WHO [3]. Previous studies have suggested an association between a decrease in the eosinophil count and acute respiratory diseases seen in COVID-19 infection [4-7]. The aim of our study was to find the association between the eosinophil count and COVID-19 in patients admitted as confirmed cases of COVID-19.

Eosinophils constitute 6% of bone marrow nucleated cells [8]. Eosinophils are potent proinflammatory cells, mainly because of the granules that contain cytotoxic proteins [9]. Although a blood cell, it is also present in various tissues, such as the gastrointestinal tract and the lungs [9,10]. Eosinopenia is the decrease in eosinophils, less than 0.01×10^9/L [11]. It has been found that the eosinophil count decreases during acute inflammation and increases during recovery from infection [12]. Since the emergence of COVID-19, there have been numerous reports of biomarkers involved in the disease, including C-reactive protein (CRP), interleukin-6 (IL-6), an increased ferritin level, the white cell count (WBC), lactate dehydrogenase (LDH), D-dimer, the platelet count, ALT, AST, an increased prothrombin time, high-sensitivity troponin, and renal markers [11]. Previous studies suggest that eosinopenia occurs as a response to acute inflammation or due to another systemic reaction

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induced by its virtue. The initial decrease in the eosinophil count was attributed to the sequestration of circulating eosinophils. Migration may happen in an inflammatory site due to the release of chemotactic factors [11].

METHODS

Study Design and Participants

This was a cross-sectional study that included 35 patients with COVID-19, confirmed either by RT-PCR or HRCT, prior to the initiation of any treatment. Patients with a CO-RADS score of 4, 5, and 6 in HRCT were considered positive. Critically ill patients and patients who were suspected cases of COVID-19 were excluded. The study was approved by the institutional ethical committee. Informed consent was not taken as this study included only routine evaluation. Information regarding demographics, clinical manifestations, vitals, laboratory data, and clinical progression of the disease and treatment were collected.

Statistical Analysis

Categorical variables were reported as numbers and percentages.

RESULTS

All 35 patients collected were cases of COVID-19, confirmed either by RT-PCR or HRCT. The median age was 62 years. Among them, 7 patients belonged to the age group of 30–49 years, 16 to the age group of 50–69 years, and 10 to the age group of 70–89 years (Fig. 1). 27 were males and the remaining 8 were females (Fig. 2). A majority of the patients presented with fever, dry cough, and myalgia. Other symptoms included a sore throat, dyspnea, and anosmia. 26 patients (74.3%) were found to have an eosinophil count of zero, 6 (17.1%) were found to have an eosinophil count of 1–2, and 1 (2.9%) had an eosinophil count of 4 (Fig. 3).

DISCUSSION

Coronaviruses are highly enveloped, positive-sense RNA viruses with a high mutation rate and infectivity [1]. They are important zoonotic pathogens infecting animals and humans [1]. The clinical features may vary from asymptomatic through severe acute respiratory distress to multiorgan failure and death [13,14]. Even if the patient is asymptomatic, they are still capable of transmitting the virus [13]. The clinical manifestations include fever, myalgia, dry cough, a sore throat, headache, dyspnea [13,14], as well as severe manifestations such as hypoxemia, confusion, chest pain, and pneumonia, with some cases requiring intensive care unit (ICU) admission and mechanical ventilation. Diarrhea, anosmia, and ageusia have also been reported in several studies [15,16]

There is the emergence of interest in the topic of eosinopenia as a biomarker of COVID-19 infection [11]. A response to acute inflammation causes the release of chemotactic factors into circulation, leading to a rapid and persistent decrease in circulating eosinophils [11,14,17]. There is also an association of adrenal corticosteroids and epinephrine, as it increases in acute stress, with the occurrence of eosinopenia [13].

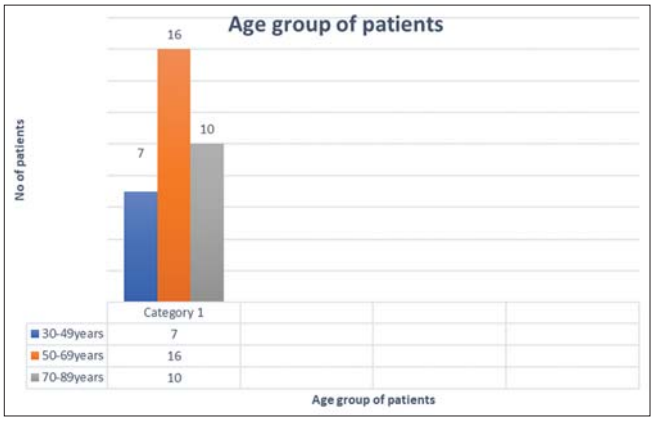

Figure 1: Age distribution of the patients.

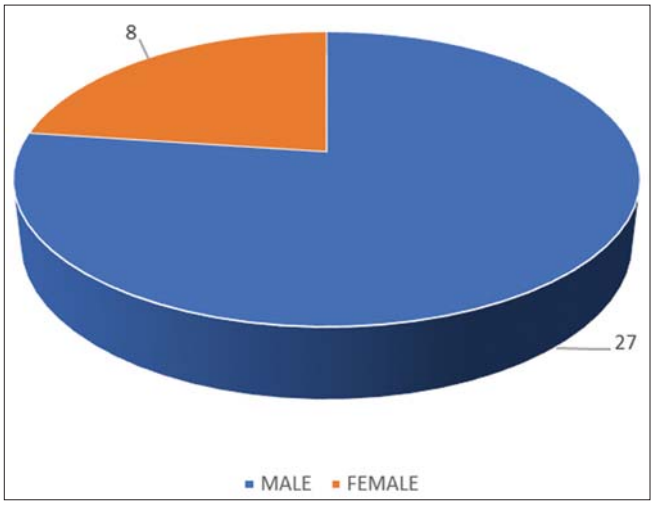

Figure 2: Gender distribution of the patients.

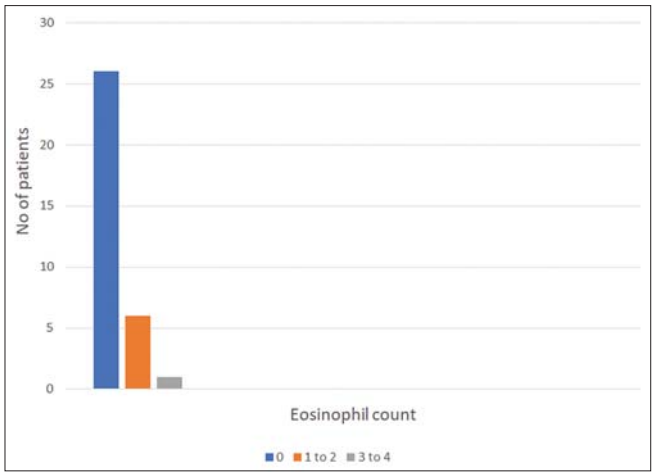

Figure 3: Eosinophil count in the COVID-19 affected patients.

EOSINOPENIA IN RESPIRATORY TRACT DISEASES

Human eosinophils may express toll-like receptors (TLR) such as TLR3, TLR7, and TLR9 that can detect molecular patterns [9,18]. TLRs may help eosinophils to identify coronaviruses and lead to degranulation, the release of cytokines, and nitric oxide (NO) production [9]. Previous studies show a direct antiviral effect of nitric oxide on parainfluenza virus and RSV [9,19]. Eosinophils may also produce extracellular DNA traps in response to viral diseases such as RSV [9]. Eosinophils may mobilize preformed granules of Th1 cytokines, such as IL-12 and IFN-g, which helps in the antiviral immune response [9,20]. Human eosinophils express MHC-II molecules and costimulatory molecules and may also act as antigen-presenting cells for viral antigens, thereby causing T-cell activation and the release of cytokines [9].

EOSINOPENIA IN COVID-19

The cause of the decrease in eosinophils in COVID-19 is multifactorial [9]. The development and maturation of eosinophils occur in the bone marrow under exposure of myeloid precursors to IL3, GM-CSF, and IL5 [11]. The suggested pathophysiology of eosinopenia includes the decrease in IL-3, IL-5, and GM-CSF, leading to a decrease in the eosinophil count, as these three cytokines regulate the production of white blood cells, and resulting in sepsis [11]. Other mechanisms are the inhibition of eosinophils from the bone marrow and eosinophil apoptosis due to type 1 interferon release during acute infection [9]. Coronaviruses target IL-33, which is responsible for the activation of eosinophil in the airways, bone marrow, and ciliated epithelial cells. IL-33 is also involved in group 2 innate lymphoid cell activation, which in turn produces IL-5 and IL-13 [21]. Previous studies have found no increase in the eosinophil count in the lung tissue in COVID-19 patients [9,22].

Li *et al*.. conducted a study on 989 confirmed cases of COVID-19, in which eosinopenia (<0.02109/L) was present in 74.7%, compared to the controls (31.3%) [4]. Bass *et al*.., by using chemotactic factors of acute inflammation, were able to induce a decrease in the eosinophil count in rabbits and in humans. In a study conducted by Hu Yun *et al*.., out of 32 COVID-19 patients, 66% showed a decreased eosinophil count [7].

CONCLUSION

Because COVID-19 follows an unpredictable course and may lead to deadly complications, there is a need for its early identification. The eosinophil count may be used as its early and low-cost indicator. In our study, around 71.4 % of the hospitalized patients had an eosinophil count of zero at the time of admission. The estimation of the eosinophil count may help in early therapeutic management. However, only several studies have been done in this regard. The relationship between the eosinophil count and COVID-19 infection needs more exploration.

ACKNOWLEDGMENTS

All authors contributed substantially to the concept and the collection, analysis, and interpretation of data. We would like to acknowledge all healthcare workers involved in the diagnosis and treatment of COVID-19 patients.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

ABBREVIATIONS

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
COVID-19: coronavirus disease 2019
WHO: World Health Organization
RT-PCR: reverse transcriptase polymerase chain reaction
HRCT: high-resolution computed tomography
CO-RADS: COVID-19 Reporting and Data System
CRP: C-reactive protein; WBC: white blood cell; LDH: lactate dehydrogenase; ALT: alanine transaminase; AST: aspartate aminotransferase
RNA: ribonucleic acid; DNA: deoxyribonucleic acid
TLR: toll-like receptor; NO: nitric oxide; IFN-g: interferon gamma; GM-CSF: granulocyte-macrophage colony-stimulating factor; IL: interleukin
RSV: respiratory syncytial virus
MHC: major histocompatibility complex

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Our Dermatology Online

Brief Report

Treatment of notalgia paresthetica with low dose pregabalin: Retrospective evaluation of 13 patients

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ABSTRACT

Background: Notalgia paresthetica (NP) is a sensory neuropathic syndrome characterized by chronic itching of the unilateral mid-back. Topical and systemic symptomatic treatments have been used to date. In recent years, neuropathic pain medicine has been used to relieve the symptoms of the disease. The aim of this study was to determine the effectiveness of pregabalin in notalgia paresthetica. **Materials and Methods:** In this study, the files of the patients with a diagnosis of NP and treated with pregabalin for at least one month in the period between 2016 and 2018 were evaluated retrospectively. **Results:** Thirteen cases of NP treated with low-dose (up to 150 mg/day) pregabalin were evaluated, and 9 (70%) patients exhibited a good response in this retrospective study. All patients were female and the mean age was 53.5 (31–71) ± 10.3 years. The mean disease duration was 6.1 (1–10) ± 4.1 years. **Conclusion:** Treatment with low-dose pregabalin may be a good option for the symptomatic treatment of NP.

Key words: Neuropathic pruritus, Neuropathic pain, notalgia paresthetica, pregabalin

INTRODUCTION

Notalgia paresthetica (NP) is a sensory neuropathic syndrome with chronic and severe itching (neuropathic pruritus) localized in the mid-back. Clinically, a hyperpigmented patch on the back that is generally unilateral and restricted to a small part of the T2–T6 dermatomal areas is observed [1-3]. NP may also be accompanied by other disturbing sensory symptoms, such as burning pain, paresthesia, dysesthesia, or hyperesthesia. Rarely, hypoesthesia is also noted. Most of the patients are middle-aged and older females [1,2]. Although the etiopathogenesis of the disease is not fully known, genetic predisposition, increased dermal innervation, viscerocutaneous reflex mechanisms, sensorial neuropathy due to neurotoxic agents, and dorsal spinal nerve injury are emphasized [4].

Numerous agents have been used for the treatment of NP. Topical agents, such as capsaicin, corticosteroids, local anesthetic drugs, or botulinum toxin A injections, are typically used. In addition to transcutaneous electrical nerve stimulation, acupuncture, exercise, and surgical decompression have been employed. Antihistamines, amitriptyline, and anti-epileptic drugs, such as oxcarbazepine, have also been used systemically in the treatment of NP [4-6]. It has recently been suggested that gabapentin and pregabalin, which are neuropathic pain relievers, may also be used for the treatment of the disease [7]. The aim of this retrospective, observational study was to evaluate the efficacy of pregabalin in patients with NP.

MATERIALS AND METHODS

In this study, the files of the patients admitted to our outpatient clinic with a diagnosis of NP and treated with pregabalin for at least one month in the period between 2016 and 2018 were evaluated retrospectively. The patients' responses to any symptomatic treatment were recorded as either none, slight, moderate, good, or

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very good in the general daily practice of our outpatient clinic. We used these descriptions in this study.

RESULTS

Thirteen patients with NP were treated with pregabalin in the period between 2016 and 2018 according to hospital records. Diagnosis was based on clinical findings in ten patients and confirmatory biopsies were performed in three patients. All patients were female and the mean age was 53.5 (31–71) ± 10.3 years. The mean disease duration was 6.1 (1–10) ± 4.1 years. The symptoms were located in the mid-back in all patients. The other clinical characteristics and accompanying diseases, as well as the doses of pregabalin and responses, are shown in Table 1.

All of the patients had previously been treated with topical corticosteroids, systemic antihistamines, or anti-inflammatory medicine. According to records, the patients were started on 25 mg of pregabalin twice daily. In one patient, at the end of two weeks, the dose was increased to 50 mg twice daily. In another patient, the dose was increased to 75 mg twice daily after three weeks.

Three of the patients had a very good response to treatment, six patients had a good response, and four had a moderate response. No side effects were recorded in any patient.

DISCUSSION

Pain and itching sensations are transmitted via peripheral unmyelinated C nerve fibers to the dorsal horn of the medulla spinalis and, then, to the thalamus and somatosensory cortex via the lateral spinothalamic tract. Microneurography studies have demonstrated that a small group of histamine-sensitive C nerve fibers transmit pruritus. These C fibers have spontaneous activity in patients with chronic pruritus [8]. The antipruritic effect of gabapentin and pregabalin has been investigated in a mouse model. Gabapentin and pregabalin inhibit hyperexcitable neurons by modulating the α_2 δ-1 subunit of voltage-dependent calcium channels. These inhibit calcium influx and the subsequent release of excitatory neurotransmitters [9].

Numerous receptors and mediators play a role in the transmission of itching. There are similarities and interactions between the neurotransmitters of pain and itching. Gabapentin and pregabalin used for the treatment of neuropathic pain are thought to be applicable to pruritus given this close relationship [9-10]. Maciel et al. reported that the response to treatment of ten patients with NP with 300 mg of gabapentin daily for four weeks was significantly better than the other ten patients with 0.025% topical capsaicin [7].

Pregabalin is a similar molecule to gabapentin, with some pharmacological advantages such as fast absorption, linear elimination, and fewer side effects. The most common side effects are sedation, dizziness, and drowsiness [10].

Pregabalin has been previously used in various clinical conditions for the treatment of pruritus in dermatology. Atış et al. reported good results with 100 mg of

POLAND_1940_Treatment

Table 1: Clinical characteristics and treatment responses of the patients

Patient No.	Age	Disease Duration (yrs.)	Mid-back Symptom Side	Accompanying Diseases	Neuro/orthopedical Problems	Pregabalin Dose (mg/day)	Response
1	54	4	Right	Hyperlipidemia	Sacroiliitis	2x25	Good
2	49	10	Bilateral	Hyperthyroidism		2x50	Moderate
3	46	10	Bilateral	Polycythemia		2x25	Moderate
4	64	5	Right	Diabetes mellitus	Cervical discopathy	2x25	Good
5	59	2	Bilateral	Hypertension		2x25	Very good
6	44	1	Right	Hypothyroidism		2x25	Good
7	31	4	Left			2x25	Good
8	58	3	Right		Fibromyalgia	2x25	Moderate
9	52	7	Right			2x25	Very good
10	71	2	Right		Lumbar discopathy	2x75	Moderate
11	47	15	Right			2x25	Very good
12	62	6	Bilateral	Diabetes mellitus	Fibromyalgia	2x25	Good
13	59	10	Right		Ankylosing spondylitis	2x25	Good

pregabalin daily in two of three cases with brachioradial pruritus, while a dose of 225 mg was needed in the third patient [11]. In thirty patients with prurigo nodularis, 75 mg of pregabalin daily was used for three months, which provided satisfactory relief in 23 (76%) patients [12].

To the best of our knowledge, this is the first report of the use of pregabalin in NP. The effective dose of pregabalin for neuropathic pain ranges between 150 and 600 mg. However, studies indicate that the use of very low doses is sufficient for itching. Although there is no standard dose for the symptomatic treatment of pruritus, it is recommended to begin with a very low dose compared with the treatment of neuropathic pain and adjust the dose and duration of the treatment according to the patient's needs. Thus, side effects are also minimized [13]. In our study, pregabalin provided satisfactory relief at a dose of 25 mg twice a day in eleven out of thirteen patients in four weeks. Two patients required slightly higher doses: 100 mg and 150 mg, separately.

Symptomatic treatment of NP is as important as the treatment of the underlying pathology if detected. A good or very good response was obtained in nine (70%) out of thirteen patients with symptomatic treatment of NP with low-dose pregabalin in this study.

In conclusion, low-dose pregabalin treatment may be a good option for the symptomatic treatment of NP. The limitations of our study were its retrospective nature and the absence of a control group. The findings of the present study encourage further prospective and controlled studies.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Brief Report

Intradermal tranexamic acid in the treatment of melasma: A prospective study of 20 Moroccan cases

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ABSTRACT

Background: The objective of this study was to evaluate the effectiveness and safety of tranexamic acid mesotherapy in the treatment of melasma in the Moroccan population. **Materials and Methods:** All the patients received an intradermal injection of tranexamic acid (5 mg/mL). No other local or general treatment was administered. The patients were kept under external photoprotection only. Pre- and post-treatment photographs were taken and analyzed with the Visioface® RD hardware. The evaluation was employed the MASI score. **Results:** All patients had a dark skin phototype. The average duration of melasma evolution was 3.67 years. The pre-treatment average MASI was 7.6. The post-therapeutic average MASI was 6. The Visioface® RD hardware estimated a 25% reduction in the surface area attained at month five. No serious side effects were reported. **Conclusion:** Tranexamic acid was proven to be an essential tool in treating melasma.

Key words: Melasma; Tranexamic acid; Intradermal injection; Therapy

INTRODUCTION

Melasma is a chronic acquired hyperpigmentation of the skin characterized by irregular brown macules symmetrically distributed on sun-exposed areas of the body, especially the face.

It is a common cause of concern in dermatological care in the Moroccan population, affecting mainly females [1]. It has long been a condition annoying for both the physician and the patient.

So far, there is no therapy with fully satisfactory results. New therapeutic options have emerged, and some of these therapies have come under increasing focus. Tranexamic acid (TA, trans-4-(Aminomethyl) cyclohexane carboxylic acid (T-AMCHA)) is a plasmin inhibitor that has recently emerged as a promising new treatment for melasma, for which different galenic forms and ways of administration are proposed [2].

The primary objective of this study was to evaluate the effectiveness and safety of tranexamic acid mesotherapy in the treatment of melasma in the Moroccan population.

MATERIALS AND METHODS

A monocentric prospective study was conducted from December 2018 through May 2019 at the dermatology department of the Ibn Rochd University Hospital in Casablanca. The study included melasma patients over the age of eighteen years who had not received any treatment in the last two months prior to the study.

The study excluded pregnant and breastfeeding women and patients with a history of hypersensitivity to the product or other associated dermatosis, endocrine disorders, photodynamic therapy, a history of vitiligo, known abnormalities in wound healing, facial warts, herpes, and patients under anticoagulant treatment, on estrogen–progestin contraception, or with a known thromboembolic or cardiovascular disorder.

The injections were performed by a dermatologist in accordance with the following protocol: the skin was

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cleansed with saline solution, then an EMLA anesthetic cream was applied for thirty minutes.

All the patients received intradermal micro-injections of TA (5 mg/mL) every fifteen days for two months, then three cycles of the TA treatment repeated monthly.

Tranexamic acid by intradermal injection (10 mg/mL). Intradermal microinjections were performed by an insulin syringe with a 30-gauge needle. An interval of 10 mm between two injections was maintained. All aseptic conditions were respected. By the end of the procedure, cold compresses were applied followed by an SPF 50+ cream.

The treatment was associated with currently external photoprotection by broad-spectrum sunscreen and SPF 50+. No other local or general treatment was administered. The patients were kept under external photoprotection only.

Each patient gave their clear consent prior to the commencement of the study and was informed of the possible side effects of tranexamic acid.

Pre- and post-treatment photographs were taken and analyzed with the Visioface® RD hardware. This device was used to analyze the number of spots and the surface area affected. The evaluation employed the MASI score.

Improvements were judged as very good (disappearance of more than 75% of the lesions), good (disappearance of 50% to 75% of the lesions), moderate (disappearance of 25% to 50% of the lesions), incremental (disappearance of less than 25% of the lesions), or no response.

The tolerance assessment took into consideration the evaluation of pain with a simple verbal scale and any adverse reactions reported by patients or observed on check-ups.

The data collection form included:
- demographic characteristics (age, sex);
- pathological history and medication in use;
- risk factors (sun exposure, hormonal imbalance, the application of irritating topical products);
- the duration of lesions evolution;
- previous treatments (depigmentation, lasers, peelings).

The statistical analysis was performed with the SPSS software.

Ethics Statement

The study was approved by the institutional ethics committee of our institution, and all patients provided written informed consent.

RESULTS

Twenty patients were enrolled, all of which were females with an average age of 41.75 years (extremes: 2–65; standard deviation: 10.63).

Ten of the patients had a family history of melasma with sun exposure among all our patients. Eleven patients were previously pregnant. Ten of them were under long-term estrogen–progestin therapy. Previous treatments were used by nineteen patients: natural masks by eight patients, depigmenting agents without hydroquinone by eleven, hydroquinone by two, and peeling by three. Fifteen had already used several therapeutic combinations before the consultation. Three patients had facial hypersensitivity.

The average duration of melasma evolution was 3.67 years.

All patients had a dark skin phototype: six patients with phototype III, thirteen patients with phototype IV, and one patient with phototype V. The clinical aspect was about pigmented macules, varying from light brown to dark brown.

The location of the melasma was centrofacial in eleven patients, malar in seven, and maxillary in two. The pretreatment average MASI was 7.6.

Interventional pain was considered moderate by five patients, intense by twelve, and unbearable by three. Post-interventional pain disappeared after one hour for all patients. Post-interventional erythema was reported by all patients and lasted for one day at most. No short-, medium-, or long-term side effects were recorded (eczematization, postinflammatory hyperpigmentation).

The patients were seen at M1, M3, and M6. One patient reported a remarkably good improvement. A good improvement was noted by six patients. A moderate improvement was noted by four patients. Three patients reported a slight improvement. No response was noted by three patients. Three patients withdrew from the study. The post-treatment average

Table 1: Protocols of intradermal TA reported by several studies

Study	No. of patients	Rhythm	Duration (in weeks)	Comparative treatment	Results
Lee & al. [11]	100	Weekly	12	None	Decrease in MASI.
Elfar & El-Maghraby. [10]	60	Weekly	N/A	Silymarin, glycolic acid	Decrease in MASI.
Saki & al. [12]	37	Monthly	20	Topical hydroquinone	No significant difference between the two groups.
Pazyar & al. [13]	49	Fortnightly	24	Hydroquinone	No significant difference between the two groups.

MASI was 6. The Visioface® RD hardware estimated a 25% reduction in the surface area achieved at month five (Fig. 1).

DISCUSSION

Intradermal injection of tranexamic acid produced an improvement in melasma in our patients. No serious side effects apart from a mild local burning sensation and erythema were reported, and these were mostly transient.

Despite several proposed therapeutic modalities of variable efficiency and tolerance, melasma remains a therapeutic challenge that evolves chronically and recurrently [3]. Some topical agents, such as hydroquinone, are limited by complications, including irritant dermatitis, allergic contact dermatitis, postinflammatory hyperpigmentation, and exogenous ochronosis [4]. Darker skin types (Fitzpatrick types IV to VI) are particularly at risk for post-inflammatory hyperpigmentation (PIH) [5], which limits the use of topical bleaching formulas [6] and physical treatments as chemical peels and lasers in our context and forces us to evaluate the efficiency and safety of other modalities [4].

Tranexamic acid is a well-known hemostatic agent. In recent years, despite its mechanism of action remaining unclear, TA has been shown to produce encouraging results in the treatment of melisma [7]. Tranexamic acid inhibits the binding of plasminogen to keratinocytes, thereby reducing the synthesis of prostaglandins, which are known stimulators of tyrosinase activity. In addition, plasmin increases diffusible forms of vascular endothelial growth factor (VEGF), leading to angiogenesis. The inhibition of plasmin by TA leads to a reduction in angiogenesis, which allows it to act on the vascular component of melasma [8,9].

Encouraging results were observed with different routes of TA administration (oral, topical, or micro-injections), with a significant drop in the MASI score in all cases [9].

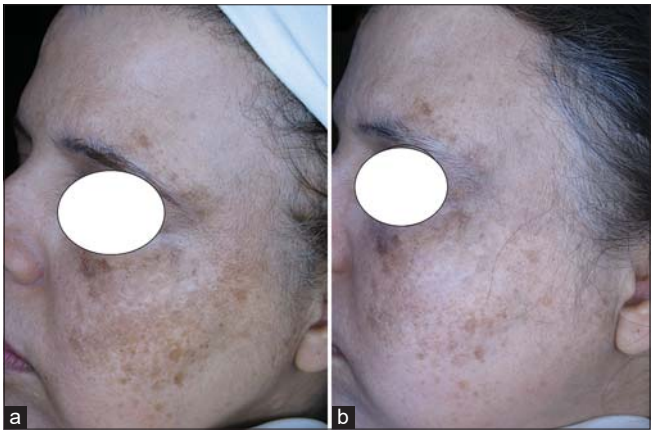

Figure 1: Photos (a) before and (b) after seven sessions of intradermal tranexamic acid therapy.

Nevertheless, given the potential for serious side effects with the use of oral TA, there has been an interest in evaluating TA as mesotherapy or topical therapy for melisma [10].

No definitive consensus on the use of TA for melasma currently exists. Several protocols have been proposed, with different concentrations and session rhythms. Variable results have been reported by trials of intradermal TA (Table 1).

TA has proven to be an essential tool in treating melasma [9].

The study was limited by a small number of patients, no control arm, and a short duration of the treatment and follow-up.

CONCLUSION

The encouraging results in our study as well as in the various studies reported make it possible to consider microinjection of TA as an effective option for the treatment of melasma in the Moroccan population. However, this data needs to be supported by larger randomized clinical trials to determine the most efficient mode of delivery.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Brief Report

Does early acne intervention provide more than just a reduction in the incidence of scars? A review of the literature

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ABSTRACT

Background: It is well established that early intervention in acne treatment reduces the incidence of scars. The purpose of this paper was to identify if early intervention in acne management also provides a cost benefit to the patient, reduces relapse rates or lessens the requirement for the treatment of acne scars. **Method**: A systematic search of The Cochrane Library, MEDLINE and Cumulative Index to Nursing and Allied Health Literature (CINAHL) was performed independently by one reviewer using predefined criteria. **Results:** Seven articles were identified from the literature – one systematic review, one review article and five expert opinion articles. Although data supports early intervention in acne management, no articles identified whether a cost benefit was also provided, if there was a reduction in the relapse rates or if there was a decreased requirement for the treatment of acne scars. **Conclusions**: This review identifies an overall lack of published data regarding multiple outcomes for early intervention in acne and allows for the possible identification of areas where primary research would be beneficial.

Key words: Acne; early intervention; scarring; cost-benefit; relapse

INTRODUCTION

Acne is a disease of the pilosebaceous unit resulting in non-inflammatory lesions including microcomedones and comedones as well as inflammatory lesions comprising papules, pustules, nodules and cysts [1]. It is one of the three most common dermatoses in the world with up to 80-90% of people between the ages of 16 and 20 affected [2]. In severe cases, acne can lead to cutaneous scarring which in most cases, is permanent. The psychological scarring that can result from acne may also be profound [3]. There is thorough evidence to suggest that early initiation of treatment in acne, in particular with isotretinoin, may reduce the incidence and extent of acne scarring [4]. Pursuing early treatment of acne may prevent or reduce psychosocial problems such as issues with self-esteem, social withdrawal, depression and unemployment [5]. Extrapolation of US data shows that acne could be costing up to $100 million per year to the Australian community [6] with justification provided given the social, psychological and physical impacts of the condition. There is however, little research on whether early intervention reduces the overall costs of acne treatment and the need for the treatment of scarring. In addition, there also appears to be a lack of concrete knowledge of whether relapse rates of acne are reduced with early intervention. Given the prevalence and significant patient morbidity resulting from acne, it is vital that robust, good-quality research is completed in this area. This review aims to investigate whether early intervention in acne provides a cost-benefit to the patient, reduces the need for treatment of acne scarring and reduces relapse rates.

