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Case Report

An atypical case of cicatricial pemphigoid vegetans in a young male and a review of the literature

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ABSTRACT

Mucous membrane pemphigoid (MMP), previously known as cicatricial pemphigoid, is the second most frequent autoimmune subepithelial blistering disorder after bullous pemphigoid (BP). MMP has a broad spectrum of both clinical and immunological features, mostly affecting the mucous membranes, mainly the oral and ocular mucosae, but around 30% of cases develop skin lesions, which heal leaving atrophic scars and milia. Herein, we report a patient with widespread vegetating cutaneous and oral plaques, oral erosions, scarring conjunctivitis, and extensive mucosal lesions, who met the immunologic and microscopic criteria of cicatricial pemphigoid vegetans (CPV). The vegetative form of MMP is a very rare entity and, to our knowledge, this is the fifth patient recorded in the global literature. We present the unusual case of a young male who developed CPV possibly caused by chronic and heavy cannabis use and who was treated effectively with rituximab.

Key words: Cicatricial pemphigoid vegetans; Cannabis; Rituximab

INTRODUCTION

Mucous membrane pemphigoid (MMP), previously known as cicatricial pemphigoid, is the second most frequent autoimmune subepithelial blistering disorder after bullous pemphigoid (BP). MMP has a broad spectrum of both clinical and immunological features. This dermatosis almost exclusively affects the elderly and mostly affects the mucous membranes, mainly the oral and ocular mucosae, but around 30% of cases develop skin lesions, which heal, leaving atrophic scars and milia [1]. Without treatment, these patients may develop ocular, esophageal, and laryngeal stenosis, strictures, and blindness [2]. Immunologically, MMP is characterized by *in vivo* bound and/or circulating IgG and IgA antibodies to the basement membrane zone (BMZ) [3]. The treatment of MMP depends on the severity: the low-risk group is treated with topical corticosteroids with or without sulphone derivatives (dapsone or sulfasalazine) while the high-risk group is treated with oral corticosteroids and immunosuppressives [4].

CASE REPORT

A 26-year-old Moroccan male, a long-term cannabis consumer for eleven years, presented with diffuse mucosal lesions, mainly ocular, and severe pain, which had persisted for the last eight months. An examination of the conjunctival mucous membranes revealed bilateral hyperemia with synechiae of the left eye (Fig. 1a). The oral mucosa exhibited extensive erosions on the hard and soft palate and gingiva, which were partly covered by thick fibrinous membranes, and well-defined vegetative and papillomatous lesions all over the tongue (Fig. 1b). The patient also had diffuse hemorrhagic erosions on the nasal, genital, and anal mucosae (Figs. 1c – 1e). In addition, the patient had extensive cutaneous lesions as well-defined vegetating erosive lesions, 1–10 cm in

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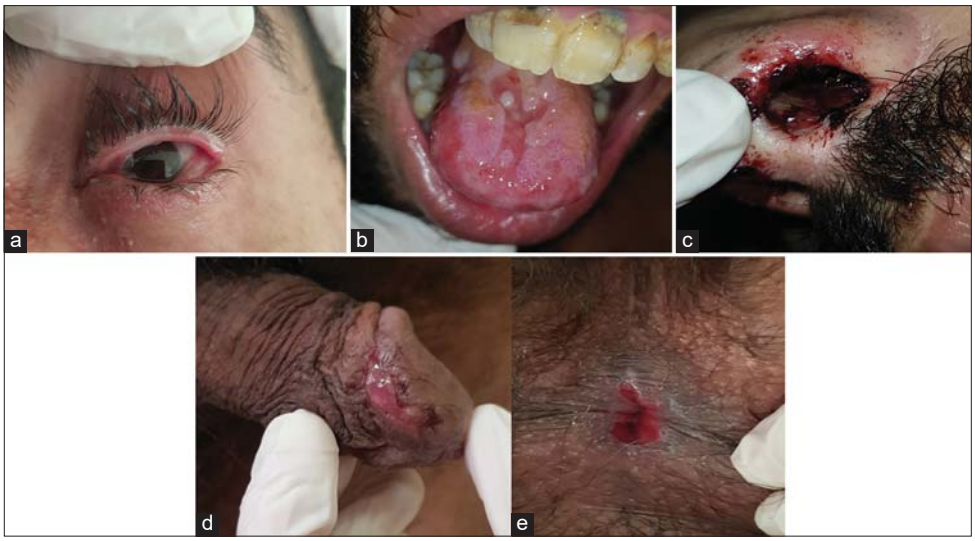