METHODS

A systematic search of The Cochrane Library, MEDLINE and Cumulative Index to Nursing and

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Allied Health Literature (CINAHL) was performed independently by one reviewer using predefined criteria. Key words used in each search engine included acne, early intervention, cost benefit, scarring and relapse. Inclusion criteria included primary research related to early intervention in acne, electronically published literature, articles written in the English language and articles from 1995 onwards. Exclusion criteria included primary research not relating to early intervention in acne, articles not written in the English language, articles published before 1995 and unpublished literature. A total of seven studies were included, which included one systematic review, one review article and five expert opinion articles. The full articles of all studies identified were analysed in depth and can be found in Table I.

RESULTS

One systematic review, one review article and five expert opinion articles were identified. Whilst ample data was identified to support early intervention in acne to reduce the *incidence* of scarring, there was no identifiable research found on whether early intervention reduces the need for the *treatment* of scarring. There was also no identifiable literature on whether early intervention in acne reduces relapse rates or whether it provides a cost benefit to the patient. Studies identified focussed on optimising acne management and patient education in order to reduce the incidence of acne scarring with Bonney et al. (2016) suggesting that acne outcomes can be improved when general practitioners are able to recognise acne scarring early [7]. Layton (2000) argues that isotretinoin instituted early on in the disease course can reduce both the physical and psychological scars that can result from acne [4]. There is evidence to suggest that optimisation of acne management should involve the use of both topical, systemic and localised therapies in order to minimise the development of acne scars [8]. There has also been extensive research performed on the treatment of atrophic scars, the most common

Table I: Analysis of articles

Reference/ Year	Level of evidence	Design	No. of patients	Major findings	Results/conclusions	Study limitations
Goodman et al. [6]/2006	N/A	Expert opinion	N/A	- Acne is costing $100 million to Australian community - It is expensive to treat a self-limiting problem - Affected adolescents report more social isolation and self-consciousness, embarrassment, unhappiness and anxiety than their unaffected peers - 5.6% of patients with acne entertained acute suicidal thoughts - Scarring may affect up to 95% of patients and is related to severity and duration of acne before adequate therapy is instituted - Early and effective treatment of acne is the most appropriate way to prevent scarring	- Early and aggressive treatment of acne has positive impacts on the social, psychological and physical effects of the condition.	- Expert opinion article
Goodman. [9]/1999	N/A	Expert opinion	N/A	- Scarring can be prevented in patients by early adequate medical intervention in the disease course.	- Post acne scarring should warrant treatment of the earliest, best and most effective treatments - Punched out scars benefit from 'coring of scars' followed by suturing or graft application - Dermal and subcutaneous augmentation methods include dermal grafting, lipocytic dermal augmentation, fat transfer and implantation of autologous collagen and cultured and expanded autologous fibroblasts - Non-autologous augmentation of atrophic acne scars include injection of bovine collagen, fibrin foam, hyaluronic acid or polymethylmethacrylate microspheres	- Expert opinion article

(*Contd...*)

Table I: (*Continued*)

Reference/ Year	Level of evidence	Design	No. of patients	Major findings	Results/conclusions	Study limitations
Layton et al. [4]/2000	N/A	Expert opinion	N/A	- Facial scarring occurs in up to 95% of acne cases - Less scarring occurred in patients who received isotretinoin early in their disease course - Reduced depression scores were seen in patients with facial acne lesions when treated with isotretinoin. - Treating acne early on the disease course reduces clinical scars - Effective therapy for acne may reduce psychological and social issues	- There is an increase in anxiety, depression and social isolation in patients who suffer from acne	- Expert opinion article
McGoldrick et al. [10] /2017	N/A	Expert opinion	N/A	- Surgical intervention within 6 months of discontinuing isotretinoin may result in hypertrophic scarring - There is level IV evidence to support dermabrasion, microdermabrasion, light or medium-depth chemical peeling and laser technologies - The time between onset of effective treatment and the extent and duration of inflammation are critical in acne scar development	- In term of acne scar prophylaxis, early appropriate medical treatment that is continued for as long as necessary is best practice	- Expert opinion article
Patel et al. [3]/2014	N/A	Systematic review	N/A	- Acne is prevalent in 90% of adolescent patients - Acne patients experienced psychological and emotional morbidity comparable to conditions such as epilepsy, diabetes and chronic pain - Evidence supports use of laser, surgery and peel therapy for atrophic scar treatment - In the adult population, 1% of patients are reported to have acne scarring persisting from adolescence	- CO2 ablative therapy, laser 1450nm diode laser/Nd YAG laser have the best evidence to support their use in atrophic scar treatment	- GRADE scoring system = subjective - Publication bias
Savage et al. [8]/2010	N/A	Review article	N/A	- Patients with acne may have impaired self-esteem, anxiety and depression - Acne can lead to social isolation, relationship issues and suicidal ideation - Early onset of acne, hyper seborrhoea, truncal acne and scarring are poor prognostic factors in acne	- Limiting the duration of active disease by early and effective treatment offers the possibility of minimising both the physical and emotional scarring caused by acne - A focus on early aggressive intervention is paramount for all patients to reduce the physical and psychological scarring that can result from acne of any severity	- Review article
Torjesen et al. [11]/2019	N/A	Expert opinion	N/A	- A lack of elastic fibres was seen from the beginning of acne inflammation - A lack of elastic fibres existed in mature atrophic scars	- TGF-B1 enhances inflammation and affects fibrosis and epidermal proliferation - Anti-inflammatory or anti-TGF B1 drugs may minimise atrophic scarring in acne. - Cutibacterium acne stimulates TNFa, IL-6, IL-12 and CXCL8 via toll-like receptor 2 signalling	- Expert opinion article

form of scars found in patients with acne. Despite this, further research with randomised controlled trials is necessary to be able to provide sound evidence for the management of atrophic scars [3].

DISCUSSION

Despite comprehensively and systematically reviewing the literature in an attempt to address our research

question, knowledge on various outcomes for early intervention in acne management are limited. Our research questions were not answerable using the literature. While there has been much research on the reduction in the incidence of scarring with early intervention, few researchers have delved into whether early intervention reduces the need for treatment of scars. Given the significant patient morbidity of acne, this points to the need for a study involving primary data collection in order to find an answer to whether or not early intervention in acne provides a cost benefit to the patient, reduces the need for treatment of acne scarring and reduces relapse rates. Limitations of our study include the small number of articles retrieved from which we are able to draw a firm conclusion as well as the fact that there is no best approach to comparing qualitative, quantitative and discussion papers. A publication bias was also noted as unpublished literature and literature not written in the English language were excluded. Other sources of limitations include unavailable and inaccessible data.

CONCLUSION

In summary, this review identifies an overall lack of published data regarding multiple outcomes for early intervention in acne and allows for the possible identification of areas where further primary research would be beneficial. Whilst it is known that isotretinoin, early optimisation of acne management and patient education can reduce the incidence of both the physical and psychological scars of acne, more research needs to be conducted to identify whether early intervention in acne provides a direct cost-benefit to the patient, reduces the need for the treatment of acne scarring and reduces relapse rates.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Our Dermatology Online

Case Series

Atypical presentations of superficial dermatophytoses associated with Ruocco's immunocompromised cutaneous district: A case series

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ABSTRACT

An immunocompromised district is an area of irregular immune control of the skin occurring due to cutaneous damage of any sort conducive to the development of infections, immune reactions, and tumors. Superficial dermatophytoses are one of the most commonly encountered cutaneous infections, which, in some cases, may have various atypical presentations. Herein, we present a series of eleven such cases in which the presentation of a superficial dermatophytosis was altered by the concurrent presence of a different unrelated dermatosis on the same anatomical site.

Key words: Immunocompromised district; Locus minoris resistentiae; Superficial dermatophytosis; Atypical tinea

INTRODUCTION

In 2014, Ruocco defined an immunocompromised district (ICD) as areas of the skin with an immune microenvironment conducive to the development of a new disease [1]. An ICD is an area of irregular immune control of skin occurring due to cutaneous damage of any sort conducive to the development of infections, immune reactions, and tumors [2]. Lately, several case reports and series documented this privileged localization of one dermatosis over another [2,3]. In fact, the Koebner phenomenon is one such example.

Herein, we describe a case series of patients presenting with superficial dermatophytosis present on top of an unrelated dermatosis.

CASES

Case 1

A 32-year-old male, an under-treatment case of post-herpetic neuralgia on the left side of the flank persistent for four months, presented with the development of annular, scaly pruritic plaques on the same dermatomes as the patient's past herpes zoster lesions from one month prior. A closer examination revealed the striking phenomenon of annular sparing seen around healed scars of herpes zoster. The patient was diagnosed with the development of tinea corporis on the healed lesions of herpes zoster.

Case 2

A 36-year-old male, a case of chronic plaque psoriasis persistent for three years, presented with a current exacerbation lasting for the past fifteen days. The patient was prescribed oral methotrexate with topical betamethasone lotion for the same condition in the past, but, for the last three months, was off all treatment. A cutaneous examination revealed, apart from silvery, salmon-colored, scaled and indurated plaques of psoriasis, widespread erythematous annular and polycyclic plaques on the existing lesions of psoriasis (Fig. 1). There was no history of preceding sore throat, fever, joint pain, or systemic involvement.

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The patient was diagnosed with tinea corporis and tinea cruris with psoriasis.

Case 3

A known case of localized morphea, 30 years of age, presented with the development of an itchy, scaly lesion on an already existing lesion in the right subscapular region. An examination revealed well-defined erythematous-to-hyperpigmented plaques with peripheral scaling. The background skin had an ill-defined, depressed plaque with a sclerodermatous appearance along with hyperpigmentation and a violaceous hue. The patient had been under treatment with 0.005% calcipotriol ointment for the last two months. The new scaly plaque had developed for the last one month. With a strong clinical suspicion, a scraping from the plaque was sent for KOH and fungal culture examination, both positive for dermatophytosis. A diagnosis of tinea incognito with morphea was reached. The patient was prescribed oral and topical antifungals, which led to the resolution of tinea incognito after four weeks (Fig. 2).

Case 4

A 50-year-old female, while under palliative radiotherapy for squamous cell carcinoma of the buccal mucosa, developed dermatophytic infection in the radiation port. The patient had been receiving radiotherapy for the last four months, while the lesions of tinea faciei had developed over the last one month, involving the left preauricular and mental area extending up to the angle of the mouth (Fig. 3). A diagnosis of radiation-port dermatophytosis was reached confirmed by a positive fungal culture.

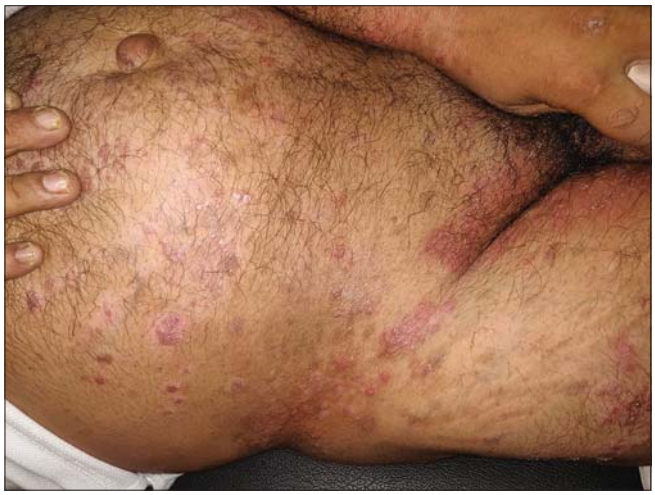

Figure 1: Round-to-oval plaques of psoriasis surmounted over tinea corporis on the abdomen.

Case 5

A 46-year-old male, a known, biopsy-proven case of dermatitis herpetiformis presented with the development of multiple annular, scaly and erythematous plaques over already existing lesions on the extensors, involving the elbows and buttocks. The patient had been taking tablet dapsone 100 mg once a day for the same condition, along with a topical preparation of 0.05% betamethasone lotion. The new annular lesions had developed over the last one month. With a strong clinical suspicion, a KOH mount of the marginal scales was performed, confirming the diagnosis of tinea incognito.

Case 6

A 63-year-old male presented with a complaint of intense pruritus and scarring and darkening of the shin of the left leg persistent for six months, because of

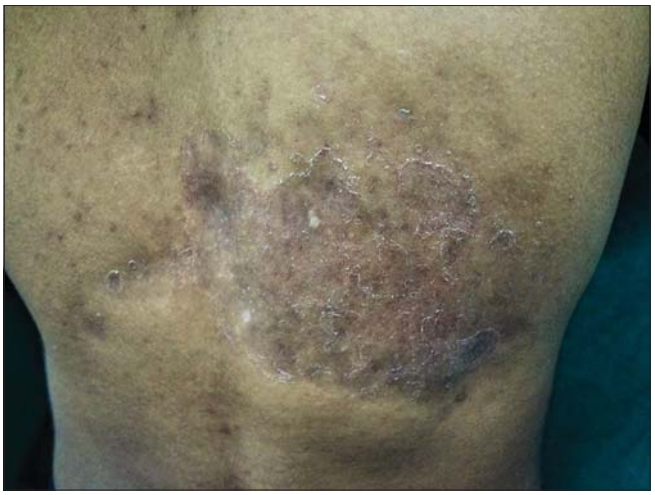

Figure 2: Tinea incognito on a localized morpheic plaque.

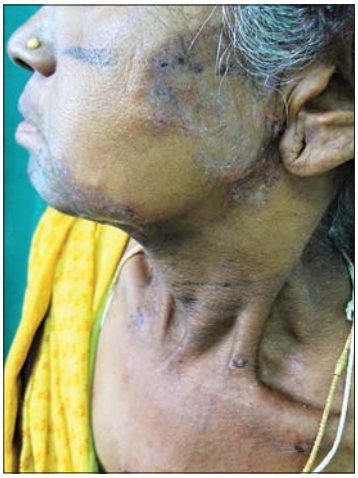

Figure 3: Radiation port dermatophytosis on the face.

which he was diagnosed with lichen simplex chronicus three months earlier and for which he was prescribed liquid paraffin. Four months after the onset of these lesions, the patient developed a progressive, raised, annular erythematous plaque around the lesion, which had progressively increased in size and surrounded the entire lesion. The patient denied the use of any topical or oral steroid. A diagnosis of tinea corporis superimposed on lichen simplex chronicus was reached.

Case 7

A 56-year-old male, a laborer by profession, presented with complaints of itchy lesions on the trunk and neck. An examination revealed lesions consistent with tinea corporis. An incidental finding, however, was made during the examining and the presence of multiple depigmented vitiliginous macules within the plaques of tinea was noted. Surprisingly, all the vitiligo plaques were completely spared from evidence of superficial dermatophytosis, and there was a sharp demarcation between the islands of sparing and the surrounding scaly plaques of tinea corporis (Fig. 4). To confirm the sparing phenomenon, a scraping from the vitiliginous plaques was sent for a fungal culture, which was negative. A diagnosis of tinea corporis with a sparing phenomenon in vitiligo macules was reached.

Case 8

A 49-year-old male, a known case of tinea corporis with tinea cruris under treatment for the last six months, presented with the presence of an irregularly shaped, well-defined atrophic erythematous plaque on the right buttock (Fig. 5). The patient admitted that the plaque was slowly progressive and had been spreading in one direction while healing toward the other end. The lesion was biopsied and histopathology was found to be consistent with lupus vulgaris, showing epithelioid granuloma and pseudoepitheliomatous hyperplasia.

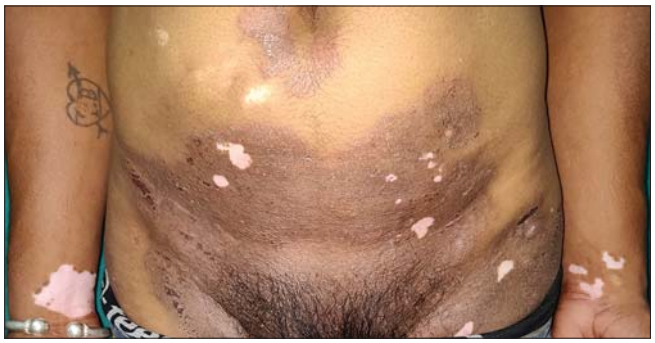

Figure 4: Islands of sparing in vitiligo macules within plaques of tinea corporis on the lower abdomen.

The patient also had a positive Mantoux test, but a chest X-ray and other routine investigations were unremarkable. The patient was put under treatment for cutaneous tuberculosis while the antifungal treatment was continued. The patient showed a marked improvement after three weeks of the treatment itself.

Case 9

A 36-year-old male presented with four days of history of high-grade fever along with an abrupt development of multiple intact or ruptured discreet vesicular lesions with crusting in some over the body. There was, however, a clustering of vesicles surmounted over well-defined, scaly erythematous plaques with raised borders on the right side of the face and in the groin area, which had been present for the last four months (Fig. 6). The patient had similar vesicular lesions over

Figure 5: The presence of a plaque of lupus vulgaris within tinea corporis.

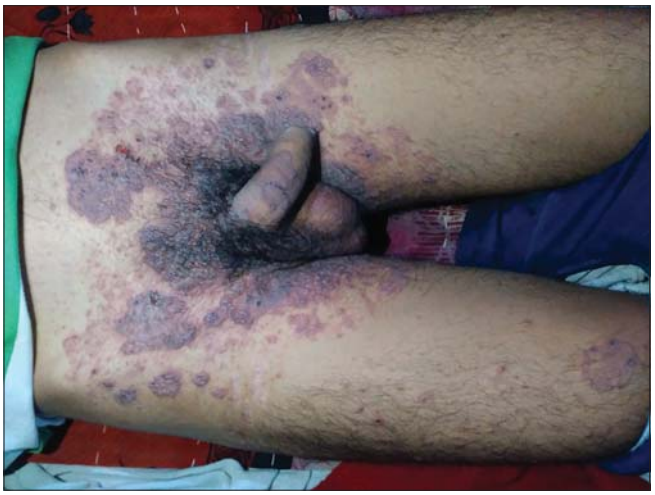

Figure 6: A clustering of varicella-zoster vesicles within plaques of tinea corporis.

the entire body. The background plaque was diagnosed as tinea faciei with tinea cruris under high clinical suspicion, further confirmed by a KOH mount and fungal culture. The fluid collected from the base of the vesicular lesion was examined by a Tzanck smear, showing multinucleated giant cells. The patient was diagnosed with varicella-zoster with tinea faciei.

Case 10

Another case, a 43-year-old married, immunocompetent female patient, presented with complaints of itchy red lesions in the groin area. An examination revealed the presence of a well-defined polycyclic annular erythematous scaly plaque with multiple shiny white papules with umbilication in some. On inquiry, the patient said that this plaque had been present for six months, while the papules had developed in the last one month, and that her husband had similar papules on the genitalia. The patient also admitted to applying topical steroids to the lesion for the last two weeks. The patient was diagnosed clinically with molluscum contagious superimposed on tinea cruris, further confirmed by a KOH mount of the background plaque, while the shiny papules on extirpation demonstrated typical molluscum bodies.

Case 11

A 33-year-old female presented with similar complaints as case three in the groin area persistent for four months. The patient had already been an under-treatment case of tinea corporis for the last one and a half months. However, the new umbilicated papules had rapidly developed over the already existing plaque in the last three weeks. The patient's serology was negative for HIV, hepatitis B, and the VDRL test. Other routine investigations, including a hemogram and liver and renal function tests, were within normal limits. A diagnosis of molluscum contagiosum with tinea corporis was reached, further confirmed by the KOH test and extirpation.

DISCUSSION

This case series highlights the concept of immunocompromised cutaneous districts (ICD) in relation to superficial dermatophytosis [1,2]. Several factors contribute to ICDs, such as prolonged lymphatic stasis, viral infections such as herpes, radiation sources such as palliative radiotherapy, post-traumas, burns, etc., all leading to localized immune dysregulation. This phenomenon is also known as locus minoris resistentiae [2]. Such ICDs are vulnerable to the development of opportunistic fungal infections. The same was seen in cases one through six.

In case 1, the development of tinea corporis over healing lesions of herpes zoster could be explained by three proposed hypotheses. According to the first hypothesis, the viral antigens and altered skin antigens lead to an atypical delayed hypersensitivity reaction or long-standing immunologic changes. Another hypothesis states that the neuropeptides, secreted from cutaneous nerves injured by the herpes virus, lead to the modulation of local immune and vascular proliferative responses. Lastly, according to the third hypothesis, herpes zoster induces anatomic changes such as scarring, the redistribution of collagen, microcirculation alteration, and defects in the skin barrier, deregulating the defense mechanism of the skin in the affected dermatome.

In case 4, the diagnosis of radiation-port dermatophytosis (RPD) was reached. RPD is an elusive and sparsely reported entity. Its pathogenesis is still not fully understood, but this is an example of an ICD as well. Various studies in the past have demonstrated a significant reduction in the Langerhans cell count in mice even with a single dose of 20 Gy. This reduction in immune surveillance coupled with a barrier dysfunction, fibrosis, and a sluggish blood flow contributes to the radiation port site becoming a privileged site for dermatophytosis. However, in all such cases, acute radiation dermatitis must be excluded first [4].

The same concept of immune dysregulation due to chronic itching altering the lymphatic and immune regulation could explain the development of dermatophytosis within a plaque of lichen simplex chronicus in case 5.

In search through the literature of the incidence of dermatophytic infections on psoriatic lesions for case 2, we found that such a combination is a very rarely reported entity, for both keratinophilic and keratinolytic dermatophytes. The parakeratotic cells of psoriasis are unfavorable for the development of such fungal infection. Although several reports in the past have mentioned the development of onychomycosis in psoriatic nails, the presence of superficial dermatophytosis superimposed on psoriatic plaques is an under-reported entity.

Case 3 was a unique case of tinea incognito secondary to topical calcipotriol application. Although several cases of the development of tinea incognito secondary to an erroneous topical administration of corticosteroids and calcineurin inhibitors have been described, to the best of our knowledge, none so far have occurred secondary to the sole application of calcium channel analogs. The application of immunosuppressive or immunomodulatory drugs leads to the downregulation of local immunity against fungi by suppression of beta-defensins and T-cell-mediated immunity. This phenomenon could be partly classified as a pharmacotopic response, secondary to calcipotriol, contributing to the development of an ICD [5-8].

The sparing of vitiligo and contact leukoderma lesions in cases of parthenium dermatitis and textile dermatitis has been described. There are also reports of sparing of nevus depigmentosus in cases of generalized drug eruption. The underlying pathomechanism included the vacuolization of Langerhans cells in these depigmented areas. However, no reports so far on the sparing of vitiligenous macules in dermatophytosis have been published.

There have been reports of lupus vulgaris masquerading as superficial dermatophytosis. The buttocks are a commonly misdiagnosed site involving lupus vulgaris due to its rarity or sporadic presentation in atypical forms [9].

The clearance of a dermatophytic infection is attributed to the upregulation of cell-mediated immunity dependent on T_h1/T_h17. However, the concurrent presence of chronic skin diseases such as untreated cutaneous tuberculosis, psoriasis, atopic dermatitis, and dermatitis herpetiformis (as seen in case 5) shifts the immune response to the T_h2 spectrum making the host site more susceptible to superficial mycosis [10]. Irrespective of the underlying cause, the precise mechanism leading to this skewing of the immune response and the absence of a cell-mediated immune response to dermatophytic invasion is still unclear. The aberrant antigen processing of the fungal hyphae and phagocytosis by the polymorph nuclear leukocytes and macrophages along with hypocomplementemia and Caspase recruitment domain-containing protein 9 (CARD9) gene mutation may be contributing factors [10].

The localization of varicella and, by extrapolation, other cutaneous viral infections such as poxvirus infection (molluscum contagiosum) on the sites of active dermatophytosis could be attributed to the presence of various migration pathways of cutaneous lymphocyte antigen memory T cells involved in immune surveillance. In the case of active inflammation, the migration of these T cells to the skin is significantly increased. Interestingly, the varicella-zoster virus has a high affinity for infecting these cells. Once these infected T cells localize to the site of active inflammation (e.g., superficial dermatophytosis), there is a clinically visible exuberant growth of these diseases over sites of tinea, as seen in cases 1 and 2. The same concept may also be applied to the acquisition of molluscum contagiosum over such sites of dermatophytic infection [11].

CONCLUSION

Our series highlights the importance of diagnosing various atypical presentations of superficial dermatophytoses with respect to the presence of other superimposed dermatoses. The concurrent occurrence of two unrelated dermatoses in the same sector of an immunocompromised district of the skin is both a diagnostic and therapeutic challenge for a dermatologist and one must always be on the lookout for such atypical cases in case of chronic and recurrent dermatophytoses. Antifungal resistant cases are an ever-rising phenomenon globally. An erroneous judgment in diagnosing such cases may add to this uprise of resistant fungal infections. Our series may be a useful tool for studies to come in the future aimed at exploring the same subject matter.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Identification of multi-exon deletion in the COL7A1 gene underlying dystrophic epidermolysis bullosa by whole-exome sequencing

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ABSTRACT

Dystrophic epidermolysis bullosa (DEB) is a rare form of genodermatosis characterized by skin blisters, milia, scarring over the entire body, and nail dystrophy. In this study, a pedigree with one affected member with skin blisters, and a clinical diagnosis of epidermolysis bullosa who was a result of a non-consanguineous marriage, was investigated by whole-exome sequencing (WES). This survey revealed that the proband is a compound heterozygote for a previously reported heterozygous missense variant (c.6205C>T) and a heterozygous deletion of exons 13–24 in the COL7A1 gene. This study indicates that the use of WES along with copy number variation (CNV) analysis gives a higher diagnostic yield for such patients. Moreover, considering the autosomal recessive and dominant forms of the disease, both caused by variants in one gene, proper interpretation and classification of novel variants in heterozygous as well as homozygous states is always a major challenge.

Key words: dystrophic epidermolysis bullosa; COL7A1; whole-exome sequencing; deletion; CNV analysis

INTRODUCTION

Epidermolysis bullosa (EB) is a group of heritable and acquired skin disorders of variable clinical severity. The heritable and severe forms of EB manifest themselves at birth or shortly thereafter as blistering and erosions of the skin and mucous membranes, with considerable morbidity during the early postnatal period, whereas the milder variants are characterized by skin fragility that does not influence the patient's overall lifespan [1]. On the basis of clinical observations and ultrastructural demonstration of the topographic level of blistering within the skin, the hereditary forms of EB have been divided into three categories: epidermolysis bullosa simplex (EBS) involving intra-epidermal blistering with autosomal dominant inheritance; junctional epidermolysis bullosa involving tissue separation within the dermal–epidermal basement membrane with autosomal recessive inheritance; and the dystrophic forms of epidermolysis bullosa involving sublamina densa blister formation within the upper papillary dermis with autosomal dominant or recessive inheritance. There is extensive heterogeneity in the severity of the phenotype and the outcome of the disease in these subgroups of EB. The phenotypic heterogeneity of different forms of EB reflects the fact that as many as twenty different genes encoding the components of the dermal–epidermal attachment complexes harbor mutations in different subtypes of EB [2]. Investigation on the genetic aspect of

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diseases provides the opportunity to explore the relationships between complex phenotypes and genomic variations [3]. Herein, with the help of next-generation sequencing (NGS) technology, we report the case of a fifteen-year-old male who had been suffering from chronic skin disease with skin blisters resulting from a compound heterozygote for a previously reported heterozygous missense variant (c.6205C>T) and a novel heterozygous deletion of exons 13–24 in the COL7A1 gene.

CASE REPORT

A pedigree with one affected member was investigated. A fifteen-year-old male with skin blisters, and a clinical diagnosis of epidermolysis bullosa who was a result of a non-consanguineous marriage, was referred to Watson Genetic Laboratory in Tehran, Iran, for genetic counseling and/or analysis. Written informed consent was taken from the patient's parents and peripheral blood samples were collected from the patient and his family (Fig. 1). Genomic DNA was extracted from whole peripheral blood with the GeneAll® Exgene™ kit (GeneAll Biotechnology Co., LTD, Seoul, Korea) [4]. Human whole-exome enrichment was performed with the Twist Human Core Exome kit and the library was sequenced on the Illumina HiSeq 4000 platform with a raw coverage of 345X and a mean on-target coverage of 149X, performed by CeGaT GmbH, Germany. Detected variations included single-point mutations and small indels (within 20bp). Furthermore, copy number variation (CNV) detection of the aforementioned genes was performed for the patient with breakpoint analysis. Breakpoint analysis was conducted by long-range PCR followed by Sanger sequencing. Long-range PCR was performed with the TaKaRa PrimeStar GXL kit (TaKaRa Bio Inc., Shiga, Japan). The thermal profile for long-range PCR was as follows: denaturation for 8 min at 96°C, then 35 cycles of denaturation (30 s at 96°C), annealing (30 s at 61°C), and extension (4 min at 72°C), followed by the final extension step of 10 min at 72°C. Primers used for genomic amplifications by which the deletion was found were as follows: F, 5'- CCCAGTACCGCATCATTGTG -3' (exon 12); R, 5'-T GTCACGGATCCTTTGCAAGA - 3' (exon 25). For PCR amplification, 1 ml (50 ng/ml) of genome DNA was used as a template in 20 ml of reaction mixture, 1 ml of each primer (5 pM), and 8 μL DH2O. The PCR products, examined by 2% agarose gel electrophoresis, were 4,899 bp (for the normal allele) and 836bp (for the mutant allele) in size, respectively. The PCR products were sequenced by an ABI 3500 automated sequencer (Pishgam Biotech Company, Tehran, Iran). Sequences obtained were analyzed with publicly available NCBI Blast, UCSC BLAT, the sequence alignment tool on UCSC (http://genome.ucsc.edu/cgi-bin/hgBlat?). In order to validate the detected missense variant, polymerase chain reaction was followed by Sanger sequencing. The sequences of the designed primers were as follows: forward primer: GAGTGAGGGAAGAGGGGTTG; reverse primer: ACAGGACTAAGGCAGGGATG. PCR reaction was performed in 20 μL of the total volume containing 8 μL of the Taq DNA Polymerase 2× Master Mix (Ampliqon A/S, Odense, Denmark), 8 μL DH2O, 1 μL of each 5 pM primers, and 1 μL of 50 ng/μL DNA. The conditions for PCR were as follows: initial denaturation at 96°C for 6 min; 32 cycles of denaturation at 96°C for 30 s, the annealing step at 60°C for 30 s, elongation at 72°C for 30 s, and the final extension at 72°C for 5 min. The PCR products were sequenced by an ABI 3500 automated sequencer (Pishgam Biotech Company, Tehran, Iran).

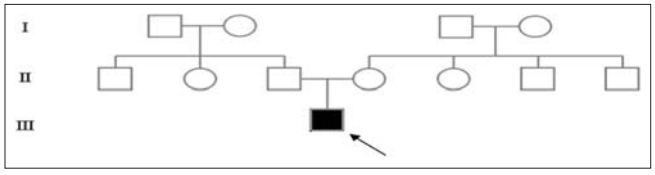

Figure 1: The investigated pedigree, with the proband indicated by filled squares and an arrow.

Whole-exome sequencing revealed a heterozygous missense variant in the proband. The variant was a C-to-T transition at the first base of codon 2069 in exon 74 of the COL7A1 gene that caused the substitution of Arg (CGT) with Cys (TGT) (Fig. 2). According to our survey, this variant (c.6205C>T) in the COL7A1 gene has been reported in the HGMD as well as several other publications as a pathogenic variant [6-11]. The bioinformatic investigation was performed with online tools, including Mutation Taster and CADD, to predict the possible effect of the variant on the function of the protein. The variant was predicted with high confidence to be "disease-causing" by Mutation Taster and with CADD to yield a Phred score of 25.6. The variant is absent in population databases (ExAC, 1000G). In addition, this variant has a frequency of zero in the largest available local database of genomic variations in the Iranian population (Pishgam Biotech Company, Tehran, Iran). Furthermore, a heterozygous deletion of exons 13–24 was detected in the COL7A1 gene. CNV analysis of multiple exon deletions in the

COL7A1 gene for the patient with breakpoint analysis is shown in Fig. 3. Long PCR analysis of genomic DNA indicated 4063 bp deletions of the COL7A1 gene in the patient (Fig. 4). This variant had been previously reported for its pathogenicity in homozygous status [5]. The nature of the deletion and multiple lines of *in silico* computational analysis support the deleterious effect of the variant on the gene or gene product(s). This variant is absent in population databases (ExAC, 1000G) and our local database.

DISCUSSION

In this study, we attempted to target a group of genes responsible for epidermolysis bullosa to detect causative mutations in an Iranian patient with skin blisters, and a clinical diagnosis of epidermolysis bullosa. As a result, a heterozygous missense variant (c.6205C>T) and heterozygous deletion of exons 13–24 in the COL7A1 gene were detected in the patient. Dominant and recessive mutations in gene COL7A1 encoding for collagen VII have been reported to cause DEB. Collagen VII is the major constituent of anchoring fibril presented below the basal lamina within the dermal–epidermal junction. Anchoring fibril appears in normal quantity and morphology on biopsy in Dominant DEB (DDEB). In Recessive DEB the amount of collagen VII was usually remarkably reduced on electron microscopy and immunofluorescence staining [12]. Mutations in the COL7A1 gene encoding for collagen

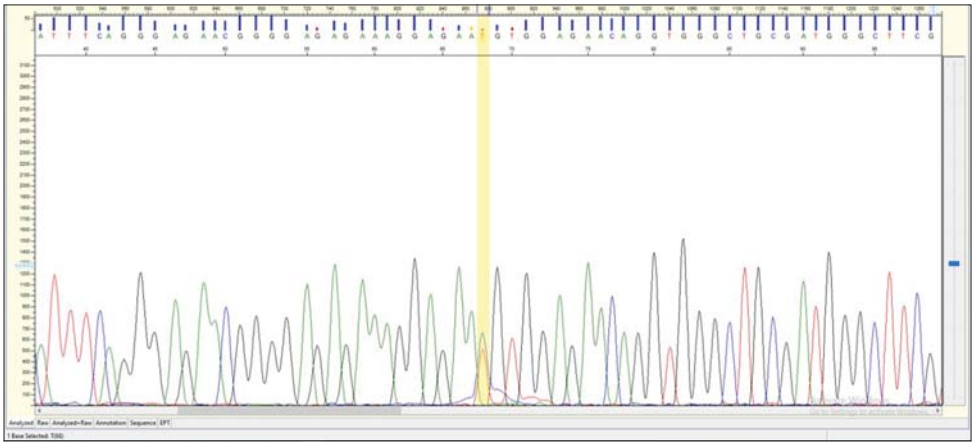

Figure 2: The result of DNA sequencing showing heterozygosity in the patient for variant c.6205C>T in the COL7A1 gene.

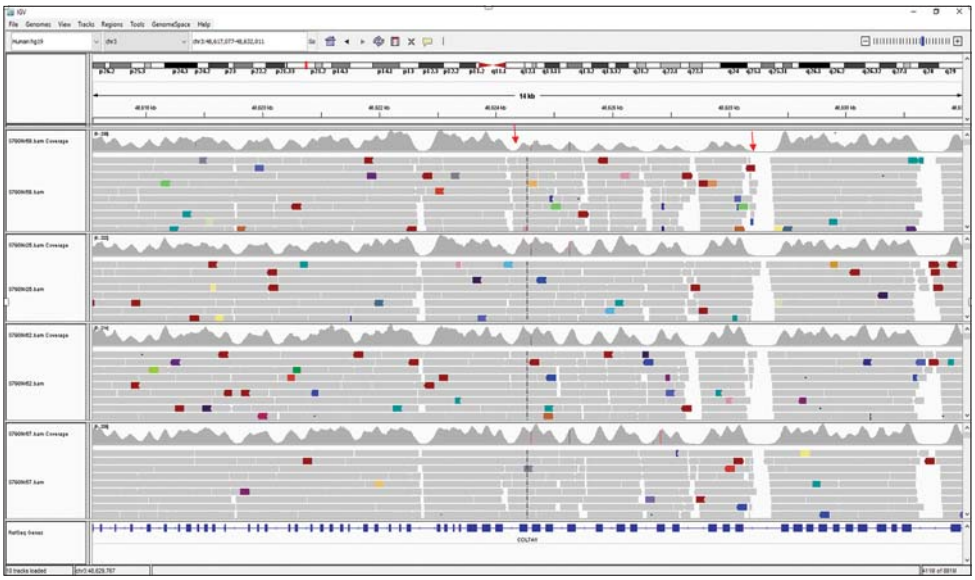

Figure 3: CNV detection of multiple exon deletions in the COL7A1 gene for the patient with breakpoint analysis. Coverage plots (IGV) of three control (ctrl) samples versus the patient (px) sample illustrate the statistical readout with a drop in coverage in the COL7A1 gene on exons 13–24 for the patient sample (double red arrows), compared to controls indicating a deletion event at this position. The 5' decrease in coverage is located at a clear-cut position at the beginning of exon 13 (red arrow). The COL7A1 gene is displayed from the right to left.

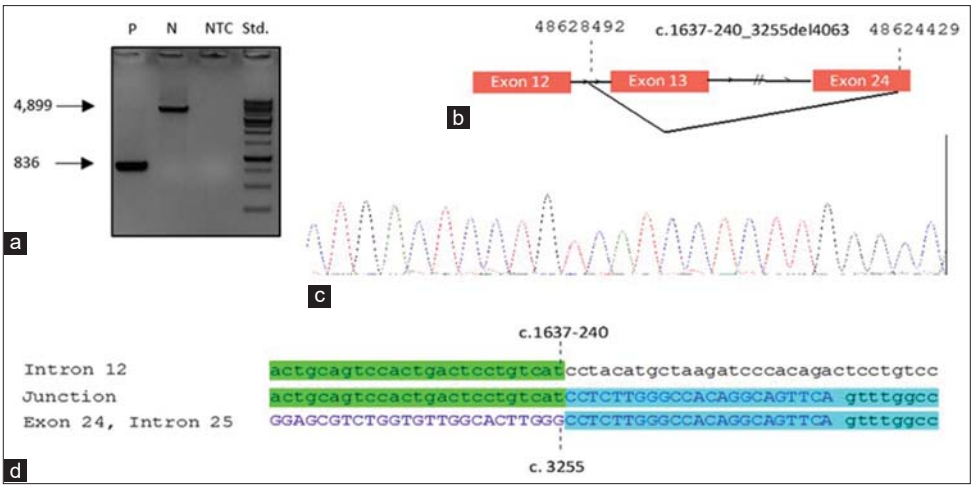

Figure 4: (a) Long PCR analysis of genomic DNA indicating 4063 bp deletions of the COL7A1 gene in the patient. Lane 1 (Std) is a 1 kb ladder. Lane 2 (NTC) is No Template Control. Lane 3 (Sample N) is amplified from the normal control. Lane 4 (Sample P) points to the abnormal fragments generated by the genomic deletion. (b) Schematic representation of the deletion regions in the COL7A1 gene. (c) The result of DNA sequencing showing heterozygosity in the patient for variant c.1637-240_3255del4063 in the COL7A1 gene. (d) Sequence analysis of junction fragments amplified by PCR revealing deleted sequences within nucleotide (c) at position c.1637-240 in intron 12 and nucleotide (g) at position c. 3255 in exon 24.

VII cause dominant and recessive forms of DEB. Genetic investigations of the COL7A1 gene in several patients demonstrated that recessive DEB (RDEB) leads to highly severe phenotypes due to deletions or small insertions and nonsense mutations creating a premature termination codon [13]. On the other hand, the substitution of amino acids causes a dominantly inherited form of DEB with a milder phenotype [14]. Therefore, the EB type was identified by accurate molecular genetic investigation of the COL7A1 gene. In the present study, WES sequencing of the patient indicated previously detected heterozygous deletion of exons 13–24, coexisting with heterozygous Single-Nucleotide Variants (SNVs) elsewhere in the COL7A1 gene that predicted to be deleterious. We could not confirm compound heterozygosity, as parental DNA was not available, but some studies have suggested an autosomal recessive pattern of inheritance for the c.6205C>T variant [6-8]. In our patient, long-range PCR confirmed the loss of exons 13 to 24 on one allele and a recombination occurring between a short sequence of three nucleotides (CCT) in intron 12 (c.1637-240) and the same sequence at exon 24 (c.3255), resulting in a deletion spanning on 4063 bp (c.1637-240_3255del4063). Descriptions by Vahidnezhad et al. and ours demonstrates that the COL7A1 gene, containing numerous repeated sequences, and the affected regions might be prone to recombination. In addition, the geographic location of the family in our study was in the northwest of Iran that was located in the same location indicated in this study [5].

CONCLUSION

Our study suggests that CNV analysis would be required to reach molecular detection of epidermolysis bullosa. Especially for centers that already employ WES or targeted gene panels, we suggest extending their analysis to include CNV detection.

ACKNOWLEDGMENTS

We would like to thank the patient and her family as well as the clinician whose cooperation made this study possible.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Rapid-onset oral isotretinoin-induced acne fulminans without systemic symptoms in a male adolescent

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ABSTRACT

Isotretinoin-induced acne fulminans without systemic symptoms (IIAF-WOSS) is an uncommon clinical variant of acne, not exhibiting systemic symptoms but with potentially severe skin lesions. Some authors believe that its occurrence is dose-dependent. Herein, we present the case of a sixteen-year-old boy with IIAF-WOSS, which developed two weeks after starting treatment with isotretinoin 0.6 mg/kg/day. The patient was successfully treated with a systemic steroid. IIAF-WOSS may cause significant disfiguring scarring, thus the physician needs to be aware of this condition, even early with low doses of isotretinoin.

Key words: Acne; Acne fulminans; Oral isotretinoin

INTRODUCTION

Acne fulminans (AF) is a rare and severe variant of inflammatory acne characterized by abrupt-onset nodules, painful erosions, and hemorrhagic crusts. Systemic symptoms, including fever, malaise, and arthralgias, may develop in its most severe forms. Isotretinoin-induced AF without systemic symptoms (IIAF-WOSS) is increasing in frequency due to widespread use of the drug.

CASE REPORT

A sixteen-year-old boy, weighing 47 kg, presented with abrupt-onset papulopustular lesions, nodules, and crusts present for one week. The patient was treated elsewhere with oral isotretinoin 30 mg daily for sixteen days. A dermatologic examination revealed thick, yellow, crusty, and hemorrhagic pustules and nodules on the forehead, cheeks, and jawline (Fig. 1). There were no triggering factors and no other systemic symptoms. Laboratory parameters were within normal limits. The patient was evaluated as having IIAF-WOSS and the oral isotretinoin treatment was discontinued. Systemic corticosteroid treatment (oral methylprednisolone at a dose of 0.5 mg/kg/day) was initiated. Due to the persistence of the crusted lesions in week two of the treatment, the dose was increased to 0.8 mg/kg/day. Once the lesions began healing in week two of 0.8 mg/kg/day doses, oral isotretinoin 0.1 mg/day was restarted. After four weeks at the same dose, the oral corticosteroid dose was tapered and isotretinoin was gradually increased to a tolerable level (20 mg/day). The lesions healed almost completely with scarring in the following four weeks (Fig. 2).

DISCUSSION

IIAF-WOSS is a recently described term for sudden worsening of acne in patients with acne vulgaris treated

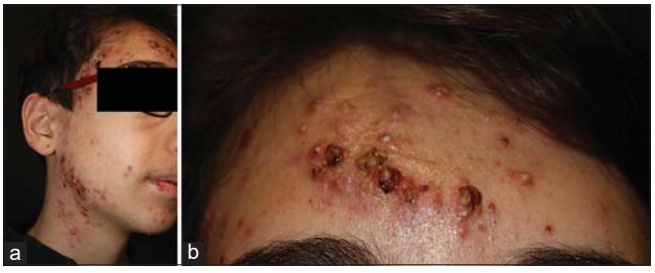

Figure 1: (a) The initial presentation of the patient. (b) A closer view of the lesions.

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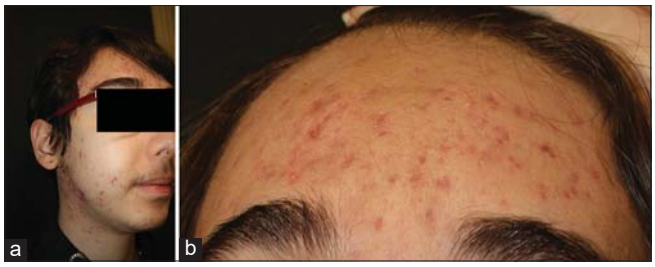

Figure 2: (a) The marked improvement at the end of twelve weeks of treatment (b) Rolling and boxcar scars seen after the resolution of the inflammatory lesions.

with oral isotretinoin. Male adolescents are more likely to be affected.

Our patient, who presented a mild form of IIAF-WOSS, was using a subtotal dose of isotretinoin (0.6 mg/kg/day) before presentation. In fact, the literature offers several reports suggesting an association of AF with a very low dose (0.1 mg/kg/day) of isotretinoin [1]. These lesions have been reported to usually develop between the fourth and eighth week of treatment. In our patient, the occurrence was earlier than expected. This may be due to the fact that the patient was underweight (with a body mass index of 17.2 kg/m^2).

The treatment mainly depends on the severity of the clinical manifestations. Our patient was treated according to the recommendations of an evidence-based expert panel [2]. This study is comprehensive guidance for the management of AF and its variants. Given the sine fulminant clinical presentation of the patient, he was initially treated with a minimally effective dose of 0.5 mg/kg/day. Because there was no clinical improvement during the follow-up period, the dose was increased to 0.8 mg/kg/day. There are several remarkable reports of IIAF with aberrant granulation tissue and subsequent scarring in the literature [3,4]. Despite the absence of systemic symptoms and large and/or widespread necrotic lesions in our patient, corticosteroid therapy for twelve weeks was required. Unfortunately, IIAF-WOSS appears to be increasing in recent years. As some authors suggest, clinicians seem to be more familiar with these indolent forms, leading to more recognition and preventing truly fulminant acne forms [5]. However, there is still a paucity of studies addressing the optimal management of this rare entity.

CONCLUSION

Considering the major psychosocial impacts of adolescence, further studies are required to determine the predisposing factors and the optimal management strategies for this rare condition that leads to undesirable, disfiguring scars.

ACKNOWLEDGMENTS

Written consent was obtained from the patient.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Advanced ulcerative tumefactive lesions of the mucocutaneous surface in previously unrecognized Langerhans Cell Histiocytosis

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ABSTRACT

Langerhans cell histiocytosis (LCH) is an uncommon systemic disease characterized by the infiltration of one organ or more by Langerhans cells. Its clinical presentation is heterogeneous and depends on the affected organs. We report the rare case of a 43-year-old female presenting herself with central diabetes insipidus and receiving nasal desmopressin spray. Later, the patient developed multiple papules and pustules progressing to multiple ulcers affecting the retroauricular and axillary folds, as well as the oral and genital mucosas. The skin lesions had been evolving for several months. A histopathological examination of a skin biopsy confirmed the clinical suspicion of LCH.

Key words: Langerhans cell; Diabetes insipidus; Ulcers

INTRODUCTION

Langerhans cell histiocytosis (LCH) is an uncommon systemic disease characterized by the infiltration of one organ or more by dendritic cells known as Langerhans cells [1]. It has an incidence rate of 3–5 cases per million [2].

Its clinical presentation is heterogeneous and affects preferentially the bone, skin, lymph nodes, and the central nervous system.

We report the case of a female with cutaneous and mucous membrane ulcers found to have systemic Langerhans cell histiocytosis lasting several years.

CASE REPORT

A 43-year-old female presenting herself with central diabetes insipidus had been receiving nasal desmopressin spray. An annually following by cerebral MRI was decided.

Five years after the first diabetes insipidus diagnosis, we received the patient in our department of dermatology. She reported a one-year history of multiple papules and pustules progressing in several days to multiple ulcers affecting the retroauricular and axillary folds, as well as the oral and genital mucosas. She described the ulcers as painful and gradually enlarging and suffered from the symptoms of fatigue, galactorrhea, and amenorrhea.

A clinical examination revealed a large retroauricular fistula complicating mucopurulent ulcers, not well-demarcated, with raised edges, with an erythematous background and a fibrinous base localized in the pinna. The right axillary fold and the oral and genital mucosas were affected by similar ulcers (Fig. 1).

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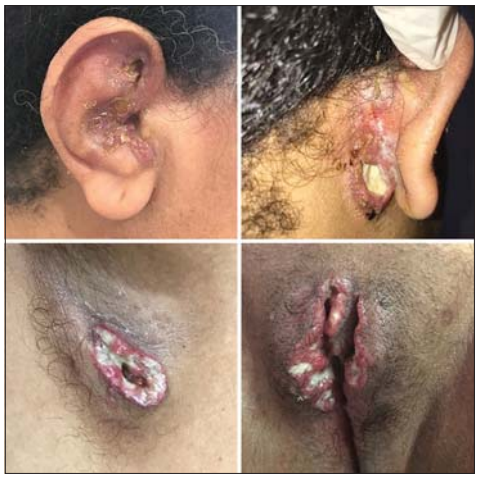

Figure 1: Multiple mucopurulent ulcers affecting the retroauricular folds with a large fistula, the axillary fold, and the genital mucosa.

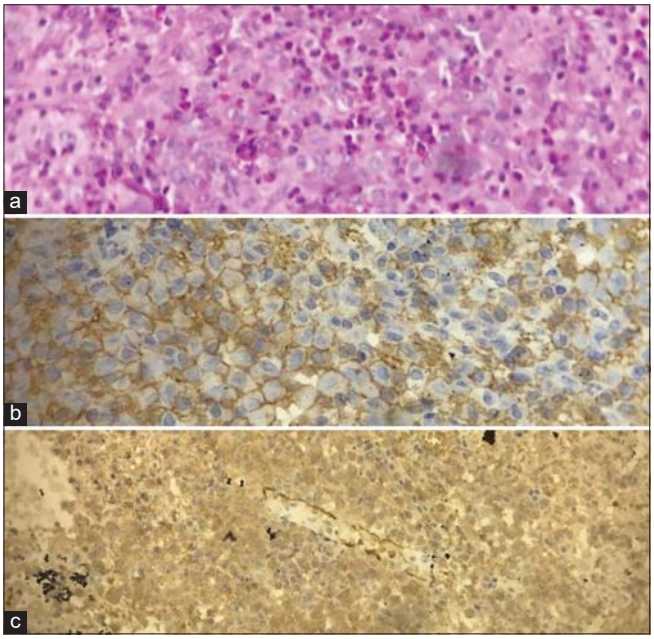

Figure 2: (a) A dense proliferation of histiocytes (H&E, 20×). (b) Immunoreactivity for CD1a (H&E, 20×). (c) Immunoreactivity for PS100 (H&E, 10×).

A histopathological examination of a skin biopsy specimen revealed a dense proliferation of histiocytes immunoreactive to PS100, CD1a, and langerin (Fig. 2).

A blood test confirmed the clinical suspicion of panpituitarism.

Gadolinium-enhanced orbito-cerebral MRI revealed a hypothalamic mass invading the optic chiasma (Fig. 3). Thoracic, abdominal, and pelvic CT revealed mediastinal and pulmonary parenchyma involvement. A skeletal X-ray examination was normal.

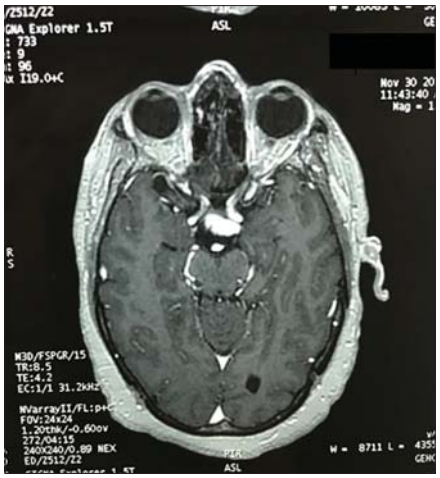

Figure 3: Magnetic resonance imaging images with contrast enhancement: Enhanced lesion invading the optic chiasma.

After the diagnosis of multisystemic LCH was confirmed and the extent of the disease evaluated, the patient received a combination of vinblastine and prednisolone as therapy.

DISCUSSION

LCH is characterized by the proliferation and accumulation of Langerhans cells in tissues, most often organized in granulomas. In 2016, the Histiocyte Society classified Langerhans cell histiocytosis as an inflammatory myeloid neoplasm [3].

Its clinical presentation depends on whether there is single- or multiple-organ involvement, which may lead to death, especially if the bone marrow, liver, spleen, and lungs are affected. Multisystemic disease is most frequently seen in younger children while unique lesions are more common in adults [4,5].

The most typical skin presentation is multiple erythematous, squamous, and crusted papules. Seborrheic or eczematiform lesions may also be part of the clinical syndrome. Cutaneous lesions most often affect the trunk, face, and scalp. External auditory canal and retroauricular fold involvement are suggestive of LCH.

The central nervous system is frequently affected. Posterior pituitary involvement is common and may precede the diagnosis of LCH. The involvement of the anterior pituitary is also possible, sometimes leading to panhypopituitarism [2,6]. MRI may reveal loss of hyperintense signals in the posterior pituitary on T1-

weighted images, as in any central DI signifying loss of ADH storage granules with contrast enhancement, a thickened pituitary stalk or, more rarely, a pituitary tumor that may press on nearby structures [7].

The bone is the most frequent location of LCH. It may be unique or multiple, symptomatic or not, preferably in the axial and cephalic skeleton. Radiology demonstrates multiple, punched out, osteolytic lesions without peripheral condensation [6].

A histological examination revealed infiltration by Langerhans cells that immunoreacted to CD1a and langerin.

The management of LCH has not been consensually defined due to its low incidence. Adults with a diagnosis of LCH must have an assessment of disease extension, which includes a hematologic, pulmonary, renal, hepatic, and skeletal systemic evaluation. Langerhans cell histiocytosis is subdivided into two types of involvement: single-organ with multifocal or unifocal involvement and multiple-organ with or without high-risk organ abnormality.

The treatment of LCH depends on the extent of the disease. Cutaneous LCH is generally treated with local therapies, whereas multisystemic LCH with multiple-organ involvement requires multi-drug therapy using, as in children, vinblastine coupled with prednisolone. The discovery of the role of the BRAF mutation as a key activator of Raf–MEK–ERK signaling in LCH opens the door to new therapeutic perspectives, especially targeted therapies [1].

The accessibility of a skin biopsy performed on the genital ulcer and the right axillary fold gave us a histopathological diagnosis of Langerhans cell histiocytosis. Given the fact that a biopsy was unattainable from the other sites, a specimen study of a shallow skin biopsy was the less invasive way to diagnose this uncommon and intricate disease. Moreover, it allowed us to reveal the etiology of the symptoms that began several years ago with diabetes insipidus before the appearance of the genital ulcers and other skin lesions.

CONCLUSION

The main characteristic observed in our patient was the clinical polymorphism of cutaneous manifestations. The atypical evolution of the papules and pustules into deep and mutilating ulcerous involvement was an uncommon skin presentation.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

An unusual case of nasal chromoblastomycosis degenerating into squamous cell carcinoma from a nonendemic region

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ABSTRACT

Chromoblastomycosis (CBM) is a granulomatous mycosis rarely described outside tropical countries. Degeneration into squamous cell carcinoma (SCC) is its most serious complication. We report the first case of nasal CBM degenerating into SCC. In 2006, a sixty-year-old male presented himself with an infiltrated plaque on the right thigh. The diagnosis of CBM was confirmed by the presence of fungal elements. In 2019, the patient had developed a mass coming from the right nasal cavity. It had rapidly involved the nasal dorsum. An ulcer-budding nasal tumor and an elevated erythematous and verrucous plaque on the thigh were noted. A biopsy revealed a granulomatous dermis with fungal elements. Other nasal biopsy fragments showed differentiated SCC. A fungal culture inoculated with tissue from both lesions showed dark colonies. The diagnosis of nasal CBM with SCC degeneration was reached. The patient presented asymptomatic endonasal CBM that had slowly evolved and recently degenerated.

Key words: Chromoblastomycosis; Nose; Squamous cell carcinoma

INTRODUCTION

Chromoblastomycosis (CBM) is a slowly progressive granulomatous mycosis of the skin and subcutaneous tissue caused by inoculation of dematiaceous fungi mainly on the lower limbs. This infection occurs in tropical and subtropical regions, but there have been several case reports from temperate regions. If not diagnosed and treated at an early stage, it may rarely undergo malignant transformation into squamous cell carcinoma (SCC), which is its most serious complication [1]. Herein, we report an unusual case of CBM from Tunisia, a nonendemic area, occurring in a distant site from the original lesion and degenerating into SCC.

CASE REPORT

In 2006, a sixty-year-old healthy male from north Tunisia presented himself to our dermatology department with an infiltrated 6 × 5 cm erythematous plaque on the right thigh. A histopathological examination revealed the presence of fungal elements. A mycologic examination confirmed the diagnosis of CBM, but the species was not identified. On interrogation, the patient reported no travels to tropical areas, but worked as a masseur in a Turkish bath in conditions of high humidity and heat. The patient also remembered having been injured in this site two years ago at work. The patient was treated with terbinafine at a dose of 500 mg/day. There was a significant decrease in the size of the lesion, but he was lost to follow-up after three months. Several years

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later, he developed a fleshy reddish mass coming from the right nasal cavity with mucopurulent discharge. Over the last three months, it had rapidly extended and involved the nasal dorsum. An examination revealed a bleeding 4 × 3 cm ulcer-budding nasal tumor with an irregular edge surmounted by telangiectasias (Fig. 1). Dermoscopy revealed a vascular pattern with polymorphous vessels. No cervical lymph nodes were palpable. On the right thigh, we found a 12 × 13 cm slightly elevated pruritic erythematous and verrucous plaque with atrophy and depigmentation in most places (Fig. 2). The rest of the examination was normal. There was no evidence of immunodeficiency. Clinically, the differential diagnoses of the tumor form of CBM and SCC were considered. Biopsies were taken from several sites of the nasal lesion and the plaque on the thigh. Histopathology revealed the presence of fungal elements in a granulomatous reaction and mixed inflammatory infiltrate (Figs. 3a and 3b). Other endonasal and nasal dorsum biopsy fragments showed moderately differentiated SCC (Fig. 3c). A direct microscopic examination showed fumagoid cells (Fig. 4a). Fungal cultures of the two samples on Sabouraud dextrose agar showed a growth of pigmented, velvety-dark colonies (Figs. 4b – 4d). A microscopic examination of the colonies revealed cylindrical septate hyphae, and conidiophores swollen at their termination carrying ovoid conidia suggestive of the *Fonsecaea pedrosoi* species (Fig. 4e). From these features, the diagnosis of nasal CBM with SCC degeneration was reached. A neck-chest-abdomen CT scan was normal. We started a combined therapy consisting of terbinafine at 500 mg and itraconazole at 200 mg daily, and referred the patient to the oncosurgery department.