Figure 1: Clinical presentation of the mucosal lesions: (a) hyperemia and synechiae in the left eye, (b) well-defined vegetating and papillomatous lesions on the tongue, and hemorrhagic erosions on (c) the nasal mucosa, (d) the penile mucosa, and (e) the perianal mucosa.

Figure 2: Clinical presentation of the cutaneous lesions: symmetrical cutaneous lesions with well-defined vegetating erosions on (a) the scalp and the nape, (b) the neckline, and (c) the right elbow.

diameter, localized symmetrically on the scalp, nape, ear auricle, neckline, and right elbow (Figs. 2a – 2c). The diagnoses considered were syphilis, HIV, mucous membrane pemphigoid, and epidermolysis bullosa acquisita. Serologies for HIV and syphilitic were negative. Biopsy specimens from the buccal mucosa revealed subepidermal blisters and eosinophilic infiltrates in the dermis. Direct immunofluorescence revealed a linear band of IgG and C3 at the dermal–epidermal junction. A skin biopsy revealed acanthosis, hyperplasia in the epidermis, subepidermal blisters, and eosinophilic infiltrates in both the lower epidermis and the dermis (Fig. 3). Direct immunofluorescence revealed the same as from the mucosa specimen (Fig. 4).

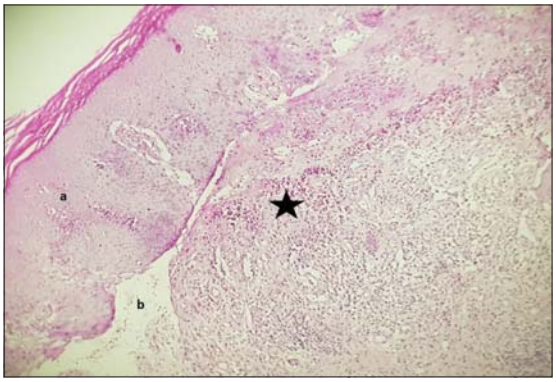

Figure 3: Histological image: (a) acanthosis and hyperplasia in the epidermis and (b) subepidermal blisters and eosinophilic infiltrates (black stars) in both the lower epidermis and the dermis.

Circulating anti-basement membrane antibodies were not detected with indirect immunofluorescence. Blood chemistry and blood count were normal. Based on the performed tests and the clinical examination, the diagnosis of vegetating cicatricial pemphigoid was reached and a corticosteroid bolus was initiated at 1 g/day for three days consecutively and then relayed orally at 1 mg/kg/day combined with Disulone 150 mg/day. Subsequently, considering the severity of the ocular involvement, the patient's young age, and, in order to be able to reduce the doses in the corticosteroid therapy later, rituximab was initiated at a dose of 1 g intravenously on day 1 and day 14, as well as assistance in cannabis withdrawal. After one month of treatment, we observed an almost complete regression of the skin lesions with scarring in milium grains, the disappearance of the inflammatory state of the mucous membranes, the persistence of scar synechia in the left eye, and the

vegetative aspect of the tongue (Figs. 5a – 5e). The patient has, to date, been stable for one year.