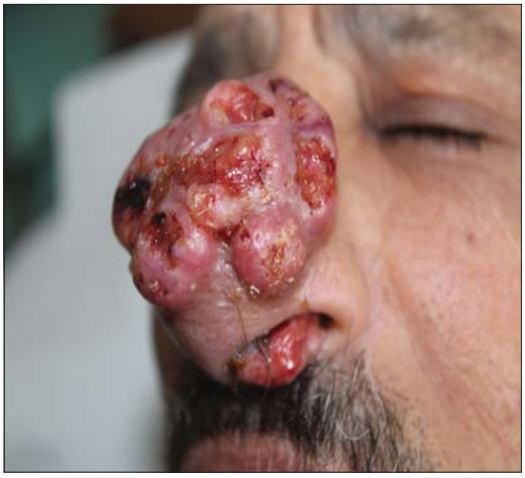

Figure 1: A bleeding ulcer-budding nasal tumor with an irregular edge surmounted by telangiectasias.

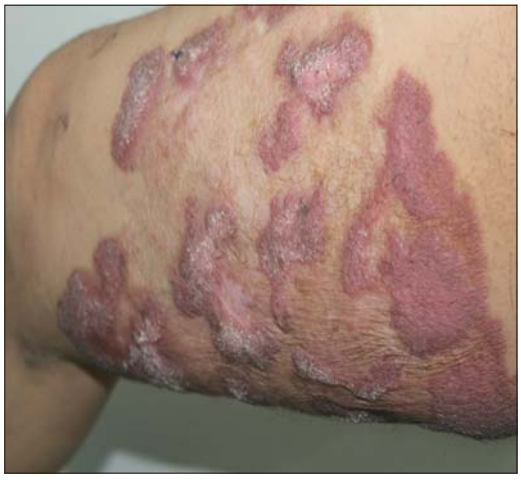

Figure 2: A slightly elevated, 12 × 13 cm, erythematous and verrucous CBM plaque with atrophy and depigmentation on the right thigh.

DISCUSSION

CBM is one of the most prevalent transcutaneous traumatic implantations in individuals living in tropical and subtropical climate areas of America, Asia, and Africa [2]. However, sporadic cases are being increasingly more often described in temperate zones, such as Western Europe and North Africa. In Maghreb countries, and particularly in Tunisia, CBM has been rarely reported: so far five cases have been published [3]. All etiological agents of CBM are black fungi with low pathogenicity thermosensitive at 40–42°C and living as saprophytes in the soil, plants, thorns, debris, and transported wood. They have also been isolated in saunas, where the conditions of high humidity and heat create a tropical microclimate that might explain the development of fungi even in temperate areas [4]. This is probably the case in our patient, who worked as a masseur in a Turkish bath.

The typical lesions usually tend to be found in exposed and nonprotected areas of the body, especially the feet and legs. According to Minotto R et al., 27% of cases involve other areas, including the medial canthus of the eye, the ears, neck, shoulder, chest, wrists, and buttocks [5]. The nasal cavity is rarely affected by CBM and there have been only a few such cases described [6]. Our patient's first lesion occurred unusually in an unexposed location—the inner part of a thigh—which might also be explained by his professional occupation. In general, CBM is a localized infection invading body sites in the immediate area of the original lesions, but usually without metastasis to distant sites. The site of our patient's second lesion might have been explained by autoinoculation due to itching.

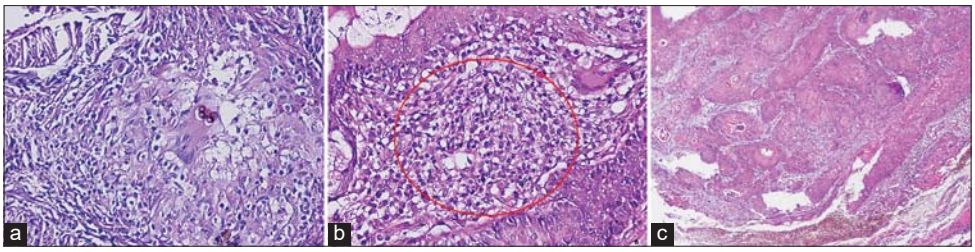

Figure 3: (a) Chromoblastomycosis, with the organisms brown, round, and with a thick wall (PAS, 400×). (b) Granulomatous dermatitis, tuberculoid granuloma (H&E, 200×). (c) Well-differentiated squamous cell carcinoma (H&E, 40×).

Table 1: A summary of reported cases of chromoblastomycosis with malignant transformation

Authors (ref.)	Sex/age	Disease duration	Geography	Affected site(s)	Agent	Type of neoplasia	Evolution
Queiroz-Telles et al. [10]	M/66	36	Brazil	Lower left limb	---	Well-differentiated SCC	Healing after surgical resection
Caplan [9]	M/60	11	Nicaragua	Left leg and thigh	*F. pedrosoi*	Epidermoid anaplastic carcinoma	Healing after surgical resection
Foster & Harris [11]	M/middle -aged	>10	Solomon Islands	Shoulder	Not reported	Well-differentiated SCC	Healing after surgical resection
Foster & Harris [11]	M/66	20	Australia	Left knee	Not reported	Well-differentiated SCC	Death after widespread metastases
Takase et al. [12]	M/62	8	Japan	Lung	*F. pedrosoi*	SCC	Not reported
Paul et al. [13]	M/67	28	Guiana	Left knee	*F. pedrosoi*	SCC	Healing after surgical resection
Jacob et al. [14]	M/47	33	India	Upper limb	-	SCC	Death after surgical resection + radiotherapy
Majeed et al. [15]	M/87	25	Pakistan	Foot	-	SCC	-
Esterre et al. [8]	F/61	6	Madagascar	Left ankle	*C. carrionii*	Moderately differentiated SCC	Healing
Esterre et al. [8]	M/39	5	Madagascar	Leg	*C. carrionii*	Moderately differentiated SCC	Healing
Torres et al. [1]	M/72	31	Mexico	Buttocks, perineum, groin	*F. pedrosoi*	Moderately differentiated epidermoid carcinoma	Death
Jamil et al. [16]	M/69	21	Malaysia	Right hand	*F. pedrosoi*	SCC	Healing after surgical resection
Rojas et al. [17]	M/63	18	Venezuela	V Lower left limb and back	*C. carrionii*	SCC	Death
Azevedo CM [18]	M/55	15	Brazil	Left leg	*Fonsecaea* spp.	Well-differentiated SCC	Healing after surgical resection
Azevedo CM [18]	M/81	20	Brazil	Left leg	*Fonsecaea* spp.	Well-differentiated SCC	Healing after surgical resection
Azevedo CM [18]	M/65	26	Brazil	Right leg	*Fonsecaea* spp.	Poorly differentiated SCC	Death after metastasis to the lower abdomen
Azevedo CM [18]	M/64	20	Brazil	Second finger of the right hand	*Fonsecaea* spp.	Poorly differentiated SCC	Following the CBM
Azevedo CM [18]	M/45	11	Brazil	Left leg	*Fonsecaea* spp.	Poorly differentiated SCC	Healing after surgical resection
Azevedo CM [18]	M/68	10	Brazil	Right arm	*Fonsecaea* spp.	Well-differentiated SCC	Following the CBM
Azevedo CM [18]	M/88	30	Brazil	Right leg	*Fonsecaea* spp.	Poorly differentiated SCC	Healing after surgical resection
Monçale Campos AG [19]	M/79	20	Brazil	Right hand	*Rhinocladiella aquaspersa*	Well-differentiated SCC	Healing
Pires CAA [20]	M/55	5	Brazil	Right leg	Not reported	Differentiated infiltrating SC	Healing after surgical resection

CBM has diverse clinical aspects, including nodular, verrucous, tumoral, plaque-like, and psoriasiform appearances. Cicatricial atrophy with central sparing may also be seen. Because of this clinical polymorphism, CBM may be confused in our country with leishmaniasis, verrucous tuberculosis, and tertiary

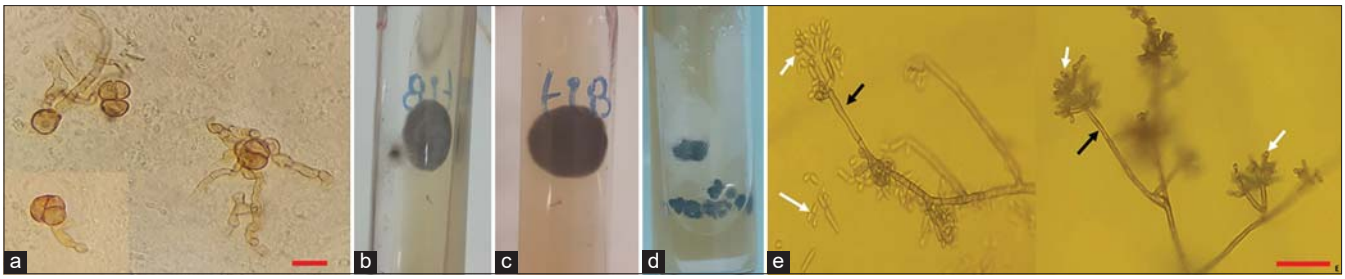

Figure 4: (a) Fumagoid cells on direct examination (scale bar at 10 µm). Colony aspects of a culture (b) of the skin biopsy and (c-d) of the nasal tumor biopsy. (e) Microscopic morphology showing dematiaceous cylindrical septate hyphae and conidiophores (black arrows) making ovoid conidia (white arrows) arranged in short chains, characteristic of *Fonsecaea pedrosoi* (scale bar at 10 µm).

syphilis. A positive diagnosis is usually confirmed by characteristic mycological and histopathological results. When skin biopsies or scrapings are examined under microscopy, pathognomonic muriform cells are seen. These rounded, cigar-colored, and cross-chambered structures are distinctive, and are also known as Medlar bodies, sclerotic bodies, and fumagoid cells [8]. Histologically, CBM typically reveals a dermal granulomatous infiltrate with a predominance of epithelioid cells surrounding fumagoid bodies [7]. A culture allows the isolation and identification of the causal organisms in about fifteen days. Initially, colonies are deep-green, depicting a dark velvet aspect with time. Presumptive species identification may be achieved by mycological morphologic methods, but molecular techniques are suggested for definitive identification.

CBM lesions are usually recalcitrant and extremely difficult to eradicate. If not diagnosed and treated early, CBM has a chronic evolutional course with numerous complications, such as secondary bacterial infection, lymphoedema, and chronic nonhealing ulcers.

The major risk is malignant transformation mainly into SCC [1]. The risk of malignant transformation is around 1%, as illustrated in a Madagascar study in which neoplasia was reported in 14 out of 1400 cases over a period of fifty years [8]. The first reported case of malignant degeneration was described by Caplan in 1968 in a patient from Nicaragua presenting with verrucous plaque lesions on the legs, left thigh, and right hand, which evolved over a period of approx. eleven years [9]. Subsequently, around 23 cases of tumors derived from CBM were documented worldwide (Table 1) [9-20]. The sex ratio was 19/2. The average disease evolution time was 19.7 years. The main affected site was the lower limbs. Cases of CBM-derived SCC were, in the majority, cured after surgical excision.

CONCLUSION

Malignancy must be suspected in the case of any suspicious change, such as the development of ulceration, a rapid growth, or a poor response to treatment. Without a doubt, the conditions of the affected tissue, which involve inflammation and chronic reparatory processes, are significant predisposing factors. Our patient had endonasal CBM that had slowly and asymptomatically evolved and had recently degenerated.

ACKNOWLEDGMENTS

The authors would like to acknowledge the patient.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Triple-negative diffuse large B-cell lymphoma: A distinct entity

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ABSTRACT

The Hans algorithm categorizes the diffuse large B-cell lymphoma (DLBCL) into two major subtypes: the germinal center B-cell-like (GCB) DLBCL and the non-GCB DLBCL. This classification is based on three immunohistochemical markers: CD10, BCL6, and MUM1. The non-GCB subtype is associated with lower overall survival (OS) and progression-free survival (PFS) rates compared to the GCB. DLBCL without positive staining for these three markers (CD10$^-$, BCL6$^-$, MUM1$^-$), also called a triple negative or TN, are classified as the non-GCB subtype. However, they show different clinical characteristics and better prognosis than others assigned to the same cell-of-origin group. Herein, we report a case of a TN non-GCB DLBCL with a complete response after R-CHOP therapy. Together with previous reports of TN non-GCB DLBCLs, our case might depreciate the prognostic value of the Hans algorithm, which was already controversial in the literature, especially in the chemoimmunotherapy era.

Key words: Hans algorithm; Immunohistochemical markers; Diffuse large B-cell lymphoma (DLBCL); Germinal center B-cell-like (GCB) DLBCL; Non-GCB DLBCL; Chemoimmunotherapy

INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most frequently encountered type of non-Hodgkin lymphoma (NHL), representing 30% to 40% of all adult NHLs [1]. It is a heterogeneous disease both clinically and morphologically [2]. In spite of advancements in clinical responses due to the advent of rituximab, the mortality rate is close to 40%. It is, therefore, essential to stratify patients conforming to its prognosis in an appropriate and cost-effective way. For this purpose, numerous immunohistochemical (IHC) algorithms have been proposed. The Hans algorithm is the most widely used in routine practice [3], relying on three markers (CD10, BCL6, and MUM1) to classify DLBCLs according to their prognosis. DLBCLs are categorized into two major subtypes: the germinal center B-cell-like (GCB) DLBCL and the non-GCB DLBCL. The non-GCB subtype is associated with lower overall survival (OS) and progression-free survival (PFS) rates compared to GCB. One category of DLBCL does not stain for the three markers CD10, BCL6, and MUM1, namely, the triple negative or TN (CD10$^-$, BCL6$^-$, MUM1$^-$), which is classified as the non-GCB DLBCL subtype. However, it shows different clinical characteristics and a better prognosis than others assigned to the same cell-of-origin group. Herein, we report a case of a TN non-GCB DLBCL with a complete response after R-CHOP therapy.

CASE REPORT

A 51-year-old male, with no significant past medical history, was referred to our department for the evaluation of a rapidly enlarging ulcerated tumor of the upper back with malaise, fever, night sweats, and weight loss. The lesion was first noticed one year ago. Bleeding after a minor frictional trauma was reported. A physical examination revealed a large polylobed

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ulcerated tumor of the upper back with multiples telangiectasias 15 cm in diameter (Fig. 1). A complete lymph node examination revealed left axillary and right inguinal lymphadenopathy. Palpation of the abdomen for hepatosplenomegaly was negative. An examination of the oral cavity showed no abnormality. Histology revealed a diffuse proliferation of round, large to medium-sized lymphoid cells (Fig. 2). On IHC, the tumor cells expressed CD45 and CD20 (Fig. 3). BCL2, CD10, BCL6, and MUM1 were negative (Figs. 4 and 5). The Ki-67 labeling index was high (60%). The complete blood count and the serum lactate dehydrogenase (LDH) level were normal. An excisional biopsy of an enlarged inguinal lymph node showed a large B-cell lymphoma. A Positron Emission Tomography (PET) scan was performed for staging. It gave evidence of widespread disease involving the liver (segment 1) and multiple lymph nodes (hepatic, pelvic, and deep inguinal). A bone marrow biopsy was negative. The patient was treated with systemic chemotherapy

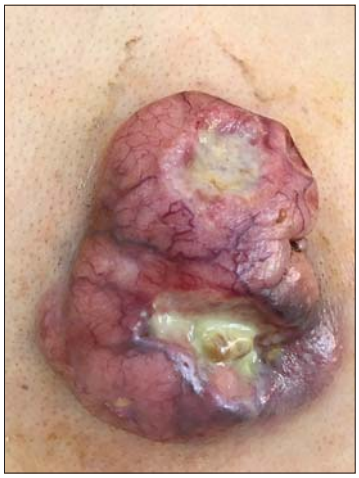

Figure 1: Large polylobed ulcerated tumor of the upper back.

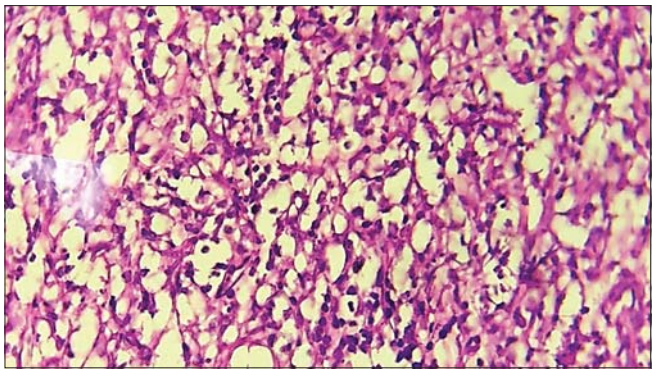

Figure 2: Diffuse proliferation of round, large to medium-sized lymphoid cells (H&E; 20×).

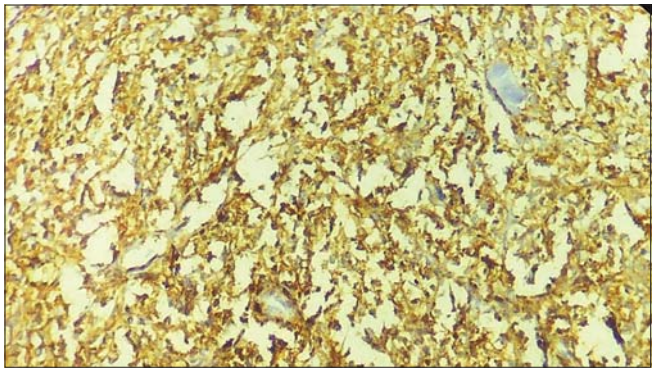

Figure 3: Expression of CD45 on IHC (H&E; 40×).

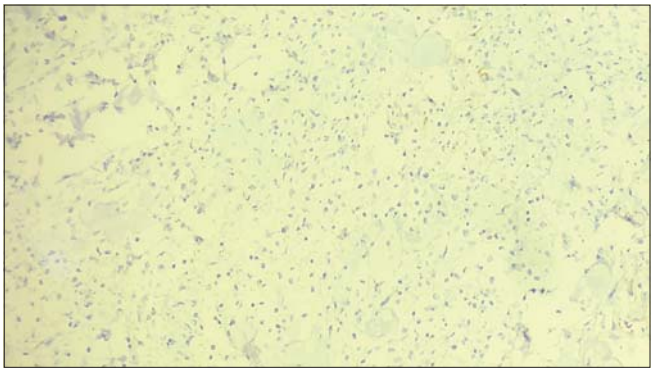

Figure 4: The tumor cells being negative for CD10 (H&E; 40×).

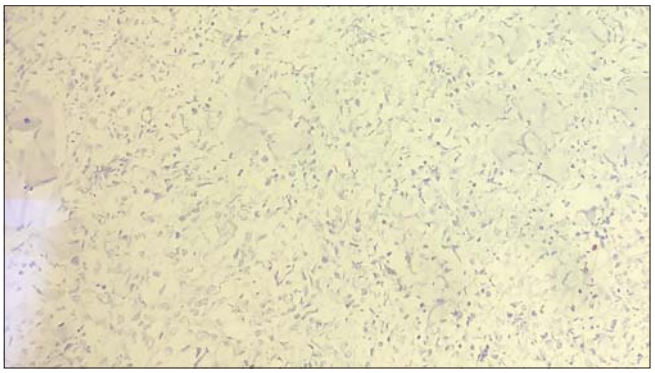

Figure 5: The tumor cells being negative for MUM1 (H&E; 40×).

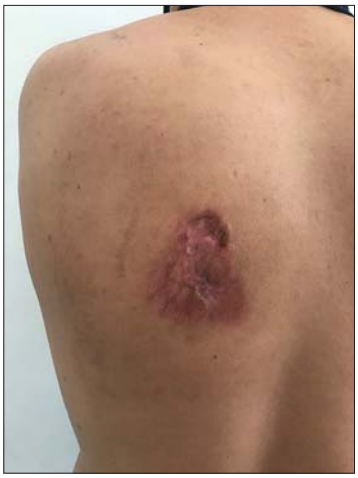

Figure 6: Complete regression of the tumor of the upper back six months after R-CHOP therapy.

(cyclophosphamide, doxorubicin, vincristine, and prednisone) together with rituximab (R-CHOP). Six months after the treatment, a follow-up examination revealed a complete regression of the tumor of the upper back and lymph nodes (Fig. 6). A PET scan showed complete clearance of all lesions. There was no relapse of the disease after three years of follow-up.

DISCUSSION

We report a case of a TN non-GCB DLBCL ($CD10^-$, $BCL6^-$, $MUM1^-$) with a complete response after chemoimmunotherapy. In the literature, the reported incidence of the TN non-GCB DLBCL is 5.5–19.1% [4,5]. In a study on the Hans algorithm, it was 19.1% [3]. The Hans algorithm is known to be a substantial and reasonable strategy for determining the prognosis in DLBCL patients. It involves IHC staining for CD10, BCL6, and MUM1 to classify cases of DLBCL into the GCB and non-GCB groups [3]. Past studies have reported a significant correlation between the non-GCB subtype and lower OS and PFS compared with the GCB [6]. However, TN DLBCLs, which should be classified as the non-GCB subtype according to the Hans algorithm, were found to have different clinical characteristics and better OS and PFS when compared with other non-GCB DLBCLs. The reason for this observation remains unknown [7]. In a study on the prognostic value of each of the markers, the expression of neither CD10 nor BCL6 was predictive of OS or PFS. However, the expression of MUM1 was a significant predictor of worse OS and PFS [8]. Immunohistochemical negativity for MUM1 in TN DLBCL may explain its relatively good prognosis, as in our patient. The existence of an entity such as ours, together with previous reports, might depreciate the prognostic value of the Hans algorithm, which has already been disputed in the literature, especially in the chemoimmunotherapy era [9-11]. The TN non-GCB DLBCL remains an ill-defined entity and, to our knowledge, there are no studies that have accurately characterized the clinical and biological behavior of this type of lymphoma. In conclusion, given the heterogeneity of DLBCLs, it is important to search for new compelling biomarkers to predict the outcome and to help in the management of the patients.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Successful ablation of giant condyloma acuminata in an adolescent

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ABSTRACT

Condyloma acuminata are usually associated with persistent and recurrent infections and early surgical intervention is often required to prevent recurrences. The Buschke–Löwenstein tumor, a locally invasive, slow-growing, cauliflower-like growth, is an example of a giant condyloma acuminatum. Herein, we report a case of sexually-acquired perianal giant condyloma acuminata in a fourteen-year-old male successfully treated by electrofulguration with radiofrequency cautery under general anesthesia in a single session with no evidence of recurrence over a follow-up period of six months.

Keywords: Giant condyloma acuminatum; sexual abuse; radiofrequency ablation

INTRODUCTION

Sexually transmitted diseases, such as genital warts, genital herpes, syphilis, human immunodeficiency virus (HIV) infection, are a worldwide health concern, with most of the patients 15 to 29 years old [1]. HPV is the most common sexually-transmitted viral pathogen [2], usually occurring in adults, but also in children, often due to sexual abuse. Four morphological variants of condyloma acuminatum are cauliflower-like growths, papular warts, keratotic warts, and flat-topped papules [3]. The Buschke–Löwenstein tumor—a rare STD characterized by verrucous lesions on the genitals and/or the perianal region—most commonly occurs due to HPV types 6 and 11 [4], and most commonly affecting adult males; although some case reports mention adult females and children [5]. Treatment modalities include an excisional biopsy, the application of podophyllin, imiquimod, electrosurgery, interferon or 5-FU injections, and CO_2 laser therapy. However, condyloma acuminata are usually associated with persistent and recurrent infections and early surgical intervention is often required to prevent recurrences. Herein, we report a case of giant condyloma acuminata successfully ablated with radiofrequency cautery under general anesthesia.

CASE REPORT

A fourteen-year-old male presented himself to the department of dermatology with the chief complaint of a massive asymptomatic cauliflower-like growth in the perianal area persistent for the previous four months. No similar lesions were present elsewhere on the body. A clinical examination revealed a hyperkeratotic, verrucous tumor 5 × 4 cm in size in the perianal area (Fig. 1). The genitals were examined and were found to be normal. On further questioning, the patient confessed to a history of a single unprotected peno-anal sexual encounter with an acquaintance one year previously.

Histopathology revealed hyperkeratosis, papillomatosis, acanthosis of the stratified squamous epithelium, and koilocytic changes suggestive of condyloma acuminatum (Figs. 2a and 2b). We planned on electrofulguration

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Submission: 26.11.2020; **Acceptance:** 27.02.2021
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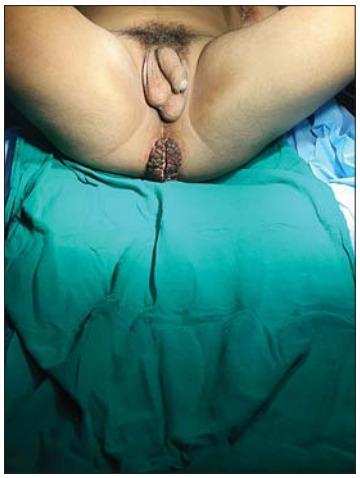

Figure 1: Hyperkeratotic, verrucous growth 5 × 4 cm in size in the perianal area.

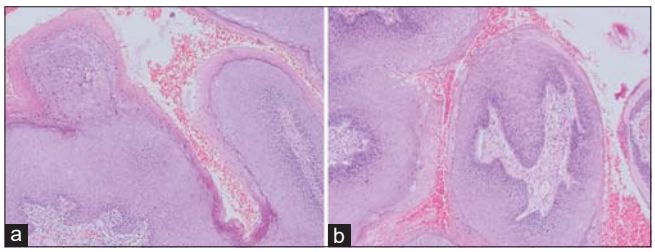

Figure 2: (a-b) Hyperkeratosis, papillomatosis, acanthosis of the stratified squamous epithelium, and koilocytic changes suggestive of condyloma acuminata (H&E, 40×).

with radiofrequency cautery in a major operation theatre under general anesthesia (Fig. 3). A routine pre-anesthetic checkup was performed. The bowel was prepared with an enema. Post-operatively, the patient was managed with a sitz bath, topical and systemic antibiotics, laxatives, and NSAIDs. The perianal wound healed in two weeks without stricture formation or other complications (Fig. 4).

DISCUSSION

Condyloma acuminata are usually seen in younger adults [2]. Nearly half of newly contracted infections are observed in the 15-to-24-year-old age group, the average incubation period ranges from three weeks to eight months, and the physical symptoms appear approx. two to three months after the initial contact [6]. Strong suspicion of sexual abuse arises in children with anogenital warts. It is, however, difficult to determine the method of HPV transmission in the pediatric population [7]. In our case, the adolescent patient was sexually abused for eight months prior to the onset of the lesion. Acrochordon, squamous cell carcinoma, and condyloma latum lie in the differential diagnosis.

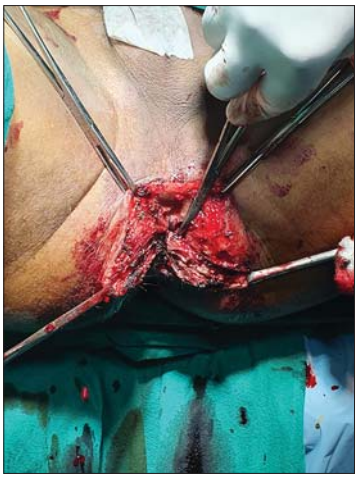

Figure 3: Intraoperative picture of the growth in the perianal area.

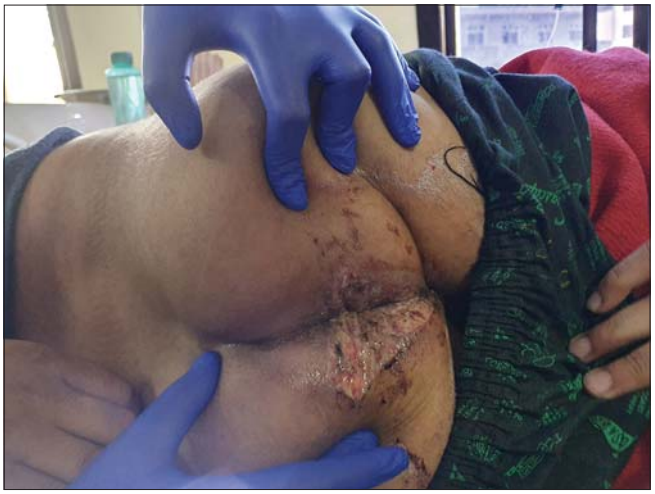

Figure 4: Postoperative picture of the wound without stricture formation or other complications.

Investigations include a PAP smear in females, a colonoscopic examination in both sexes, an HPV DNA test, and an excisional biopsy. Our case was confirmed by histopathology. Treatment includes an excision biopsy, interferon or 5-FU injections, epinephrine gel implants, the local application of podophyllin, imiquimod, curettage, electrosurgery, and CO_2 laser ablation. Giant condyloma acuminata, especially in the perianal area, are difficult to treat due to the possibility of complications such as strictures and a secondary infection and because of a high recurrence rate.

Gürbulak et al. [8] performed a wide surgical excision of a large perianal condyloma acuminatum in a seventeen-year-old female, including the surrounding skin area, and the wound had to be reconstructed with a bilateral gluteal fasciocutaneous V-Y advancement flap.

In 2013, Nambudiri et al. [9] treated a 46-year-old leukemic male with giant perianal condyloma acuminata after two unsuccessful surgical ablations with cryotherapy, a high dose of IL-2, fulguration, and topical cidofovir therapy.

Nonetheless, we were able to successfully ablate the giant perianal condyloma acuminata with radiofrequency cautery under general anesthesia, which was required to relax the anal sphincter and reveal any intra-anal extensions and to remove the entire tumor in one sitting.

CONCLUSION

Giant perianal condyloma in a child mandates thorough sexual history-taking to rule out a sexual history and abuse. As a therapeutic option, surgical ablation of the entire lesion should be attempted in one sitting.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Diode laser in the management of faun tail nevi

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ABSTRACT

Faun tail nevus is a rarely reported congenital cutaneous marker of an underlying spine or spinal cord anomaly characterized by the presence of a hypertrichotic patch affecting the lumbosacral region since birth. In addition to spinal dysraphism, it also affects the psychosocial life of the suffering patient. Herein, we report two cases of faun tail nevus, one with associated diastematomyelia. In both cases, cosmetic improvement was achieved with triple-wavelength diode laser. This article aims to present this sparsely reported clinical entity and describe our experience in its management with diode laser.

Key words: Hypertrichosis; faun tail nevus; diode laser; triple wavelength

INTRODUCTION

Faun tail nevus is a localized patch of hypertrichosis affecting the lumbosacral region. It may be associated with an underlying spinal cord anomaly. We report two cases of faun tail nevus, one with underlying diastematomyelia and a cosmetic disability. Both experienced cosmetic improvement with a triple-wavelength diode laser.

CASE REPORT

A 17-year-old female presented with excessive hair growth on the lumbosacral area since birth. She was born to a nonconsanguineous marriage, had an older sibling with no similar complaints, and had a normal vaginal delivery.

On local examination, a 12 × 25 cm area of localized hypertrichosis with coarse dark terminal hair of varying lengths was present overlying the T10 to T12 vertebrae (Fig. 1). The underlying skin was normal. There were no other visible gross spinal defects. On further examination, she showed restricted forward bending with a normal gait and had achieved normal developmental milestones.

An MRI scan of the dorsolumbar spine revealed mild scoliosis with a convexity to the right, diastematomyelia at D11 to L2 level with a bony spur in the canal at the D12 to L1 level, and a conus at the L5 level, while the cervical spine and the CV junction were normal (Figs. 2 and 3).

A neurologist opinion was taken in view of the above, and the patient was advised conservative therapy as she had almost completed the growth curve and was asymptomatic.

The second patient presented to our OPD with similar complaints present since birth. No similar complaints were present in family members. On examination, a 15 × 30 cm area of localized hypertrichosis was observed overlying the T9 to T12 vertebrae (Fig. 4). There were no visible gross defects, and an MRI scan was normal.

Because both patients were psychologically affected by their cosmetic disfigurements, laser hair removal

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DOI: 10.7241/ourd.20214.19

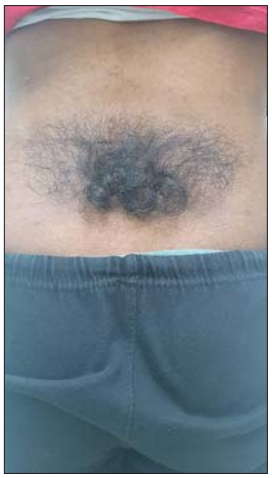

Figure 1: Clinical picture of faun tail nevus in the first patient.

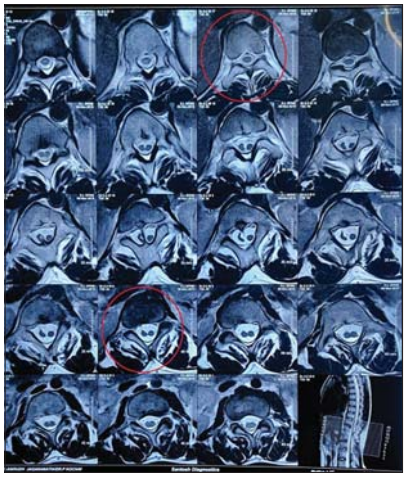

Figure 2: MRI scan showing a single and split spinal cord.

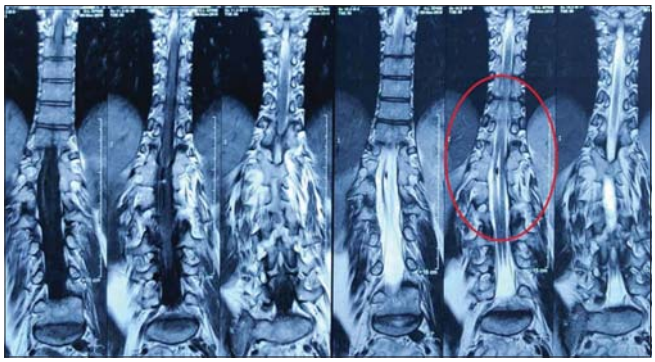

Figure 3: MRI scan showing diastematomyelia.

using a triple-wavelength diode laser was advised. Before initiating the treatment, the area was shaved and cleaned, and during the course of four treatments, the patients had not been using any other method of hair removal and followed the pre- and post-treatment instructions. The treatments were given monthly once. On the initial sitting, a total energy of 6 KJ, an energy density of 7–8 J/cm^2, and a frequency of 8 Hz were used. On each sitting, the total energy was increased by 0.5 KJ. After four sittings, both patients had minor regrowth of thin and light hair. The patients are still under therapy.

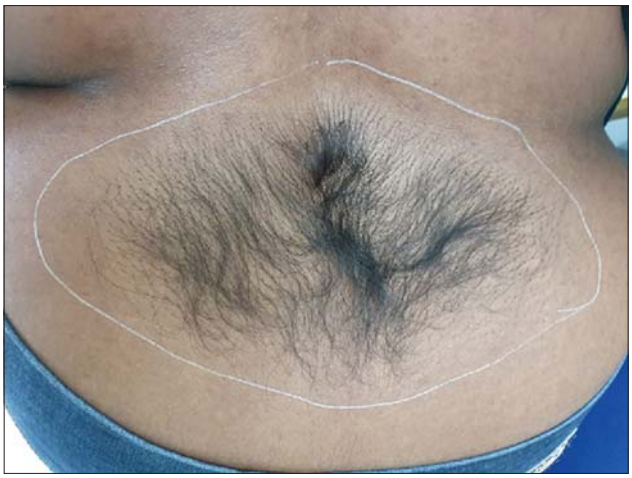

Figure 4: Clinical picture of a faun tail nevus in the second patient.

DISCUSSION

Lumbar hypertrichosis may present itself in three forms: (a) simple nevoid hypertrichosis (abnormal hair away from the spine), (b) silky down (soft nonterminal hair at the midline), and (c) faun tail (a wide patch of coarse terminal hair several inches long at the midline) [1].

A faun tail is abnormal lumbosacral hypertrichosis characterized by a patch of coarse terminal hair usually several inches long. The word *faun* refers to the Italian deity in human form with horns, pointed ears, and a goat's legs and tail [1]. Failure of the caudal neuropore to close at the end of the fourth week of intrauterine life results in neural tube defects such as spinal dysraphism, which may also involve tissues overlying the spinal cord [2,3].

Faun tail nevus is associated with spinal defects, most commonly spina bifida, intraspinal lipoma, dermal sinus, lipomeningomyeloceles, diastematomyelia, a tethered cord [4]. In our case, MRI revealed diastematomyelia, which is characterized by longitudinal splitting of the spinal cord into two parts. An osseous, cartilaginous, or fibrous septum in the central portion of the spinal canal produces a complete or incomplete sagittal division of the spinal cord into two hemicords. In occult cases of dysraphism, treatment is rarely required for a tethered cord or spinal instability, except for the cosmetic disfigurement [5].

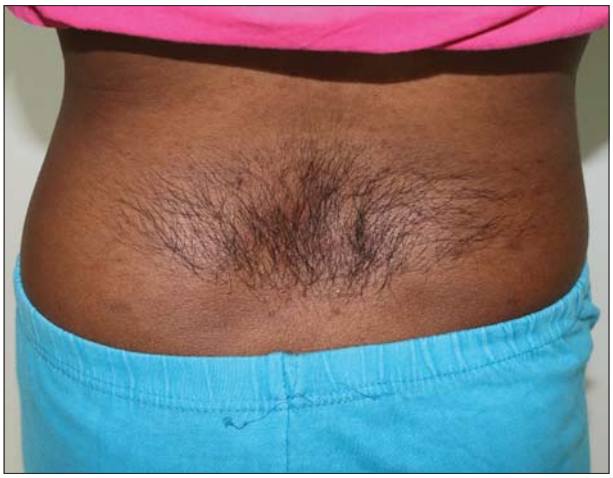

Figure 5: Effects after 4 sittings of diode laser in the first patient.

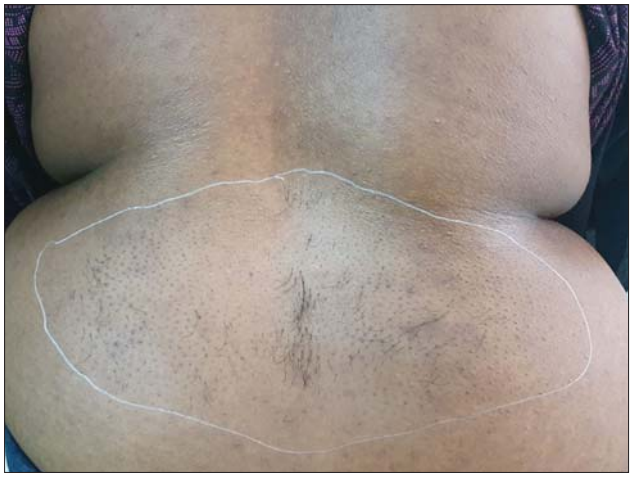

Figure 6: Effects after four sittings of diode laser in the second patient.

To achieve a better cosmetic appearance, various types of lasers have been found useful, for instance, the alexandrite laser, the ruby laser, the diode laser, the Nd:YAG laser [4], and intense pulsed light (IPL) [6]. The principle underlying these therapies is the selective absorption of laser energy by the melanin pigment in the hair follicle, which leads to its thermal destruction. Additionally, there is minimal absorption of energy by the surrounding tissues and, thus, skin damage does not happen [4]. Phototypes I–III require a broader choice of densities with a shorter length of the pulse, while the darker skin types (phototypes IV–VI) need lower densities and a longer duration of the laser pulse [7]. After the procedure, redness, burns, and pigmented lesions may be observed [8]. Both our patients had redness following each sitting and experienced a good cosmetic improvement after four sittings of triple-wavelength diode laser therapy (Figs. 5 and 6).

CONCLUSION

This article aimed to present the rare cases of a faun tail nevus and our experience in improving their cosmetic aspect with a triple-wavelength diode laser.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Two shades of malignancy in a psoriatic patient

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ABSTRACT

Psoriasis is a chronic inflammation of the skin, affecting approx. 120 million people worldwide. The risk of developing skin cancer in psoriatic patients has been stressed, although with a significant amount of conflicting data in the literature. The most consistent findings suggest that psoriatic patients are at an increased risk of non-melanoma skin cancer. An increased risk of melanoma has not been well established. Herein, we report the case of a patient with a history of pustular psoriasis present since the age of ten, who developed an SCC and a melanoma, and discuss the etiopathology of this association.

Key words: Psoriasis; Melanoma; Squamous Cell carcinoma; Inflammation

INTRODUCTION

Psoriasis is a chronic inflammation of the skin, affecting approx. 120 million people worldwide. The association between psoriasis and a substantial increase in the risk of systemic and skin cancers has been debated increasingly often. The association between squamous cell carcinoma (SCC) and psoriasis is well established. Several cases of melanoma in psoriatic patients, however, have been reported in the literature. Herein, we report the case of a psoriatic patient who developed an SCC and a melanoma in the same area.

CASE REPORT

A fifty-year-old male with skin phototype IV was admitted to our department in December 2016 with a bleeding tumor on the right leg. The patient had a history of pustular psoriasis present since the age of ten. There was neither a history of intensive sun exposure nor a family history of skin cancers. The patient was treated for many years with acitretin and topical steroids. In 2010, the patient had extensive exacerbations requiring several hospitalizations. Acitretin was temporarily replaced with MTX, which was discontinued after two weeks due to anemia and digestive intolerance. Since then, the patient experienced severe involvement on the feet, legs, and arms. An examination revealed multiple erythematous plaques covered by yellowish scales on the upper and lower limbs. A bleeding and ulcerating plaque with everted edges and 6 × 5 cm in size was present on the anterior surface of the right leg (Fig. 1). The patient also had two irregular pigmented plaques on the inner side of the same leg 2 x 1.5 cm and 2 x 3 cm in size (Fig. 1). Skin biopsies of the lesions were performed, concluding to an invasive SCC (Fig. 2) and a superficial spreading melanoma corresponding to the pigmented plaques with a Breslow thickness of 1 mm and a mitotic rate of 1/mm^2) (Fig. 3 and 4). A cervico-thoraco-abdominal CT scan revealed bilateral inguinal lymphadenopathy. The patient was referred to the surgical oncology department. Amputation of the leg was indicated, given the difficult healing of the pathological skin, but the patient refused to undergo this surgically invasive procedure.

DISCUSSION

Several factors may increase the risk of carcinogenesis in psoriatic patients, including chronic inflammation,

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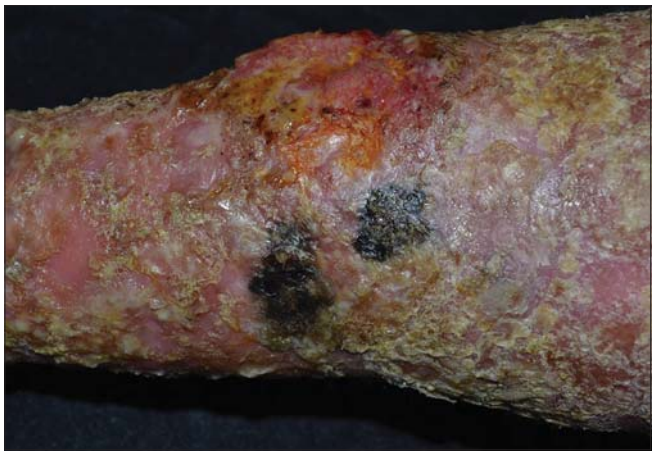

Figure 1: Multiple erythematous plaques covered by yellowish scales: a well-defined ulcerative plaque 6 × 5 cm in size on the anterior surface of the right leg and two pigmented plaques on the inner side of the same leg 2 × 1.5 cm and 2 × 3 cm in size, respectively.

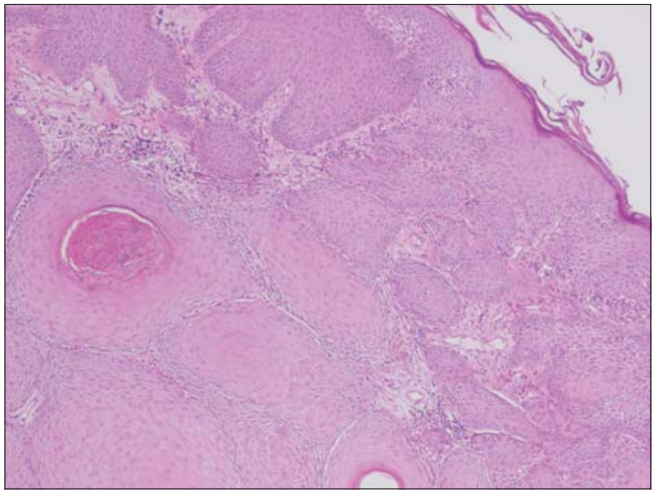

Figure 2: Lobules of malignant squamous epithelial cells arising from the epidermis with a dermal infiltration (H&E; 20×).

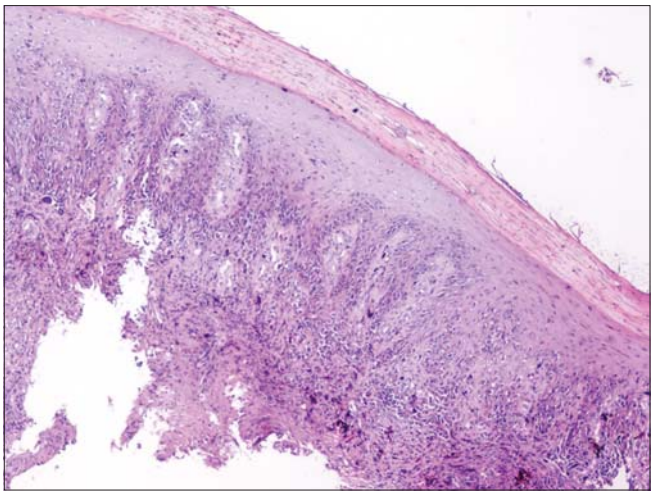

Figure 3: Proliferation of atypical melanocytes in the epidermis and the upper dermis (H&E; 40×).

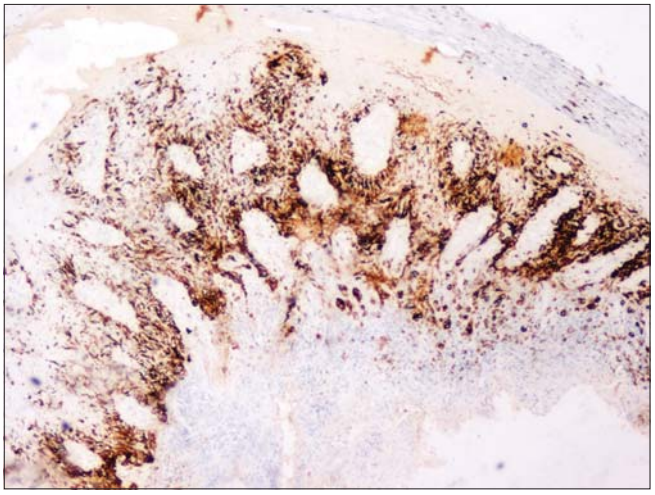

Figure 4: Presence of Melan-A positive dermal cells (immunohistochemical staining; 40×).

immunosuppressive treatments, and UV therapies [1]. Inflammatory mediators may contribute to neoplasia by inducing proneoplastic mutations, resistance to apoptosis, and the stimulation of angiogenesis [2]. SCC has been reported to be associated with phototherapy, cyclosporine, and MTX [3,4]. As an immunosuppressive drug, MTX may inhibit cancer-related immune surveillance. Thus, drug-induced immunosuppression is a risk factor for malignancies, particularly squamous cancers [5]. The association between PUVA therapy and an increased risk of SCC is well established. A systematic review of 46 studies on PUVA therapy concluded that SCC may develop with low-level UVA exposure and the risk increases linearly with the number of treatments [6]. However, the risk of developing a melanoma in psoriatic patients remains unclear, with studies concluding to an increased risk [7,8] and others showing no increased risk when compared with cancer rates in the general population [3,9].

As for our patient, besides the chronic inflammation of psoriasis, there were no other risk factors for skin cancer. However, the patient was treated with acitretin for years, which could have been a protective factor against the development of skin cancer [10,11]. In this sense, chronic inflammation in psoriasis may be a precursor of skin cancer, mainly non-melanoma skin cancers. Numerous transcription factors and cytokines thought to play a role in psoriasis may also promote tumor development. These include interleukin (IL)-6, TNF-α, and signal transducer and activator of transcription (STAT)-3 [12]. Proinflammatory cytokines, such as TNF and IL-1, activate nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), which is an intracellular transducer

of inflammatory signals [13] whose activation may enhance tumor cell proliferation.

CONCLUSION

We reported the particular case of a psoriatic patient who developed two types of skin cancer: SCC and melanoma.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Treatment of venous ulcers in drug addicts: A case report

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ABSTRACT

Venous ulcers are common in drug addicts and, although the management of these wounds is the same as in other patients, there are differences in the approach and the outcome of treatment. Those injecting drugs are at risk of serious infections, such as necrotizing fasciitis, wound botulism, and cutaneous anthrax due to the nature of the substances being injected. Herein, we present two cases of venous ulcers in drug addicts in their thirties. Both patients had been suffering from a venous ulcer for several years and the final result differed in the two patients. We concluded that it is necessary to raise awareness of the importance of treatment and lifestyle changes. The multidisciplinary approach in these patients may contribute to the improvement of wound healing.

Key words: Drug addiction; Venous ulcer; Wound healing

INTRODUCTION

Venous ulcers are common in drug addicts and, although the management of these wounds is the same as in other patients, there are differences in the approach and the outcome of treatment. Patients with a history of intravenous drug use are affected by numerous risk factors for developing chronic venous insufficiency due to damage to superficial veins through repeated trauma and thrombophlebitis.

The reason for the appearance of venous ulcers in these individuals is of course the injection of narcotics in the femoral vein, which leads to deep vein thrombosis. Repeated injections and additional damage to the venous wall cause poor blood flow, which, in combination with inactivity, emphasizes preexisting venous insufficiencies.

The preference for injection into the femoral vein is usually due to its size and easy availability. Over time, the vein becomes scarred and thickens, making it difficult to puncture, thus the addict is forced to employ thicker needles, which further damages the vein wall [1].

Through reinjection, the lumen of the femoral vein narrows, creating pressure in the back and venous hypertension in the lower legs, causing swelling of the collateral veins and dilation [2]. Leg ulceration is the end-stage venous disease [3]. A frequently traumatized vein that is no longer functional is an excellent basis for opening the skin barrier and creating an ulceration.

People injecting drugs are at risk of serious infections, such as necrotizing fasciitis, wound botulism, and cutaneous anthrax due to the nature of the substances being injected [4]. Illegal narcotics are often diluted with other toxic substances, whose acidity contributes to accelerated sclerosis of the veins and faster damage to and opening of the ulcers [5]. The most commonly used drug is heroin.

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CASE REPORTS

Case 1

A 34-year-old male and heroin addict had suffered from venous ulcers persisting for about three years with occasional and partial closures. The patient repeatedly refused to be hospitalized and made the bandages on the wound by himself. During an examination, it was revealed that, during the last several days, he noticed an increase in the size of the wounds and an unpleasant odor.

The ulcerations were on the medial side of the left lower leg on erythematous bases, 6 cm in length in the bigger and 2.5 cm in the smaller (Fig. 1), with a bottom with fibrin patches and pus and with serrated edges. The patient reported continuous intravenous injection of heroin until one year ago, when he began a rehab program and methadone therapy.

After three years of outpatient treatment, the patient finally agreed to be hospitalized. During the hospitalization, intravenous antibiotic therapy, daily dressing, and compression therapy were performed. Blood counts, differential blood counts, and extended laboratory tests were within normal limits.

Doppler ultrasound showed normal arterial circulation, but significant damage to the venous system, reflux of the saphenous–femoral mouth, remnants of the post-thrombotic process, and significantly dilated and branched *v. saphena magna* and *v. saphena parva*, with numerous perforators at the level of the left lower leg.

The patient was discharged one month after admission with a significant improvement in his dermatological status, and complete closure of the ulcer occurring after six weeks. We believe that the improved clinical picture and the closure of the chronic venous ulcer were due to the changed lifestyle, the intermission of heroin injections in the femoral vein, and the constant care of the wound in the hospital.

Case 2

A 35-year-old patient addicted to heroin since the age of seventeen visited the dermatological clinic for numerous venous ulcers in the lower extremities. She had a long history of venous ulcers that had only become worse and asked for help several times but was never hospitalized. The wounds were treated badly, without professional treatment and without daily dressings. The patient had been in a bad condition for a long time, and during an examination, it was revealed that she had been in the third month of pregnancy, her gynecologist advised her to undergo an abortion, but she refused and did not return for a fetal check-up. The baby's father was also addicted to drugs and supported her intention not to stay in the hospital and not to visit doctors often. It was almost impossible to do Doppler ultrasound of the blood vessels of the lower extremities due to the poor dermatological status of the lower legs. Extensive, shallow venous ulcers with livid and infiltrated borders (Fig. 2) were present on both lower legs. Therefore, we suspected papillomatosis cutis carcinoides of the foot (Fig. 3), which required a biopsy, but we again encountered rejection. The patient's ulcers were treated and a bandage was applied. The patient did not come for a follow-up examination and refused hospitalization. The patient has had a miscarriage and still has a problem with the open lower leg ulcers.

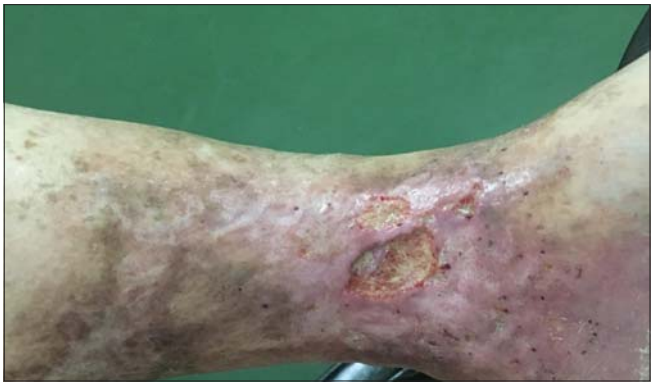

Figure 1: The two ulcers, 6 cm and 2.5 cm in size, with a bottom with fibrin patches on erythematous bases and serrated edges.

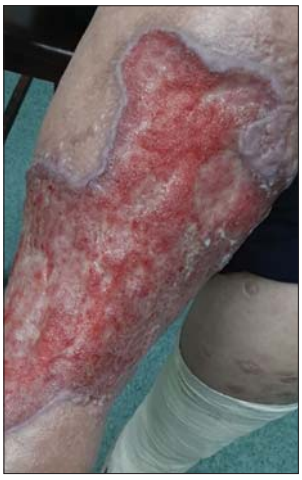

Figure 2: The venous ulcers with livid and infiltrated borders on the right leg.

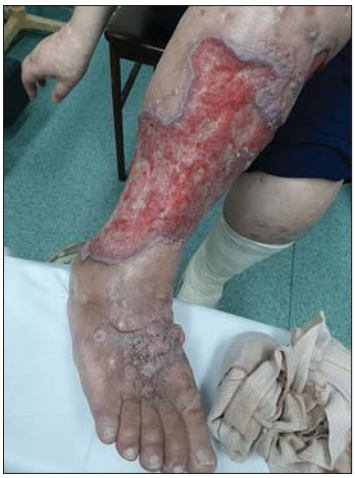

Figure 3: Papillomatosis cutis carcinoides.

DISCUSSION

In the presence of chronic venous ulcers that last for years, the outcome depends on lifestyle changes. A rehabilitation and hospitalization programs and proper wound care give satisfactory results. Unfortunately, in many young addicted patients, indiscipline and prolonged venous trauma from drug injections lead to greater complications and problems.

The most common problems that we face as medical staff in treating venous ulcers in drug addicts are lack of diligence, often insufficient hygiene, non-adherence to prescribed medical treatment, and refusal of hospitalization, which is probably caused by fear of abstinence. Staff should be careful when treating wounds in these patients as most of them are hepatitis C positive and some are HIV positive. Working with this type of patients is more complicated than usual as it requires more attention and patience.

Some studies show that problematic drug users also report feelings of worthlessness and shame, and many of them have co-existing mental health problems [6].

CONCLUSION

It is therefore important to pay attention to informing drug addicts on the consequences of intravenous drug injection and limb care. It is necessary to raise awareness of the importance of treatment and lifestyle changes. The composition and quality of the injected heroin and the duration of the addiction also play a role in the treatment as the degree of sclerosis of the veins depends on these factors. In our case, the patients' mental health and the support and influence of the environment that they have had proved to be crucial. In this context, a multidisciplinary approach in these patients may contribute to the improvement of the venous insufficiency, wound healing, and lifestyle. Quitting drug addiction is a long and arduous process, yet it requires sacrifice, strong will, and work with professionals in the field.

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Our Dermatology Online

Case Report

Dural venous sinus thrombosis: A rare complication of pulse corticosteroid therapy in pemphigus vulgaris

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ABSTRACT

Systemic pulse corticosteroid therapy is used widely in the treatment of pemphigus vulgaris. Dural venous sinus thrombosis as a complication of pulse therapy has not been reported in the literature. A middle-aged female with pemphigus vulgaris was started on monthly pulse dexamethasone therapy with daily azathioprine as an adjuvant. After two pulse therapies, she developed throbbing headache, which on further evaluation was determined to be due to dural venous thrombosis. Other causes of dural venous thrombosis were excluded. Pulse therapy was stopped and other medications were started. The headache subsided within two weeks of stopping pulse therapy. Corticosteroids may play the role of a procoagulant in producing cerebral venous sinus thrombosis. Herein, we report a rare case of dural venous sinus thrombosis due to pulse steroid therapy in pemphigus vulgaris.

Key words: Venous sinus thrombosis; pulse therapy; pemphigus

INTRODUCTION

Pemphigus vulgaris is a rare autoimmune bullous dermatosis that presents with intraepidermal blisters affecting the skin and mucosae. It results from the formation of IgG autoantibodies against the transmembrane desmosomal glycoproteins DSG3 and DSG1, leading to the loss of cell-to-cell adhesion (acantholysis) [1]. Therapeutic options include systemic corticosteroids, immunosuppressives such as azathioprine and cyclophosphamide, and more recently rituximab, which is a chimeric monoclonal antibody to CD20 present on B cells and pre-B cells [2]. Systemic steroids remain the mainstay of treatment. Systemic steroids are administered conventionally in daily doses. Steroids may also be administered as pulse therapy, in which high doses of methylprednisolone or dexamethasone are given intravenously for three days every four weeks. It is proposed that pulse therapy, apart from the induction of a quicker remission, also results in less HPA suppression than conventional daily doses. However, such high doses also involve some inherent risks, including volume overload, electrolyte disturbances, and cardiac rhythm disturbances, mainly bradyarrhythmias. The efficacy of dexamethasone–cyclophosphamide pulse therapy in patients with pemphigus was documented by Pasricha et al. in an Indian setting [3]. Since the advent of steroid pulse therapy, there has been a radical improvement in the survival of these patients [4]. We report a case of dural venous sinus thrombosis in a patient with pemphigus vulgaris on corticosteroid pulse therapy, which, to the best of our knowledge, has not been described in the literature.

CASE REPORT

A 40-year-old female—a resident of New Delhi, India—presented to the outpatient dermatology department complaining of multiple fluid-filled lesions on the chest, back, and upper limbs. A clinical examination revealed multiple flaccid vesicles and bullae ranging in size from 0.5 × 0.5 cm^2 to 2 × 2 cm^2 on the chest, upper back, arms, and forearm. The lesions were filled with clear fluid and lay on non-erythematous bases. The bulla-spread sign and Nikolsky's sign were positive.

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A presumptive diagnosis of pemphigus vulgaris was reached and the patient was investigated. A Tzanck smear from the vesicle revealed acantholytic cells. An H&E-stained skin biopsy revealed a suprabasal split in the epidermis with acantholytic cells in the blister cavity. On direct immunofluorescence, IgG and C3 deposits in a fishnet pattern were observed on cell surfaces. An enzyme-linked immunosorbent assay (ELISA) determined that anti-nuclear antibody (ANA) was negative. Based on the clinical examination and laboratory parameters, the diagnosis of pemphigus vulgaris was thus made.

The patient was started on dexamethasone pulse therapy every four weeks with azathioprine 50 mg twice daily as an adjuvant. Immediately after the second pulse therapy, the patient developed throbbing headache, which did not subside with analgesics. The vitals, including blood pressure, ECG, serum electrolytes, and a thyroid profile were normal. A fundus examination performed to exclude benign intracranial hypertension revealed small hyperemic discs, shallow cup margins with normal vessels. The intraocular tension on tonometry was normal. A neurologist's opinion was taken and MRI angiography of the brain was advised. MRI of the brain showed a lack of normal flow voids in the right transverse and sigmoid venous dural sinuses, which was suggestive of dural venous thrombosis. Magnetic resonance venography (MRV) revealed the attenuation of flow-related enhancement of the right transverse sinus and the most distal part of the superior sagittal sinus with non-visualization of the right sigmoid sinus (Fig. 1).

Investigations were done to evaluate the cause of the thrombosis. The prothrombin time was 13.7 seconds and the INR was at 0.98 (normal range: 2–3). Antiphospholipid screening was negative. An ENT examination and referral revealed no localized infection in the ear or mastoid. Thus, a diagnosis of steroid-induced right transverse and sigmoid sinus thrombosis was made in view of no other known causes and a temporal association with dexamethasone pulse therapy. The patient was started on oral anticoagulants and acetazolamide tablets 250 mg twice a day. Oral corticosteroids and azathioprine were stopped. Pulse therapy was withheld. The headache subsided in the next two weeks. To manage the pemphigus, the patient was started on oral mycophenolate mofetil at a dose of 1 g twice daily with gradual control of disease activity.

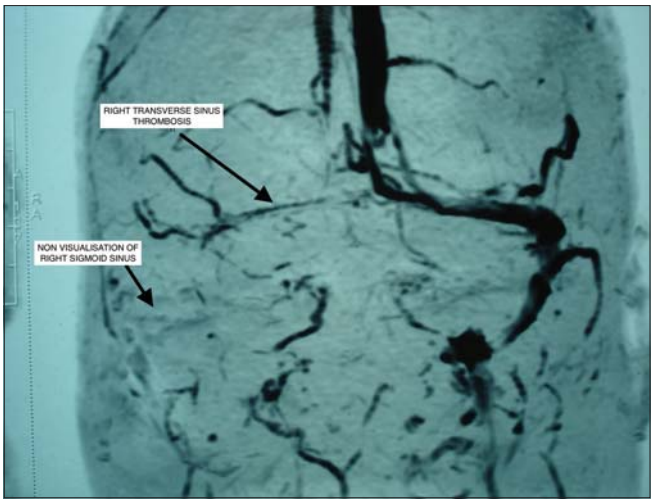

Figure 1: Magnetic resonance venography revealing the attenuation of flow-related enhancement of the right transverse sinus and the most distal part of the superior sagittal sinus with non-visualization of the right sigmoid sinus.

DISCUSSION

Cerebral venous thrombosis is a rare disease that accounts for 0.5% of all strokes [5]. It is characterized by clotting of the blood in the cerebral venous or dural sinuses or even the cortical veins [6]. The etiological factors include infections (mastoiditis, otitis, meningitis) and inflammatory diseases. The other predisposing factors are pregnancy, puerperium, trauma, neoplastic disorders, obesity, thrombophilia, contraceptives, and prior neurosurgery [6].

The role of corticosteroids as a procoagulant causing cerebral venous thrombosis has not been elaborately documented in the literature. Cushing's syndrome is a condition involving elevated levels of glucocorticoids. It is also associated with increased von Willebrand factor, a short APTT, the development of thrombin, and the impairment of fibrinolytic activity. All these factors are associated with a procoagulant state [7]. The presence of hypercoagulability causing femoral head necrosis has been reported, even with physiological doses of steroid therapy [8].

CONCLUSION

The thrombosis in our patient might be attributed to the high dose of corticosteroids in the absence of other risk factors. To our knowledge, there has been no report of cerebral venous thrombosis in a patient with pemphigus vulgaris with the absence of comorbidities and risk factors. However, a case of cerebral venous

thrombosis due to a high pulse dose of intravenous methylprednisolone in a patient with multiple sclerosis has been reported [9].

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Zinc-responsive acral hyperkeratosis as a mimicker of cutaneous tuberculosis

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ABSTRACT

Zinc-responsive acral hyperkeratosis is regarded as a novel entity masquerading numerous skin disorders, such as psoriasis, acral necrolytic erythema, and tuberculosis. Tuberculosis itself is a great imitator and so is its cutaneous form. Herein, we present the case of a female misdiagnosed as a case of tuberculosis verrucosa cutis due to clinical, biochemical, and histopathological features. The patient completed a full course of anti-tubercular therapy without an improvement and showed a dramatic response after a therapeutic trial of oral zinc. Thus, the patient was diagnosed as a case of zinc-responsive acral hyperkeratosis. In any form of acral hyperkeratotic lesions, zinc-responsive acral hyperkeratosis must be considered as a differential diagnosis.

Key words: Acral hyperkeratosis; Cutaneous tuberculosis; Nepal; Tuberculosis verrucosa cutis; Zinc

INTRODUCTION

Zinc-responsive acral hyperkeratosis (ZRAH) is a rare dermatological disorder recently announced as a novel entity, which clinically presents itself as acral hyperkeratosis and shows a dramatic response to zinc [1]. Cutaneous tuberculosis (CTB) is uncommon and varies in its clinical manifestations depending on the host's immune status and is also a great classic imitator. Even with diagnostic advancements, misdiagnosis and undertreatment are likely, and consideration of this particular problem is recommended [2]. Herein, we present a complex case of a novel tuberculosis imitator: ZRAH in an adolescent female with clinical and pathological misdiagnosis of cutaneous tuberculosis of the bilateral foot cured with a dramatical response with a micronutrient for growth and development, elemental oral zinc. To our knowledge, this is the first case report of zinc-responsive acral hyperkeratosis from Nepal.

CASE REPORT

This is a case of an adolescent female with skin lesions in the dorsum of the bilateral feet present for one year. The patient had hyperpigmented and hyperkeratotic skin plaques ranging in size from 5 × 5 cm to 5 × 7 cm in the dorsum of the foot, ankle, and tendinous–calcaneus region up to the distal lower leg (Figs. 1a and 1b). The patient underwent multiple biopsies with multiple treatment modalities in multiple clinical settings before being admitted to our hospital. Our initial differential diagnoses were tuberculosis verrucosa cutis, acral necrolytic erythema, and psoriasis. Biochemical (high ESR and Monteux at 15 cm in 72 hours) and clinical parameters and histopathological findings with a chronic lymphocytic infiltrate, with Langerhans cells and epithelioid cells in the dermis, were supportive of tuberculosis verrucosa cutis (TVC). On serological screening, the patient was negative for HIV, hepatitis B, and hepatitis C and non-reactive for the venereal disease research laboratory (VDRL) test. Because of the high prevalence of tuberculosis in the community and other supportive parameters, a therapeutic trial of anti-tubercular therapy (ATT) was initiated along with keratolytics agents such as salicylic acid and emollients. The patient was put under conventional antitubercular therapy (ATT) for six months, including two months of the intensive phase and a continuation

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phase of four months. Even after the standard antitubercular regimen administered for nearly six months, she had no significant improvements in the lesions, which were present on the legs. As CTB is an imitator of numerous clinical entities, an alternative diagnosis was considered. Regarding the clinical features of the bilateral hyperkeratotic lesions and acral involvement, a presumptive diagnosis of zinc-responsive acral dermatosis was considered and the patient was put under a therapeutic trial of a high dose of zinc sulfate (300 mg/day). To our surprise, she improved dramatically in two weeks of therapy and was almost cured in two months (Figs. 2a and 2b) Thus, a clinicohistopathological mimicker of cutaneous tuberculosis was treated and cured with oral zinc therapy and a retrospective diagnosis of zinc-responsive acral hyperkeratosis was reached. Figure 3 shows the timeline progression of the disease.

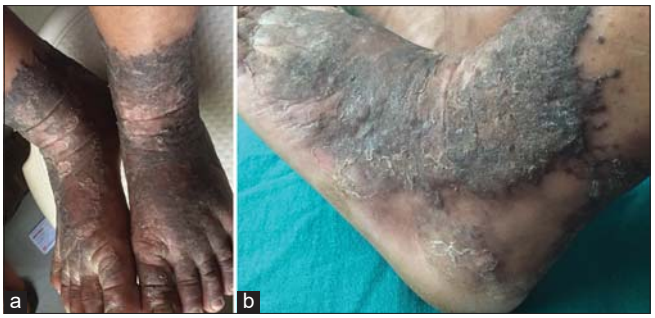

Figure 1: (a) Anterior view of the lesion before the treatment. (b) Lateral view of the lesions before the treatment.

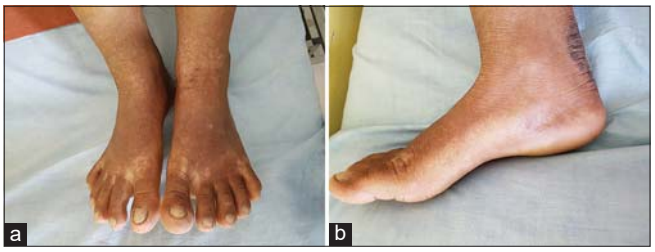

Figure 2: (a) Complete resolution after the zinc therapy. (b) Complete resolution after the zinc therapy.

DISCUSSION

Acral hyperkeratosis may be present in various skin diseases, such as acral necrolytic erythema, psoriasis, lichen simplex chronicus, verrucous tuberculosis, and ZRAH [1]. Acral necrolytic erythema has a clinical presentation similar to ZRAH but the response to zinc is not very dramatic and is usually associated with viral hepatitis C infection. Although the use of zinc in dermatology has been suggested for numerous skin diseases, its role in cutaneous tuberculosis is not discussed in the literature [3]. Clinically and histologically, lichen simplex chronicus and psoriasis vulgaris outweighed the diagnosis in our case. CTB, which is caused by the invasion of the skin by *Mycobacterium tuberculosis* or *Mycobacterium bovis*, or following a BCG vaccination, may be present in various forms. It is a less common form and only accounts for about 1% to 2% of all extrapulmonary cases [4]. Tuberculosis verrucosa cutis, a type of CTB, occurs after direct inoculation into the skin and presents as a brownish-red warty growth most often in the feet, buttocks, and hands. Because it has various clinical and histopathological mimickers, diagnosis and treatment become a challenge, even with diagnostic and therapeutic advancements [2,5]. The patient's clinical presentation of tuberculosis also varies with immune status, with patients with HIV infection possessing even more bizarre presentations [6]. There is suggested evidence of a change in serum zinc levels in tuberculosis but no proven evidence as diagnostic or therapeutic markers [7]. Our patient presented with multiple acral warty lesions over the bilateral dorsal foot with positive Manteaux, a high ESR, and histology suggestive of TVC. However, the poor response to ATT led to us revise our diagnosis and consider a therapeutic trial of high-dose zinc. There was a dramatic response to the zinc therapy with almost complete clearance of the lesions. The additional high dose zinc therapy would not only be supplemental to ATT, as there was no change in ATT for almost six months and a dramatic response was achieved with zinc therapy. There have been reports of acral plaques and significant response to oral zinc dilemmas in nomenclature as novel entities or subsets of well-known dermatoses [1].

CONCLUSION

Clinicohistologically diagnosed cases of verrucous cutaneous tuberculosis, if non-responsive to conventional therapy, require a high suspicion of mimickers as zinc-responsive acral dermatoses may mimic the hyperkeratotic variant of CTB.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images

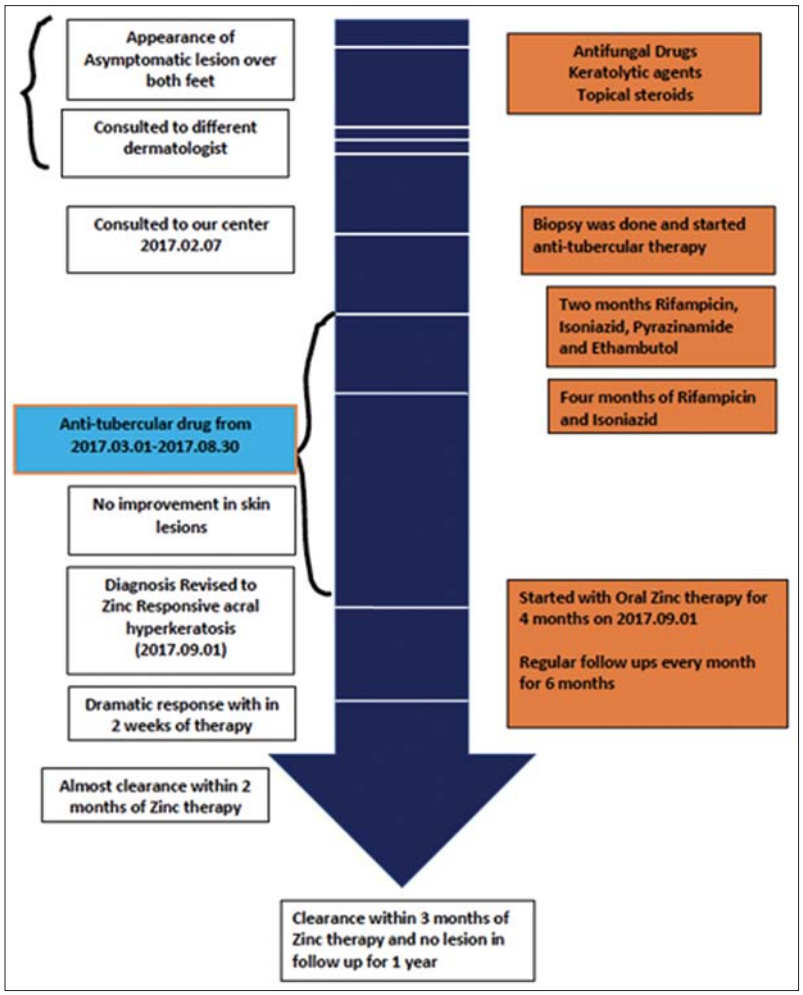

Figure 3: Progression timeline of the disease and its clearance.

and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Case Report

Favre–Racouchot disease: A clinico-dermoscopic profile

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ABSTRACT

Favre–Racouchot disease (FRD) is clinically characterized by the presence of open comedones, small papules, and cystic lesions with deep wrinkles and furrows on sun-exposed areas, especially the face. FRD is a purely cosmetic disorder, with most patients not requesting treatment. Dermoscopy may play a vital role in diagnosing early lesions of FRD, averting the need for an invasive procedure such as a skin biopsy, and helping to differentiate it from close mimics. The dermoscopic features of FRD have not been reported in the literature before. We report a clinicoepidemiological profile and dermoscopic findings in patients presenting with features suggestive of FRD.

Key words: Favre–Racouchot disease; dermoscopy; yellowish background; circular homogenous areas; keratin plugs

INTRODUCTION

Favre–Racouchot disease (FRD), originally described in 1932 by French dermatologist Maurice Favre and reviewed in detail by Favre and Racouchot in 1951, is also known as senile comedones, solar comedones, and nodular elastosis with cysts and comedones [1]. FRD is clinically characterized by the presence of large, open comedones, small papules, and cystic lesions with deep wrinkles and furrows on an underlying area of actinic damage. It usually develops in the periocular region and on the nose. However, the lateral neck, retroauricular areas, earlobes, and forearms may sometimes become involved [2,3]. Diagnosis is mainly clinical since most of the patients are often reluctant to undergo an invasive procedure such as skin biopsy and because of the benign and asymptomatic nature of the disease and, often, the lack of concern at an advanced age. Dermoscopy may improve the accuracy of diagnosis in an older age, helping to distinguish it from close mimics. Herein, we present a clinicoepidemiological profile and dermoscopic findings in a series of five patients with clinical features suggestive of FRD.

CASE SERIES

Five consecutive patients presenting to our outpatient department with features suggestive of FRD were enrolled and subjected to history taking and clinical examination. The criteria for diagnosing FRD included the presence of large, open, black comedones, symmetrically distributed in the temporal and periorbital areas, a diffuse yellowish hue of the skin, and the presence of deep wrinkles and furrows on a background of actinically damaged and atrophic skin. Only three of the five patients were subjected to a dermoscopic examination with a hand-held dermoscope (3Gen DermLite DL4, 10×). No case underwent histopathological confirmation.

As for the clinicodemographic profile of the patients (Table 1), the mean age on diagnosis was 66.4 years. All were chronic cigarette smokers with pack-years ranging from 25 to 30. The only female patient was a chronic hookah smoker. All were farmers by occupation with a history of significant daily sun exposure and had never followed any specific sun protection measures or applied sunscreen.

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Table 1: Patient characteristics of FRD

No.	Age	Sex	Body area	Anatomic sites	Lat.	UV exp.	Smoking	Occupation/hobby	RT
1	62	M	Face	Malar, periocular, temporal, forehead, nasal, chin, earlobe, helix, neck	Bilateral	Yes	Yes	Farmer and bricklayer	No
2	75	F	Face	Malar, periocular, temporal, forehead, nasal, chin, earlobe, helix,	Bilateral	Yes	No	Housewife with outdoor work	No
3	69	M	Face	Malar, periocular, temporal, forehead, nasal, chin, earlobe, helix, neck	Bilateral	Yes	Yes	Farmer	No
4	74	M	Face	Malar, periocular, temporal, forehead, nasal, chin, earlobe, helix, neck,	Bilateral	Yes	Yes	Farmer	No
5	54	M	Face	Malar, periocular, temporal	Bilateral			Laborer and farmer	No

Anat.: Anatomical; Lat.: Laterality; UV exp.: UV exposure; RT: radiotherapy; M: male; F: female

On clinical examination, all cases exhibited a classical triad of multiple, large, open—with few closed—comedones and numerous 0.5–6 mm yellow-to-brown papules and nodules clustered around the temporal and periocular region in a symmetrical fashion, deep wrinkles and furrows involving predominantly the forehead and the zygomatic and malar areas, and a background of actinically damaged and atrophic skin with a diffuse yellowish hue. The surrounding skin had a thickened, soft, and waxy appearance. Similar lesions were observed on the dorsum of the patulous nose in three patients. Accompanying cutis rhomboidalis nuchae was seen in two patients. One patient bore an actinic comedonal plaque, considered a variant of FRS, presenting as a skin-colored, lobular plaque with comedones and yellow cysts localized in the right malar region. Other areas involved were the lateral sides of the neck (two cases), the retroauricular areas (two cases), and the earlobes (three cases). Cases with severe disease had a peculiar facial appearance with coarsening of facial features. Lateral madarosis of both eyebrows was present in three cases (Figs. 1a – 1i).

DERMOSCOPIC FINDINGS

The following dermoscopic findings were noted (Figs. 2a – 2j):

- Numerous circular homogenous areas in shades of light-to-dark brown, sometimes black, depending on the openness of comedones, with remarkable keratin plugs, situated superficially (all cases);
- Multiple, large, black, barrel-shaped rings surrounding hair follicles against a creamy white to yellowish background (open comedones);
- Multiple, small, well-defined, structureless, yellowish-brown homogenous circular areas surrounding keratin plugs (closed comedones);
- Intervening, apparently normal skin showing an atypically yellowish hue, corresponding to solar elastosis of the skin, linear arborizing vessels, numerous small comedones, and pigmentary changes, together representing chronic actinic damage of the skin, seen mainly on the forehead, cheeks, and nose, and in the periorbital areas;
- Linear arborizing vessels corresponding to telangiectasias (three cases);
- Enlarged facial skin pores and embedded blackheads correlating with well-defined dilated pilosebaceous openings visible on dermoscopy (five cases).

DISCUSSION

Six percent of the population in the 54-to-76-year-old age group are said to be affected by FRD. [2,3]. The mean age of 66.4 years, the age of onset, the male predominance, and the typical clinical presentation observed bore resemblance to other studies. The exact pathogenesis of FRS remains unexplained. A number of risk factors, such as chronic UV exposure, cigarette smoking, and therapeutic radiation, have been suggested to play a role [4]. All our patients proved to be heavy smokers of 25–30 pack-years with significant UV exposure. This was mainly linked with occupational exposure as nearly all were farmers by occupation and had other sorts of outdoor jobs as laborers. Clinical evidence of actinic epidermal damage or solar elastosis was present in all cases.

Although a biopsy-proven diagnosis for a majority of cases of FRD has been described in the literature [3,4], histopathology was not performed in our study as most of the patients came to us with other cutaneous complaints and it was a coincidental diagnosis, with the patients showing no concern for it.

The associated cutaneous disorders in our patients were basal cell carcinoma in one, eyelid papilloma in one, and actinic keratosis in two. Cutaneous myxoma, actinic keratosis, basal and squamous cell carcinoma, trichostasis spinulosa, keratoacanthoma, and eyelid papilloma have been reported in patients with FRD [5].

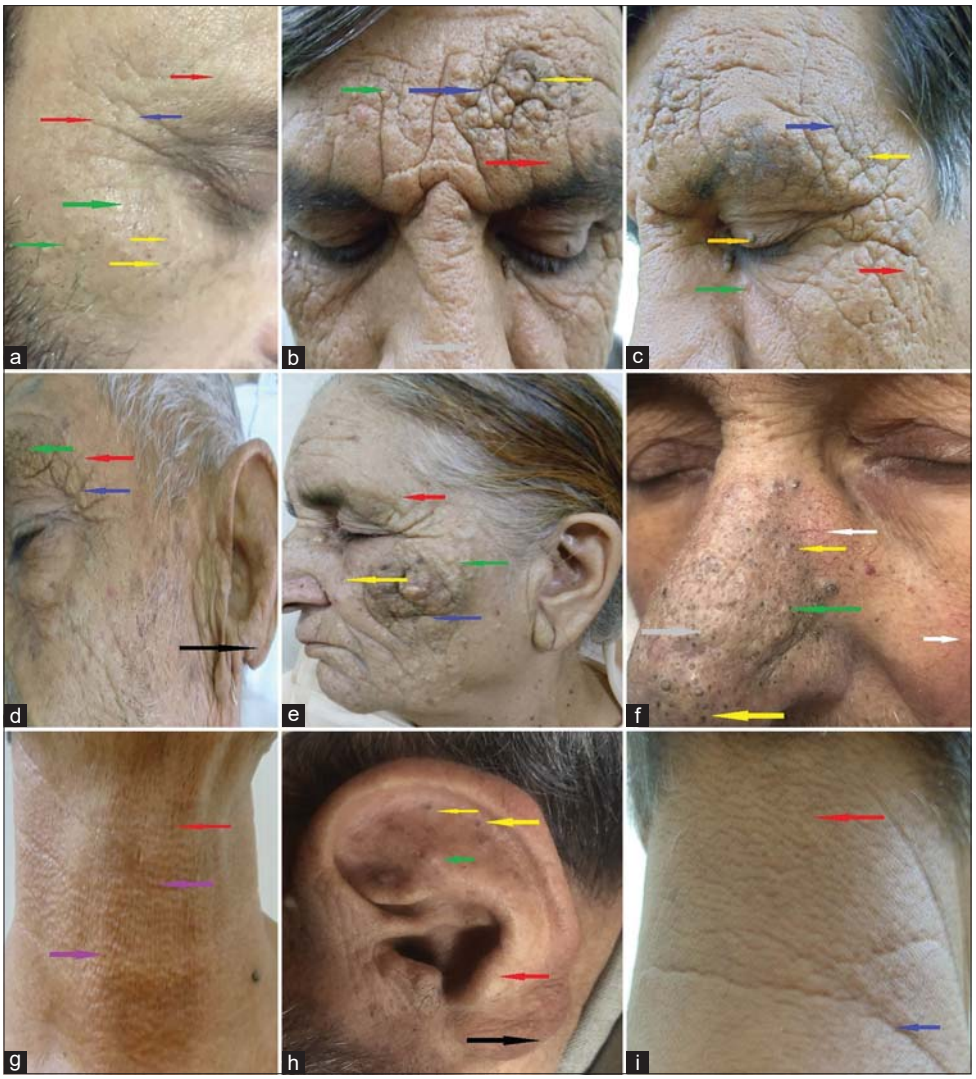

Figure 1 (a-i): Clinical spectrum of FRD showing periorbital wrinkles with cysts and comedones (yellow arrows) distributed symmetrically and preferentially in the malar and periocular areas. Deeply wrinkled, furrowed (blue arrows), and atrophic facial skin with multiple comedones, papules, and nodules on the nose, cheeks, and forehead. An inflamed plaque with comedones in the right malar region (green and yellow arrows). (c) Eyelid papillomas (orange arrow). (d) Thick and coarse skin on the earlobes (black arrows). (e) An actinic plaque with comedones and yellow cysts in the right malar region. (f) A yellowish hue with skin-colored papules on the face and neck (red arrows). (g) Skin-colored papules and telangiectasias on the ear (white arrows). (g) Skin-colored papules distributed in a linear reticular pattern on the neck (purple arrows). (h) Deep furrows and elastotic changes on the back of the neck (blue arrows).

The dermoscopic features of FRD have not been reported in the literature before. Only one report, describing the dermoscopic finding of an inflammatory lobular plaque on the cheek in a case of FRD, has been published [6].

FRD needs to be differentiated from acne comedones, milia, colloid milium, syringomas, trichoepitheliomas, and sebaceous hyperplasia. Comedones are very similar to those of acne vulgaris but without perilesional inflammation or associated inflammatory lesions. A central white structure and a surrounding brown ring are the typical findings in milia; a whitish structure surrounded by an erythematous halo is seen in trichoepithelioma; glittering yellowish white globules are a feature of syringoma; and multiple dull, yellowish-white globules with surrounding vessels are seen in sebaceous hyperplasia. Sebaceous nevi show bright, yellow dots not associated with hair follicles [7,8].

No standard treatment protocols have been devised so far. Preventive measures include the avoidance of sun exposure, the use of broad-spectrum sunscreen, and the discontinuation of smoking. Topical retinoids, alone or as part of combined strategies, have been described as the mainstay of treatment. The use of superpulsed CO_2

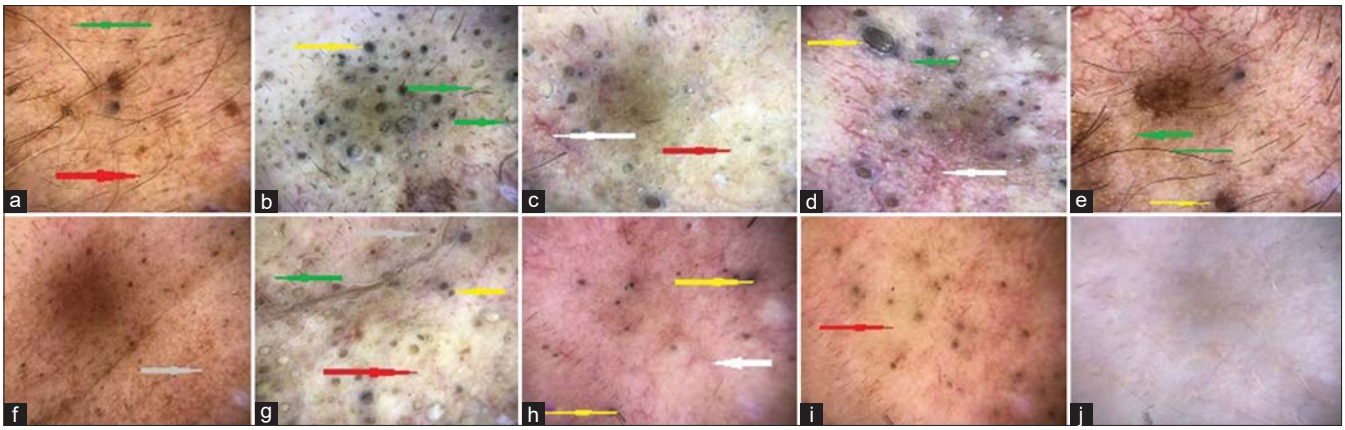

Figure 2 (a-j): Dermoscopic findings varying with the type of lesion in FRD. Polarized dermoscopy showing the presence of multiple, well-defined, structureless, homogenous superficially placed circular areas, light-to-dark brown, sometimes black, surrounding keratin plugs.Open comedones typically showing a hair follicle surrounded by a central black ring that is small, yellowish, and surrounds white/closed comedones (yellow arrows). Circular, homogenous areas, light-to-dark brown, sometimes black, with remarkable keratin plugs, situated superficially (yellow arrows). Multiple, large, black, barrel-shaped rings surrounding a hair follicle representing open comedones (yellow arrows). Multiple, small, well-defined, structureless, yellowish-brown homogenous circular areas surrounding keratin plugs representing closed comedones (green arrows). A yellowish hue (red arrows) corresponding to solar elastosis of the skin, linear arborizing vessels (white arrows), numerous small comedones, and pigmentary changes, together representing chronic actinic damage. Linear arborizing vessels corresponding to telangiectasias (white arrows). Enlarged facial skin pores and embedded blackheads correlating with well-defined dilated pilosebaceous openings (grey arrows).

laser followed by the extraction of cystic and comedonal material, dermabrasion, curettage, and chemical peels have been used with mixed cosmetic results [4].

CONCLUSION

FRD is a purely cosmetic disorder, with most patients not asking for treatment. Dermoscopy may play a vital role in:

- An accurate diagnosis if dealing with early lesions specifically;
- Determining whether a biopsy is needed or not in light of clinical observations;
- Averting the need for an invasive procedure such as a skin biopsy and helping to differentiate it from close mimics.

To the best of our knowledge, no Indian literature exists on the dermoscopic appearance of FRD and ours is the first from this part of the globe.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Our Dermatology Online

Review Article

Properties and parameters for effective laser hair removal: A review

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ABSTRACT

Because some people seek consultations for the removal of unwanted body hair, a permanent, safe, and non-invasive method of hair removal is needed. Laser hair removal has been a popular cosmetic procedure. It is a monthly treatment that may take up to ten sessions for permanent results. However, its efficacy varies due to the patient's biological skin hair traits, the adjustment of the optimal parameters of the laser, and the protocols. The purpose of this review is to discuss the properties and parameters employed for laser hair removal. Once parameters for laser hair removal have been optimized, this treatment offers an effective and permanent solution for unwanted body hair.

Key words: Laser hair removal; Fluence; Frequency; Pulse width; Skin type

INTRODUCTION

Unwanted or excess hair is a prevalent condition affecting various aspects of life, including medical, social, and cultural. Because people tend to seek consultations for the removal of unwanted body hair, a permanent, safe, and non-invasive method is needed. Laser hair removal has been a popular cosmetic procedure. It is a monthly treatment that may take up to twelve sessions for permanent results [1]. Results may be understood as the elimination of hair or a decrease in the density of hair follicles or their diameter. Laser hair removal may be employed in preparation for surgery [2], for hirsutism [3], and to treat scars [4], folliculitis, and hypertrichosis. A correct initial diagnosis is necessary for optimal results [5]. These depend upon factors that affect the hair cycle, such as the location of hair growth, the sex, the age, and the season of the year; as well as factors that influence hair growth, such as genetic predisposition, fetal development, medications taken, and other hormonal, nutritional, and psychological factors.

However, the efficacy varies due to the patient's biological skin hair traits, the adjustment of the optimal parameters of the laser, and the protocols.

The purpose of this review is to discuss the properties and parameters employed for laser hair removal.

LASER PROPERTIES AND PARAMETERS

Simply put, a laser is a light-producing device with an active medium—which may be liquid, solid, or gaseous—within a cavity, called the optical cavity, bounded by two mirrors (Fig. 1). When the proportion of the excited atoms is increased, exceeding the medium and raised to a higher energy level, the LASER (light amplification stimulated by emissions of radiation) effect is produced inside the cavity. The light escapes from the cavity through a partial reflection mirror, continuously or in pulses, and has specific properties:

- Coherence (all photons follow the same direction);
- Monochromacy (all photons are emitted with the same wavelength, which makes the laser beam one-color);
- Collimation (the waves have the same direction and the light is parallel, not divergent, narrow, and concentrated);
- Small area of focus: the light may be focused on a very small area, allowing it to reach an extremely high luminous intensity (Fig. 2).

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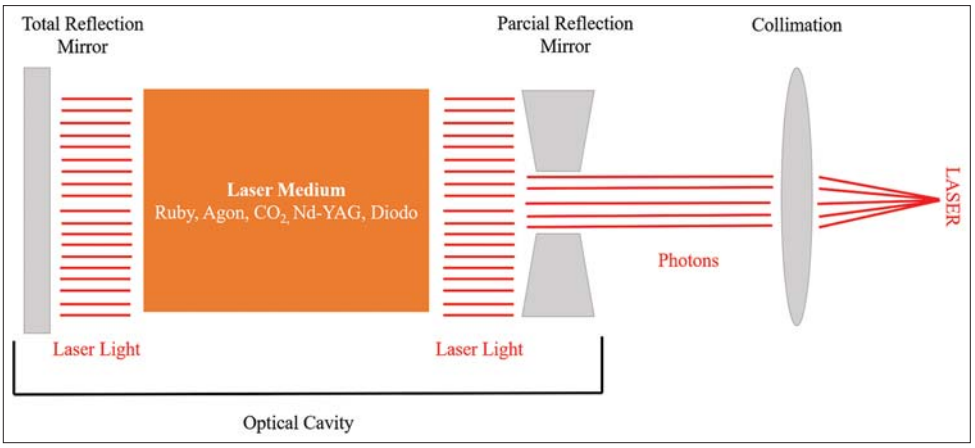

Figure 1: Laser scheme.

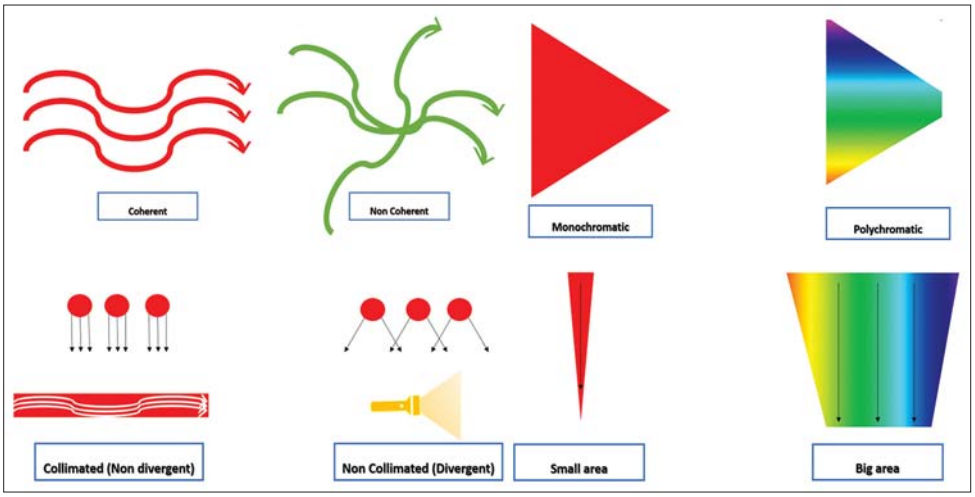

Figure 2: Properties of LASER light.

When laser light falls on the skin it may be reflected, transmitted, dispersed, or absorbed. However, it only produces an effect on tissues if absorbed. Absorption happens because of the presence of chromophores in the skin—elements that selectively absorb specific wavelengths. Energy transmitted into the dermis eliminates chromophores; that is, it fragments the molecules of a chromophore into smaller particles without damage to the surrounding tissue and with minimal epidermal damage.

Laser hair removal is a process that involves complex selective photothermolysis via the epidermis–dermis matrix, aimed to cause hair follicle damage while sparing the epidermis. The thermal action that causes the hair removal effect is caused by heat accumulation in the dermis [1] under strict safety and preservation parameters for the epidermis (Fig. 3). Prolonged exposure to a temperature above 45°C causes the destruction of the hair follicle [2], with the consequent elimination of the hair in that area [3].

Lasers carry various characteristics:

- Wavelength: a band from the electromagnetic spectrum from which a laser emits its light; wavelength is chosen according to the depth to be reached and the chromophore in the target tissue;
- Emission type: the method of energy supplying: continuous or pulsed; continuous emission is a constant energy supply, while pulsed is the application of the energy in intervals and is further divided into:
    - o Semicontinuous: pulsed emission at a frequency equivalent to continuous emission;
    - o Multipulsed: emission of a "train" of pulses (two, three, or more);
    - o Superpulsed: emission that, by means of electronic devices, is able to generate high-power pulses with emission times as small as microseconds;
    - o Q-switched: exceedingly high-power pulses and short emission times, as small as nanoseconds or femtoseconds [6];

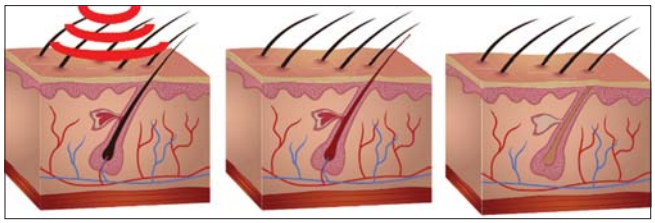

Figure 3: Principle of action of selective photothermolysis.

- Pulse duration: the time that the light takes to emit, measured in picoseconds, nanoseconds, microseconds, or milliseconds:
  - o Thermal Relaxation Time (TRT): the time that the tissue needs to reduce the temperature generated by the emission of the laser light by 50%; the pulse duration must not be below the TRT; this way, less energy dissipation in the underlying structures and no undesirable effects, such as epidermic damage, happen [7]:
    - TRT for the epidermis: 3–10 ms;
    - TRT for the hair follicle: 40–100 ms;
  - o Thermal Damage Time (TDT): the time required to heat the target chromophore;
- Pulse frequency: the number of pulses of laser light emitted per second, measured in hertz (Hz);
- Delay: the time between each pulse; especially important parameter related to the TRT;
- Fluence: the relation between the energy supplied by the light emitter and the surface of the radiation beam—not of the total area of treatment—measured in joules per square centimeter (J/cm^2); this is the energy that heats;
- Irradiance: the relationship between the actual output power of the light emitter and the surface of the radiation beam—not of the total area of treatment—measured in watts per square centimeter (W/cm^2);
- Spot: the size of the irradiation beam at the point of application; although not an adjustable parameter of a laser machine, it is equally as important; the spot is the size of the crystal through which the laser light escapes and large spots sizes are associated with greater power; one must pay attention to note that a spot of 2100 W and 1 cm^2 is different from a spot of 2100 W and 6 cm^2, with small spots more suitable for the face and large spots for the body, as smaller spots lead to greater dispersion and a lower energy density (Fig. 4a), and larger spots lead to less dispersion and a higher energy density (Fig. 4b).

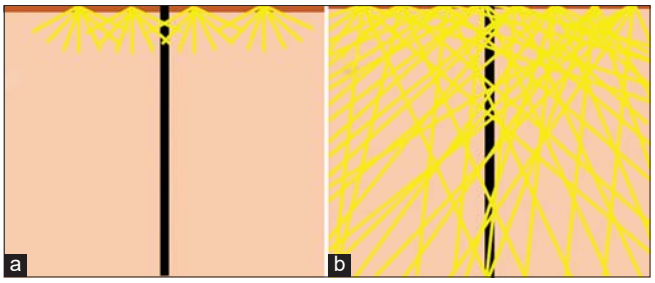

Figure 4: (a and b) Difference between small and large spot sizes.

Effective Hair Removal

Two types of factors are involved in effective hair removal: patient-dependent and laser-dependent [8].

The patient-dependent factors include:

- Amount of melanin in the hair follicle: As melanin is the target of the laser light, the higher its concentration and the closer it is to the capillary matrix, the more effective the treatment will be. For this reason, gray or less pigmented hairs are unaffected by the laser [9].
- Amount of melanin in the skin: Melanin is also found in the epidermis. Epidermal melanin competitively absorbs the same wavelengths as employed for hair removal. In darker-skinned individuals, the greater epidermal melanin content competes with the hair follicle for light absorption, increasing the risk of thermal blisters and hyperpigmentation. It is important to determine the skin's phototype and choose the appropriate laser parameters. The darkest phototypes are those with the highest risk of burn and they require a laser with a longer wavelength and a longer pulse duration.
- Hair thickness: The thicker and more pigmented the hair, the greater the energy absorption and the better results from laser hair removal. Fine hairs absorb less energy and results take longer to appear.
- Depth of the hair follicle: It is important to consider this aspect with lasers reaching certain depths. For more superficial hair, such as facial, lasers of shorter wavelengths are employed; for deeper hair, such as that of the back in most males, longer wavelengths are employed.
- Growth stage: During the anagen phase, the hair is thicker and more pigmented, making it the most appropriate phase to perform laser hair removal.

The laser-dependent factors include:

- Wavelength: The selection of the most appropriate laser wavelength is essential.

  - o Lighter skin types respond well to shorter wavelengths, while darker skin types respond well to longer wavelengths.
  - o The hair follicle may reside between 2 to 7 mm below the surface of the skin, so different wavelengths are required for the best results.
  - o Light-colored and fine hair requires a laser with a high attraction to melanin, while darker and thicker hair will respond well to a laser with a low attraction to melanin [10].
- Pulse duration: An appropriate pulse duration is essential and allows the professional to reach hairs of different diameters. Longer pulses are often needed as it is necessary to heat the hair follicle to the outermost portion and not only to carbonize the hair rod. In the beginning, the ideal pulse duration was thought to be between the TRT of the epidermis and that of the hair follicle. However, fine hair heats up more quickly than thicker hair, yet it is unable to hold the heat and, thus, requires short pulse durations (5–10 ms), while thicker hair requires longer pulse durations (40–60 ms).
- Spot size: A larger spot means higher penetration and higher efficiency. A small spot size causes the photons to scatter radially not reaching the hair bulbs, leading to greater dispersion and a decreased fluence. The spot size should be larger than the depth of the light penetrating the tissue, namely 5–10 nm [11].
- Pulse frequency: The number of shots per second that helps to reduce the time of the treatment session.
- Delay: A larger delay leads to the epidermis protecting itself more effectively.
- Number of pulses: Splitting the energy into multiple pulses enables the application of a higher fluence and more effectively protects the epidermis.
- Fluence: The efficiency is proportional to the fluence. If the fluence is too high, heat is produced in excess, leading to skin burns. A too low of a fluence may lead to a temporary hair loss lasting one to three months. Permanent hair reduction requires high-quality lasers that are capable of generating large amounts of energy, ensuring irreversible damage to the hair.

Pre- and Post-Treatment Recommendations

Complying with the following recommendations is of utmost importance to obtain satisfactory results from laser hair removal.

The pre-treatment recommendations are the following [8]:

1. Remove make-up from the areas to be treated: Makeup prevents the laser from reaching the hair root, compromising the results.
2. Do not apply creams or deodorants to the areas to be treated: Creams and deodorants prevent the correct application of the ultrasound gel, in addition to the fact that, after the action of the laser, it sticks, hindering the progression of the handle.
3. Cut the hair in the areas to be treated: It is advisable for patients to cut their hair at home with a razor and depilatory cream if needed.

Table 1: Laser parameters from studies: fluence, pulse width, and frequency

Year	Skin Type	Fluence (J/cm²)	Pulse Width (ms)	Frequency (Hz)	Reference
2011	IV–V	5-8	20	10	[12]
		25–35	30	2	
2012	II-V	15	15	5	[13]
2012	I–IV	25–35	30	N/A	[14]
2012	N/A	7–9	10	10	[15]
2012	III–IV	5–10	20	10	[16]
2013	IV	40	20	1	[17]
2013	IV–VI	24	6	10	[18]
		10	20		
2013	N/A	30	12	N/A	[19]
2014	II–V	6–12	20	N/A	[20]
		6–12	30–70		
2015	II–IV	25–33	30–45	N/A	[21]
2016	N/A	60	30–80	N/A	[22]
2016	IV–VI	3–10	N/A	10	[23]
2016	III–V	10	30	10	[24]
2018	IV	26–30	30	N/A	[25]
	V	22–26			
2020	III	24	30	1	[26]
	IV	22			
	V	20			

4. Between the sessions, only cut the hair: Plucking the hair at the root makes laser hair removal less effective. Patients who have had their hair removed must wait 15 to 21 days before the next session.
5. Always use a body scrub before each session: This helps to unravel hair.

The post-treatment recommendations are the following:

1. Avoid sun exposure in the following 48 hours and indoor tanning 5 days after treatment: The skin after laser hair removal is especially sensitive and the pores are open. Sunlight and indoor tanning may lead to hyperpigmentation.
2. Use high-SPF sunscreen and protect the treated area from the sun. Tanning after a session may increase melanin regeneration, leading to in hyperpigmentation.
3. Minimize the use of makeup immediately after the treatment: The face is especially sensitive after having come in contact with laser light.
4. Moisturize the treated areas: With each session, the skin will acquire an increasingly better appearance. The use of moisturizer accelerates this process.

Parameters from Studies

The PubMed database was used. An initial query yielded 52 results and, after filtering these against the last ten years, 24 results. After reading the abstracts, 15 studies remained, eliminating 9. Table 1 shows all the parameters gathered.

CONCLUSION

Although the ideal patient is one with light skin and dark hair, this is not always the case. Parameters need to be adjusted to the patient's characteristics. The operator of a laser hair removal machine needs to perform a correct evaluation of the patient, determining the presence of a health condition that might compromise the results, but also assessing the skin phototype and the hair color correctly to optimize the parameters (Table 1).

The fluence, pulse frequency, and pulse duration seem to play an important role. The authors recommend a high fluence (20–30 J/cm^2), a high frequency (10 Hz), and a medium pulse width (30 ms). Once the frequency is set on the machine, fluence and pulse width will automatically adjust since they are linked to one another. A high frequency requires a low pulse width and fluence, and a low frequency allows for a higher pulse width and fluence. Most machines are equipped with predefined values, parameters ideal for an operator new to the machine. However, it is important to adjust the parameters from session to session for the most satisfactory outcome.

Because parameters for laser hair removal continue to evolve as further understanding is being reached, further investigation on the optimization of these parameters is needed.

Ethics Statement

The procedures followed were in accordance with the ethical standards of the responsible Committee on Human Experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2000 and 2008.

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Clinical Image

Pink plaque on the hypogastrium

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Bowen's disease is a type of intraepidermal squamous cell carcinoma usually affecting the elderly and occurring on sun-exposed areas, such as the face, scalp, and limbs. The development of Bowen's disease in other locations such as the abdomen is rare. In these cases, dermoscopy proves to be a helpful tool in making the diagnosis [1].

A 65-year-old male with no previous medical history presented himself with a nonhealing asymptomatic lesion on the abdomen slowly growing for the last ten years. A dermatological examination revealed a 6-cm well-limited erythematous plaque on the hypogastrium with peripheral pigmentation (Fig. 1). Dermoscopy found central keratin as well as white shiny structures, including white shiny lines, white shiny areas, and rosettes (Fig. 2) as well as brown linear globules and dots on the periphery and looped vessels (Fig. 3). Bowen's disease was the most likely diagnosis, which was confirmed by histopathology. The patient underwent surgery for excision of the lesion with 5-mm margins.

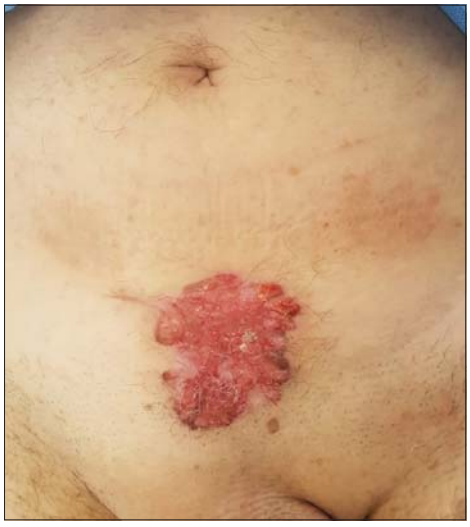

Figure 1: A well-limited erythematous plaque on the hypogastrium with peripheral pigmentation.

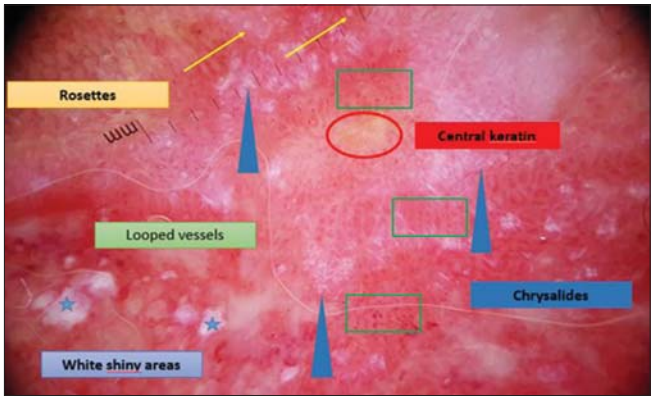

Figure 2: Dermoscopic image showing central keratin and white shiny structures (white shiny lines, white shiny areas, and rosettes).

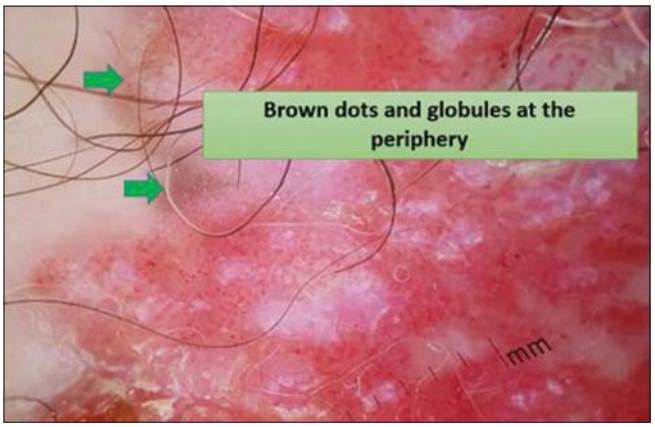

Figure 3: Dermoscopic image showing brown linear globules and dots on the periphery.

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Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Image

Keloid-like dermatofibroma

Fatima Azzahra El Gaitibi[1], Soumaya Hamich[1], Asmae Abdelmoutalib[1], Kaoutar Znati[2], Mariame Meziane[1], Badereddine Hassam[1], Karima Senouci[1]

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Dermatofibroma is a common benign skin tumor, mainly occurring in young to middle-aged females. It is frequently localized in the lower extremities. A typical dermatofibroma usually presents itself as a single firm papule or nodule, of variable color, bluish, brownish, or pinkish. Its clinical, dermoscopic, and histological features usually allow easy diagnosis [1]. However, it is possible to observe some variations of these typical features. Keloid-like dermatofibroma is one of these atypical presentations rarely reported in the literature [2].

A 40-year-old patient with no previous medical history presented to our dermatology department with a lumbosacral lesion evolving for several months. A physical examination revealed a firm, well-demarcated, asymptomatic erythematous nodule, 5 × 12 mm in size, localized in the lumbosacral area (Fig. 1). The patient denied any trauma preceding the onset of the lesion. There was no personal or familial history of keloidal scars. A dermoscopic examination revealed erythema, telangiectatic vessels, a shiny white streak, and a brownish-yellow pigmentation (Fig. 2). A biopsy was performed. A histological examination revealed an atrophic epidermis. The dermis contained a fibroblastic proliferation of low cell density haphazardly arranged, located on a fibromatous background (Figs. 3 and 4). Dermatofibroma with a keloidal presentation was the diagnosis.

In the present case, dermoscopic features were different from the signs usually found in dermatofibroma, which are a central white patch and a delicate pigment network. Indeed, a keloidal-like dermatofibroma presents itself as a pink nodule with other dermoscopic features. Erythema and vascular structures (arborizing vessels or/and dotted vessels) are the most frequently reported features. Besides, the shiny white streaks are

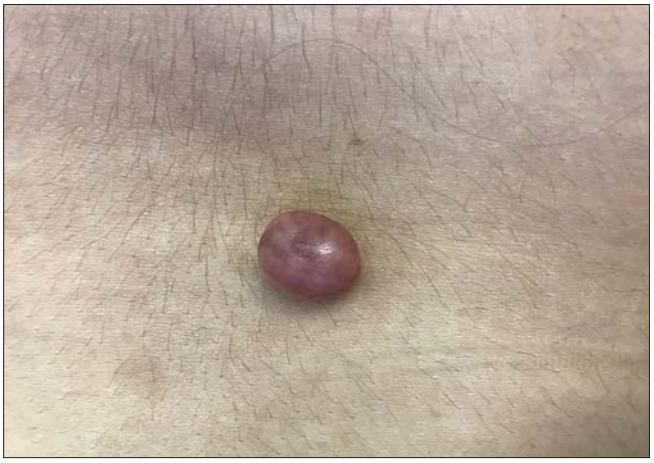

Figure 1: The firm erythematous nodule in the lumbosacral area.

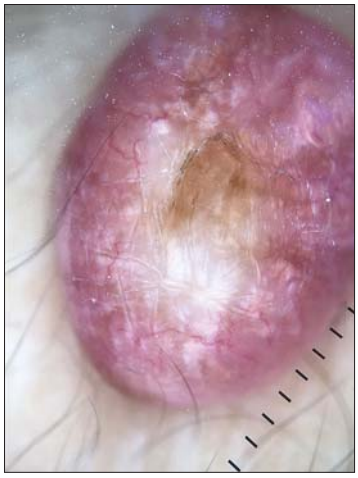

Figure 2: Erythema, telangiectatic vessels, a shiny white streak, and a brownish-yellow pigmentation.

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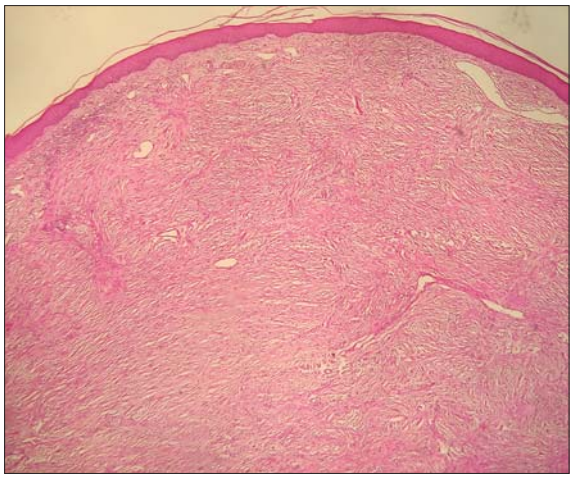

Figure 3: An atrophic epidermis and a fibroblastic proliferation on a fibromatous background (H&E; 10×).

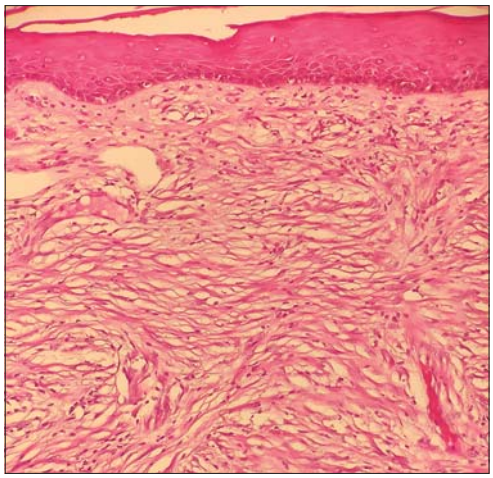

Figure 4: A fibroblastic proliferation of low cell density haphazardly arranged, located on a fibromatous background (H&E; 40×).

present in around half of cases. These features may be suggestive of malignant lesions, especially amelanotic melanoma and basal cell carcinoma [3].

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Letter to the Editor

Dermatoses in the hospital and their impact on quality of life

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Sir,

Dermatological pathologies may be responsible for the creation of a real handicap, affecting the patient's self-esteem and their professional and social life. The aim of this study was to assess the impact of diseases on the quality of life of patients hospitalized at the dermatology department.

The following was a retrospective study that included patients over eighteen years of age, hospitalized at the dermatology department of Hospital Mohammed VI in Oujda from January 2018 through December 2019. The Arabic version of the validated DLQI was used for all patients [1].

A total of 294 patients were collected, with a mean age of 53.95 years and a male-to-female ratio of 0.85.

The most frequent reasons for hospitalization were infectious dermo-hypodermitis ($n = 51$), autoimmune bullous dermatosis ($n = 23$), severe drug eruption ($n = 20$), genodermatosis ($n = 17$), melanocytic ($n = 9$) and non-melanocytic skin tumors ($n = 17$), severe psoriasis ($n = 17$), cutaneous lymphoma ($n = 11$), alopecia areata ($n = 10$), dermatomyositis ($n = 8$), and Verneuil's disease ($n = 5$).

The DLQI was impossible to calculate in eleven patients. The mean DLQI in all patients was 10.20, corresponding to a moderate effect on quality of life.

The mean DLQI was as follows: Verneuil's disease at 17.4, severe psoriasis at 16.6, dermatomyositis at 14.42, genodermatosis at 12.37, cutaneous lymphoma at 11.45, severe drug eruption at 11, alopecia areata at 10.5, AIBD at 9.67, skin tumors at 7.76, and infectious dermo-hypodermitis at 7.52.

The DLQI was the first index measuring quality of life in dermatology and is still widely used today[2]. The number of publications concerning the impact of dermatological pathologies on quality of life has increased in recent years [3].

Our results showed that the DLQI was higher in patients with Verneuil's disease, severe psoriasis, and dermatomyositis.

These results agree with the data of the literature, many publications have shown that psoriasis seriously impaired the quality of life and was responsible of social anxiety in patients [4]. Verneuil's disease is also responsible of a significant impairment on quality of life mainly due to the sexual disorders caused by this pathology [5].

Another study on dermatomyositis showed that there is a significant correlation between the severity of skin signs and the quality of life of patients [6].

Dermatological pathologies are distinguished from other pathologies by their displaying character, which is responsible for a significant impact on the patient's quality of life. The management of dermatology patients requires psychological support in addition to conventional therapy. However, these pathologies are still not recognized as long-term illnesses in Morocco.

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Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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Letter to the Editor

Herpes zoster following mRNA-1273 COVID-19 vaccination

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Sir,

Skin rashes have been associated with COVID-19 and studies suggest the inclusion of skin diseases in the list of COVID-19 symptoms. Skin eruptions are also associated with the mRNA-1273 COVID-19 vaccine. Findings by Baden et al. [1] describe immediate injection-site reactions observed in 84.2% of participants after the first dose, with delayed onset reactions—on or after day eight—occurring much more infrequently, 0.8% after the first dose and 0.2% after the second dose. Blumenthal et al. [2] discuss twelve cases of delayed vaccine reactions, with all patients experiencing reactions in the vaccination site. Herein, we describe two cases of herpes zoster within days of receiving their first mRNA-1273 vaccine.

Figure 1: 77-year-old male with a unilateral rash with scattered vesicles and edematous plaques in a dermatomal distribution.

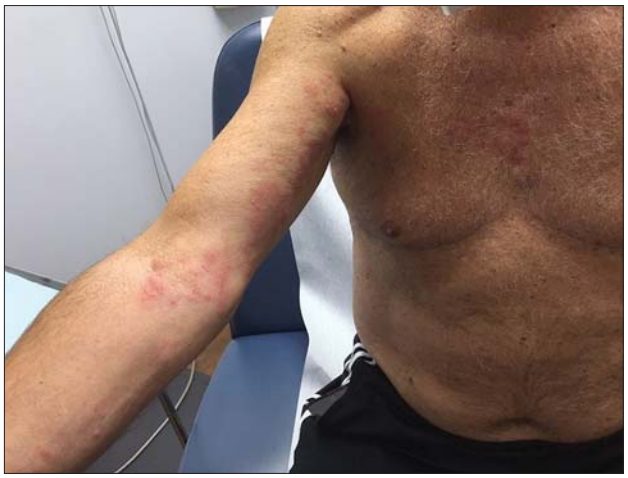

Figure 2: 77-year-old male with a unilateral rash with scattered vesicles and edematous plaques in a dermatomal distribution.

Both cases presented to the same dermatology clinic. A 77-year-old male presented with a bumpy, itchy, red rash on the upper right arm and axilla three days following an mRNA-1273 vaccine injection. The symptoms continued to worsen and the patient was clinically diagnosed with herpes zoster and treated with valacyclovir (Fig. 1). Another patient, also a 77-year-old male, complained of a rash located on the right upper arm and axilla. It was a red, itchy, bumpy rash that the patient developed two days after an mRNA-1273 vaccine injection (Fig. 2). Both rashes demonstrated a similar distribution pattern and both patients responded well to valacyclovir with the resolution of the erythema; however, one patient did have residual post-herpetic neuralgia.

Herpes zoster infection is caused by the reactivation of the varicella-zoster virus (VZV). After the primary infection, VZV remains latent in the dorsal root ganglia and reactivates spontaneously or in association with stress, immunosuppression, or fever [3]. It is possible that the administration of the mRNA-1273 vaccine

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causes an immunomodulatory response leading to the reactivation and development of herpes zoster. Recently, six cases of herpes zoster have been reported after the BNT162b2 COVID-19 vaccine; however, there are no documented cases of herpes zoster occurring after the administration of the mRNA-1273 vaccine [4]. These cases mostly involved patients with underlying rheumatologic disorders, a comorbidity not observed in our patients. While most cases of herpes zoster are self-limited, roughly 10% of affected patients will continue to develop post-herpetic neuralgia, a chronic pain disorder that affects the nerves and the skin [5]. It is important that providers are aware of these potential dermatologic manifestations to provide appropriate treatment and avoid unnecessary use of antibiotics. Our findings of multiple cases of herpes zoster, in a limited patient population, demonstrate that herpes zoster may be more common following COVID-19 vaccination than was initially thought. These observations provide important information for clinicians as mass vaccination continues to be performed.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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Letter to the Editor

Skin infection with *Saccharomyces cerevisiae* in an immunocompetent patient: An exceptional infection

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Sir,

Saccharomyces cerevisiae is a ubiquitous yeast used as a probiotic for antibiotic-associated diarrhea prophylaxis. It is part of the normal flora of the oral, gastrointestinal, and respiratory tracts and the vaginal lining. Severe opportunistic infections due to *S. cerevisiae* have been reported in patients with immunosuppression with fungemia, endocarditis, pneumonia, and urinary tract infection [1-3].

Herein, we describe the first case in the literature of a skin infection with *S. cerevisiae* in an immunocompetent patient.

A 72-year-old patient with no particular history had had pruriginous skin lesions for five years in the context of general state preservation and apyrexia.

A skin examination revealed erythematous and maculopapular lesions diffused throughout the body (Figs. 1a–1d). The phaners and mucous membranes were without abnormality, and there was no adenopathy. The rest of the examination was unremarkable. The patient had been treated several times with topical and oral antifungals and dermocorticoids but without any improvement.

Biological examination revealed no immunodepression. Two mycological examinations of the skin lesions revealed the presence of *S. cerevisiae* (Figs. 2 and 3). Unfortunately, the patient proceeded against medical advice and discontinued attendance without treatment.

The genus *Saccharomyces* comprises several species, with the most well-known being *S. cerevisiae*.

Saccharomyces cerevisiae is a common colonizer of mucous surfaces and part of the normal flora of the gastrointestinal tract, respiratory tract, and vagina [1]. Invasive *S. cerevisiae* infections have been identified for the past three decades, with the microorganisms recovered from the blood, lungs, esophagi, peritoneal cavities, urinary tracts, and vaginas. Clinical and commercial strains are being identified with genotyping studies, and the contribution of commercial strains to the colonization and infection has been documented [1]. The predisposing risk factors are similar to those associated with invasive candidiasis. The treatment of choice has not been established: *S. cerevisiae* is persistently sensitive to amphotericin B and fluorocytosine while resistant to fluconazole and itraconazole. A literature review by Munoz et al. reported a favorable response in 60% of 19 patients with invasive *S. cerevisiae* who received fluconazole alone, in contrast to a favorable response in 77.7% of 31 patients receiving amphotericin B [2]. The role of echinocandins has not yet been established and was not reported in the study [1,2].

Ours is the first case of *S. cerevisiae* discovered in an immunocompetent patient, whose immunodepression might be explained by advanced age; however, it remains uncertain whether this is necessary for a skin infection with *S. cerevisiae*.

Reports of *Saccharomyces cerevisiae* infections in dermatological publications are nonexistent, and, to

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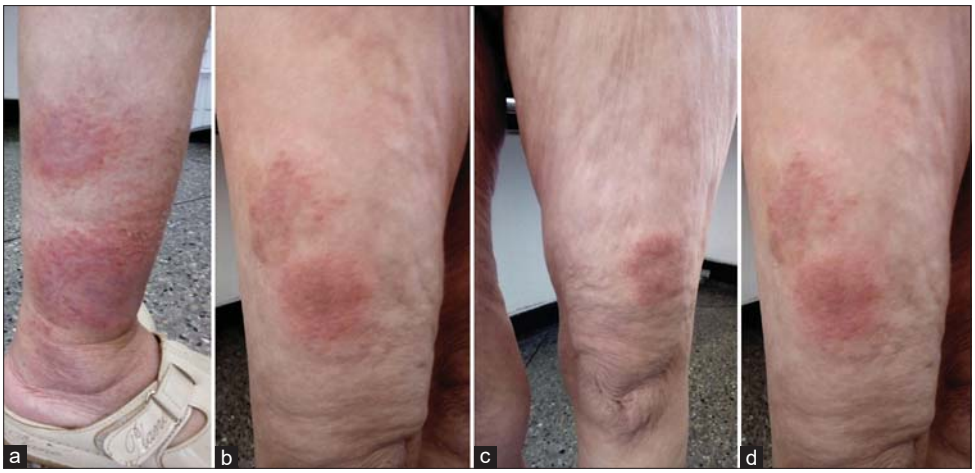

Figure 1: (a-d) Erythematous maculopapular lesions of the lower members.

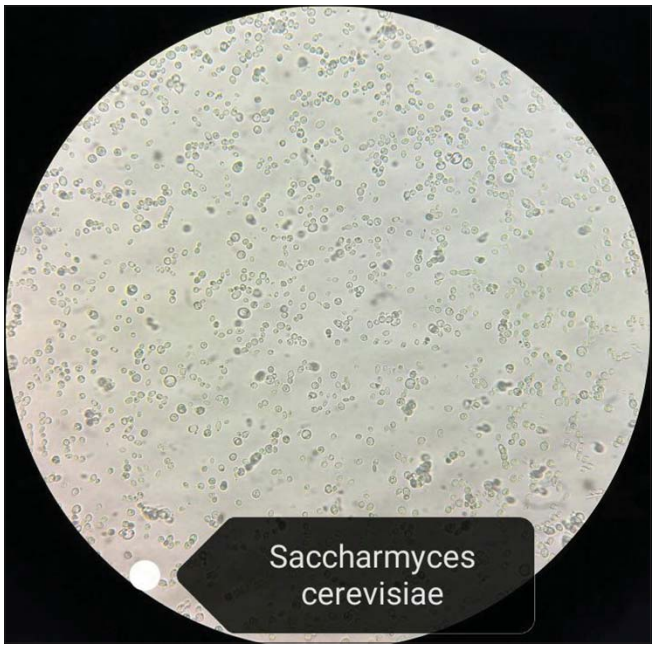

Figure 2: A microscopic image highlighting the arrangement of Saccharomyces cerevisiae yeast.

date, they remain exceptional. Studies are needed to elucidate their pathophysiological mechanism as it still remains poorly understood.

Although skin infections with *S. cerevisiae* remain exceptional to this day, it is preferable to perform a cultured mycological examination in front of ring lesions resistant to the usual treatments, especially in elderly persons.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients have given consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

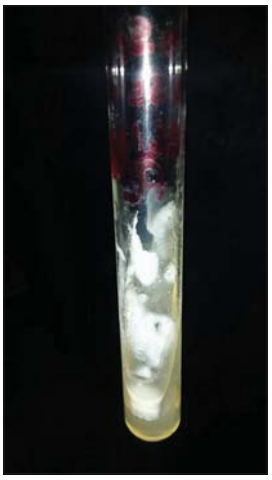

Figure 3: *Saccharomyces cerevisiae*.

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Letter to the Editor

Linear lichen planus associated with primary aldosteronism

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Sir,

Lichen planus (LP) is categorized as a chronic inflammatory skin disease of unknown etiology that involves immune reactions. It is characterized by flat-topped, polygonal, violaceous papules and plaques. It has various clinical presentations, such as classical LP, hypertrophic LP, LP pigmentosus, and linear LP (LLP). Primary aldosteronism (PA) is known to pose a higher risk of causing multiple autoimmune diseases [1]. Herein, we report a case with LLP and PA present at the same time.

A 72-year-old Japanese female presented herself to our hospital with a three-month history of slightly itchy skin lesions on the lower right leg. A physical examination revealed flat-topped plaques on the lower right limb extending from the middle of the leg to the dorsum of the foot (Fig. 1a). There was no oral or nail involvement. The patient had a history of hypertension from the age of 62 years and was diagnosed with PA afterward. The patient had been treated with an antihypertensive drug since then without change in internal medication. The patient had no history of a preceding trauma, dental metal fillings, hepatitis, metastatic cancer, or any other infections. A histopathological examination of a skin biopsy from a lesion on the right leg revealed hyperkeratosis, a saw-tooth appearance of the epidermis, and severe liquefaction degeneration. A band-like lymphocytic infiltration was present in the upper dermis (Figs. 2a and 2b), as well as lichenoid infiltration into the dermis composed of CD4+ and CD8+ T lymphocytes. Predominantly, CD8+ T lymphocytes infiltrated into the epidermis (Figs. 2c and 2d). Clinical and histological findings confirmed the diagnosis of LPP.

The patient was treated with a topical corticosteroid. The lesions improved after six months (Fig. 1c).

LP is a chronic inflammatory autoimmune disease affecting not only the skin but also the oral and genital mucosas, scalp, and nails. It usually appears as itchy shiny flat-topped papules that may persist for several weeks. It has various clinical presentations, such as classical LP, hypertrophic LP, LP pigmentosus, and linear LP (LLP). LLP is observed in less than 0.2% of all LP patients [2]. It sometimes occurs alongside autoimmune disorders, viral infections, allergic reactions from certain metals and chemicals, stress, radiation, and genetic conditions [3-5]. Mild cases of lichen planus clear up in weeks to months.

Our case had no history of recent vaccination or episodes of allergic reaction to metals. The patient had been taking eplerenone, an oral aldosterone antagonist, for eight years since the diagnosis of primary aldosteronism, but the medication remained unchanged after blood pressure became well controlled. The lesions improved without change in drugs. We excluded drug-induced LP.

The exact etiology of our patient's LLP is unknown and we speculated that the coexistence of primary aldosteronism could have been one trigger. A study by Herrada et al. showed that aldosterone augmented the activation of CD8+ T cells in a dendritic cell-dependent fashion, and that this condition contributed to inflammatory damage, leading to hypertension and cardiovascular diseases. In addition, stimulation with aldosterone imposed a Th17 phenotype on CD4+ T cells, which has recently been associated with the promotion of inflammatory and autoimmune diseases [6]. In our case, bilateral adrenal venous sampling revealed high levels of plasma

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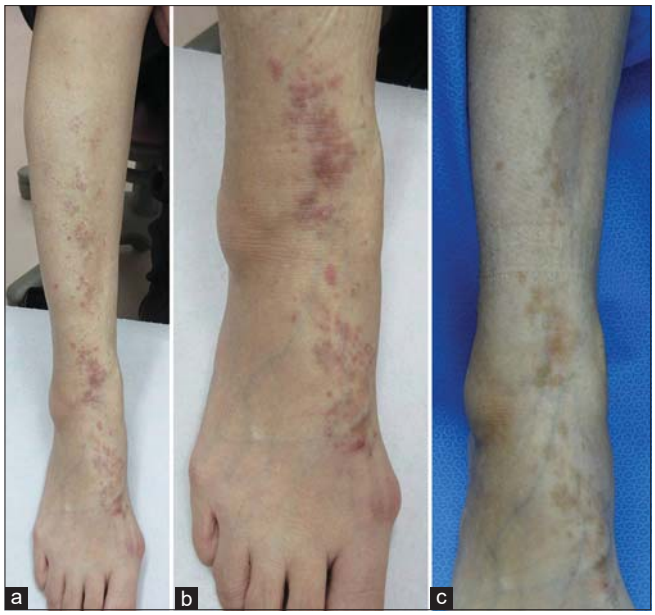

Figure 1: (a-c) Flat-topped plaques on the lower right limb extending from the middle of the leg to the dorsum of the foot.

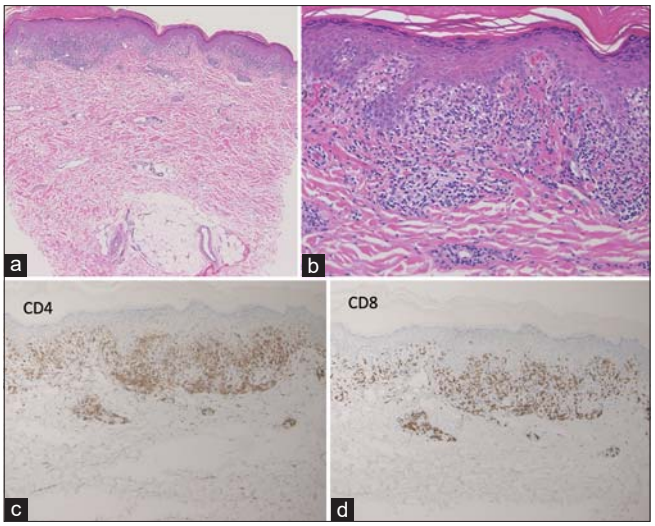

Figure 2: (a-b) A saw-tooth appearance of the epidermis and severe liquefaction degeneration (H&E; (a) 200×); a band-like lymphocytic infiltration in the upper dermis. (c-d) Lichenoid infiltration into the dermis composed of CD4+ and CD8+ T lymphocytes; CD8+ T lymphocytes infiltrating into the epidermis (H&E, 200×).

aldosterone. We presume that the excessive production of aldosterone might have led to an inflammatory state, which may have been promoted by T cell immunity and led to the abnormal keratinocyte cloning on the patient's right foot to unmasked LLP. We were unable to find any report in the literature of the coexistence of LLP and primary aldosteronism as seen in our case. Recent studies have suggested that lichen planus is associated with an increased risk of cardiovascular comorbidities. Baykal Selcuk et al. observed a positive correlation between the duration of the disease and arterial stiffness in a patient with lichen planus [7]. Our case seems to have needed immediate treatment and careful follow-up.

In summary, primary aldosteronism poses a risk of promoting an inflammatory state and autoimmune diseases. Therefore, patients with primary aldosteronism should be assessed for the presence of inflammatory skin diseases, including LLP.

Consent

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Letter to the Editor

Isolated café-au-lait macules: Think of neurofibromatosis type V

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Sir,

Segmental neurofibromatosis (SNF) is a rare form of neurofibromatosis (NF) with a reported prevalence of 0.0014%–0.002%. It is included in Riccardi's classification as type V NF [1].

It is characterized by café-au-lait macules and/or neurofibromas distributed in only one dermatome, less commonly in two or more dermatomes [2]. Roth et al. reclassified SNF into four subtypes: true SNF, localized SNF with deep involvement, hereditary SNF, and bilateral SNF. A limited number of cases of SNF have been reported with systemic involvement, such as visceral neurofibromas, skeletal abnormalities, and renal agenesis [1]. Laser therapy may be performed if an aesthetic demand arises.

Herein, we report a case of SNF in a young boy with no systemic disease.

An eleven-year-old male was sent by his pediatrician for skin spots that appeared at the age of four. The young patient came from a non-consanguineous marriage and had no family history of skin disease. A general physical examination revealed normal parameters, such as weight, size, intelligence, speech, auditory function, and visual acuity. A dermatological examination found unilateral café-au-lait macules with a ranging size of 1 to 5 mm in the right half of the trunk with no crossing of the midline (Figs. 1a and 1b). We thoroughly examined the boy and found no other features of neurofibromatosis, including neurofibromas, neurological deficits, or bone abnormalities. We assured the patient and his parents that this was a benign disease, so the risk of developing any disease-related complications was low. Annual monitoring was started. No therapy was proposed because the patient expressed no aesthetic demands.

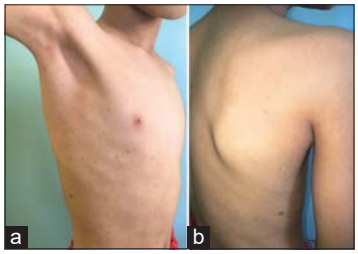

Figure 1a and 1b: Unilateral cafe-au-lait macules of different sizes in the right half of the trunk with no crossing of the midline.

Consent

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Letter to the Editor

Squamous cell carcinoma mimicking a wart

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Sir,

Cutaneous squamous cell carcinoma, a malignant proliferation of the cutaneous epithelium, represents the second most common non-melanoma skin cancer after basal cell carcinoma [1]. Verrucous carcinoma (VC) is a rare, low-grade, well-differentiated squamous cell carcinoma most commonly seen in the mucosa, infrequently reported to occur in the skin, where it is a slow-growing and locally aggressive tumor. It is not uncommon for cutaneous verrucous carcinomas to be mistaken for the more frequent wart (verruca vulgaris) and treated accordingly [2]. The etiopathogenesis of VC is not completely known. One theory mentions the human papillomavirus (HPV) infection; with plantar lesions, the types involved are reported to be 16 and 11 [3]. Histopathological diagnosis is difficult and needs one or more broad and in-depth biopsies. Morbidity results from the local destruction of the skin and soft tissues and, occasionally, from a perineural, muscular, and even bony invasion. Metastasis to regional lymphatic ganglia is rare, found in 5% of cases [4]. VC bears a high risk of local relapse. No matter the treatment employed, the rate of recurrence varies from 30% to 50% and usually is not the result of incomplete surgical interventions. The treatment of choice is complete surgical excision with safety margins [5].

A forty-year-old female patient with no previous history presented herself with a hyperkeratotic lesion on the right foot persistent for two years, which she had been manipulating routinely, which had progressively been increasing in size for the previous year, and which, for the previous three months, had become painful and bleeding. An examination revealed a hyperkeratotic plaque with a hyperpigmented border, hard on palpation, adherent to the deep plane, and with an eroded surface (Fig. 1). Dermoscopy was able to find a papillomatous appearance surrounded by dotted vessels (Fig. 2). This dermoscopic aspect typical of vulgar warts was confusing. Indeed, dermoscopy of the foot wart shows red or black dots in the center of papillomatous structures, which are thrombosed vessels supplying the wart; hence the importance, in our opinion, of the clinical and pathological correlation. For this reason, we performed a skin biopsy; an anatomopathological study found a squamous cell carcinoma of the verrucous type.

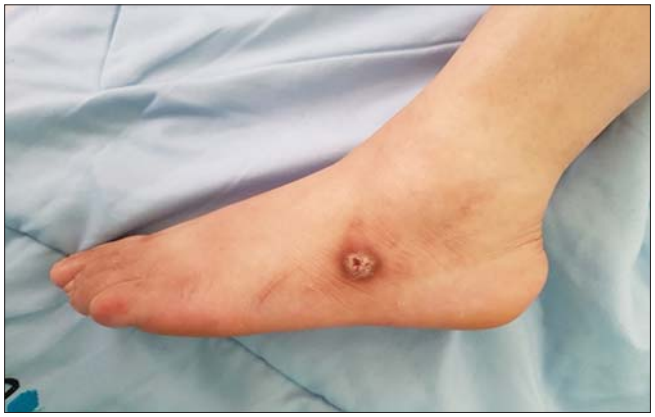

Figure 1: Hyperkeratotic plaque with a hyperpigmented border and an eroded surface on the lateral side of the right foot.

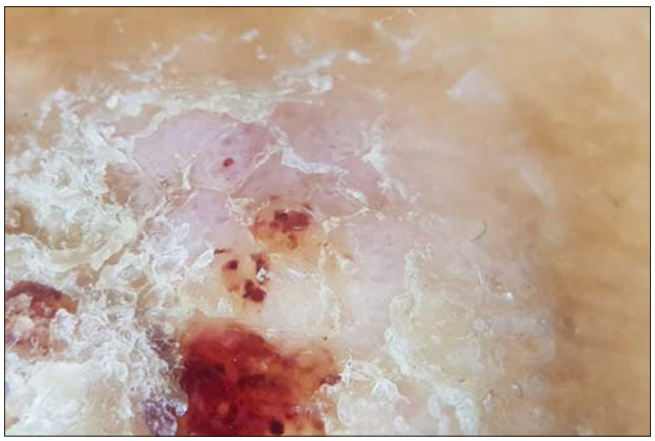

Figure 2: Papillomatous appearance surrounded by dotted vessels.

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Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

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Our Dermatology Online

Historical Article

Jonas Lelis and the syndrome that bears his name

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ABSTRACT

Jonas Lelis (1914 – 2011) was a professor and one of the Lithuanian pioneers in dermatology. In the 1970s, Lelis described four unrelated patients of eastern European origin with an association of ectodermal dysplasia and acanthosis nigricans, a rare congenital genodermatosis that was to be known as Lelis syndrome. The syndrome is characterized by hypotrichosis, hypohidrosis, and acanthosis nigricans. This report sheds light on Jonas Lelis and the syndrome that bears his name.

Key words: Acanthosis nigricans; Ectodermal dysplasia; Lelis syndrome

Jonas Lelis (Fig. 1) was a world-renown Lithuanian professor of dermatology and venerology and a pioneer in dermatology [1-3]. Among his great contributions to dermatology, he is credited for describing a syndrome that was to be known as Lelis syndrome (LS) [4-10].

Lelis syndrome (MIM ID %608290), also known as Ectodermal dysplasia and hypohidrosis with acanthosis nigricans [10], is a rare autosomal recessive condition with only several cases reported worldwide [9].

It is characterized by hypotrichosis, hypohidrosis, and acanthosis nigricans. Additional features reported include perioral radial furrowing, hypodontia, palmoplantar hyperkeratosis, a furrowed tongue, nail dystrophy, disturbances in skin pigmentation [4] (perioral and periorbital hyperpigmentation, vitiligo, and perinevic leukoderma), and mental retardation [10].

Some authors have suggested that LS occurs secondary to mutations in the EDA gene [2].

The syndrome has, so far, been reported in Europe [4,7,9], Saudi Arabia [6], and Brazil [4,8]. Van Steensel et al. suggested that Lelis syndrome may be a manifestation of X-linked hypohidrotic ectodermal dysplasia [9].

Some authors reported successful treatment with acitretin of skin lesions seen in LS.[8]

Jonas Lelis was born on July 5, 1914 [1,3], in Skaistgirys, Pušalotas District, Lithuania. In 1933, he finished Panevėžys Secondary School for Boys. Between 1933 and 1939, he attended the Medical Institute at Kaunas University, named after Vytautas Magnus. After graduating from Kaunas University in 1938, J. Lelis practiced medicine in Šakiai, Panevėžys, Akmenė and Ylakiai. In the years 1946-1957, he worked at the Vilnius Institute of Dermatological and Venereal Diseases, since 1948 as a director; and he also was the chief medical inspector in the Ministry.. From 1948 through 1993, he continued his scientific career. He held the position of a lecturer at the Medical Faculty of Vilnius University and received the title of associate professor and professor [3]. He had written more than 300 scientific articles in both Lithuanian and foreign journals and 10 monographs on dermatology and venereology [1]. He had developed interest in numerous dermatological diseases, but genetic skin diseases were one of his favorites.

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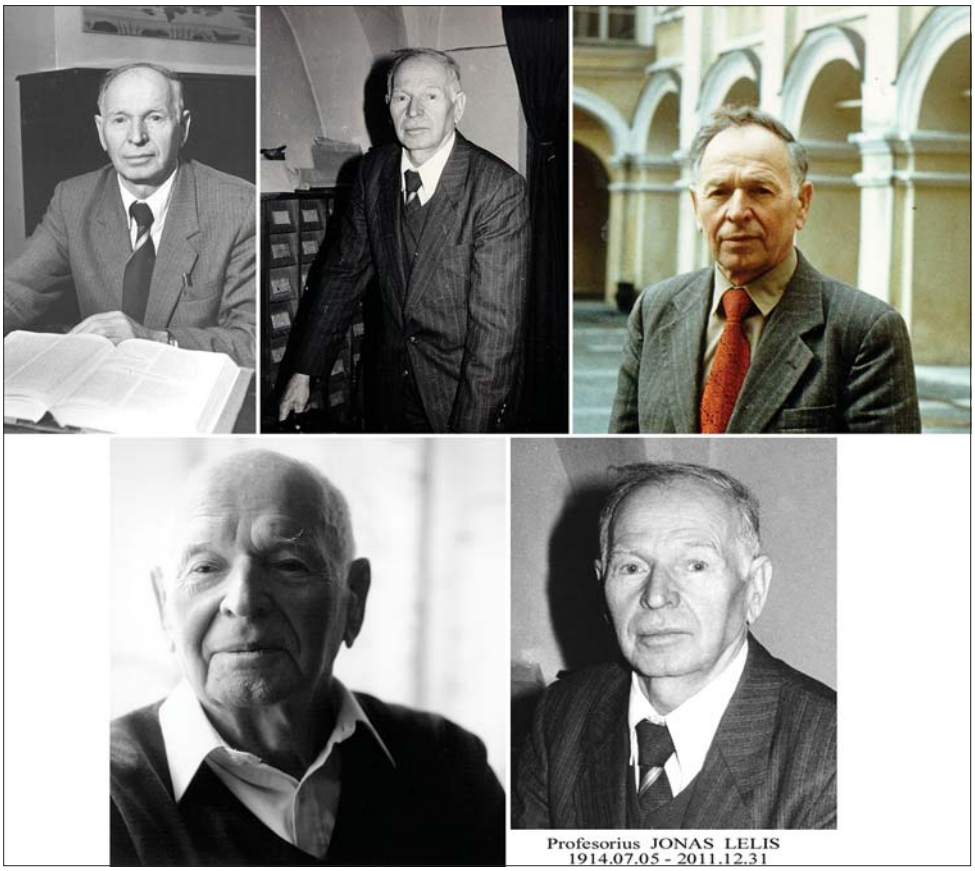

Figure 1: Jonas Lelis (1914–2011).

In three of his publications, he described an autosomal recessive disease, ectodermal dysplasia (Lelis syndrome), in seven patients of eastern European origin. He had also published fiction books and biographical essays [1]. In 1965, he become a republican prize winner for his monograph "Red gum" [3]. His other monographs are widely known as well, to name a few, "F. Schaudinn: The discoverer of the pale monster" (on Fritz R. Schaudinn as a scientist of Lithuanian roots) (1971), "Inherited dermatoses and syndromes" (1981), "The atlas of dermatological and venereal diseases" (by Lelis and a co-author, 1998), and "Tragical and comical miniatures" (1998) [3]. Lelis was a member of the medical corporation Fraternitas Lituanica. He is widely known for a high degree of intelligence and erudition. He did sports, played chess, and was a polyglot with a good command of about ten foreign languages. He had shared his knowledge lavishly with his students and doctors alike [3]. Lelis died at the age of 97 on December 31, 2011.

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