DISCUSSION

In 1979, Winkelmann et al. described a patient with vegetating and pustular lesions that were clinically indistinguishable from pemphigus vegetans, but histologically and by immunohistopathological criteria were classified as part of the bullous pemphigoid spectrum [5]. The term *vegetating pemphigoid* was coined and further observations confirmed that this vegetating subset of bullous pemphigoid indeed exists [6,7].

The vegetating type of MMP was first described by Wolff et al. in 1987 [8]; the patient had blistering and scarring mucosal lesions of cicatricial pemphigoid of the mucocutaneous type and widespread vegetating and purulent cutaneous eruptions of pemphigoid vegetans. The authors suggested that a third subset of cicatricial pemphigoid may be added to the two other and proposed to designate this heretofore undescribed condition vegetating cicatricial pemphigoid (VCP). MMP with vegetating lesions is particularly rare, and the literature reports five cases, including ours (Table 1).

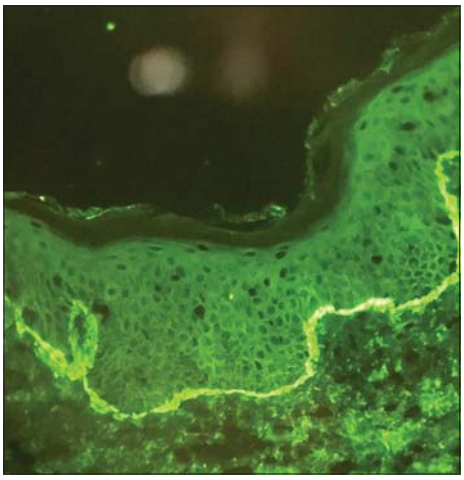

Figure 4: Direct immunofluorescence revealing a linear band of IgG and C3 at the dermal–epidermal junction.

VCP predominates in females, with a female-to-male ratio of 3:2, coinciding with the common form. The age of onset was above forty years in all patients, except the case of our patient, who was much younger and with a strong suspicion of a drug-induced form.

Clinically, the four cases described in the literature present an almost similar aspect with initially pustular lesions progressing toward vegetative plaques located mainly in the folds, but our patient is an exception, since the elementary cutaneous lesions were, by interrogation, bullous lesions with clear contents, which had evolved into vegetative lesions on the scalp, the ear's auricle, the nape of the neck, and the upper part of the trunk.

With the exception of a case reported by Narbutt et al. [9], all patients, including ours, presented extensive erosions and ulcerations involving almost the entire oral mucosa. The vegetative lesions of the tongue in our patient have not been previously described.

Erosions on the penile mucosa have been described in two male patients in one series, including our case [2].

Figure 5: Clinical presentation after one month of treatment: (a) synechiae in the left eye, (b) the persistence of the vegetative aspect of the tongue, (c-e) a regression of the skin lesions.

Table 1: Review of the literature on cases of cicatricial pemphigoid vegetans.

Study/ years/ country	Gender/ age	Coexisting/ triggering factors	skin involvement	Mucous membrane involvement	Histopathology	Diagnostic procedures	IIF	Therapy	Time to remission
Wolff et al. (5) 1987/ Austria	F/79	Not detected	**Type of lesions :** Pustular, vegetating lesions **Localization :** Intertriginous, umbilical, periocular	**Oral** : blistering, ulceration, scarring, **Conjunctival :** synechiae	Subepidermal cleavage, Epidermal hyperplasia with acanthosis, papillomatosis, hyperand parakeratosis Dense and eosinophilic infiltrate at the dermal-epidermal junction, sub-epidermal eosinophilic abscess	DIF: IgG and C3 along BMZ	Neg	Dapson: 100 mg/d, methylprednisolon: 60 mg/d	4 Weeks
Woźniak et al.(10) 2007/poland	F/58	ulcerative colitis	**Type of lesions :** pustules, vegetating erosions **Localization :** inguinal and axillary folds and on the upper inner thighs	**Oral** : erosions **Conjunctiva:** subtle scarring	Subepidermal blisters Epidermal acanthosis, papillomatosis, hyperplasia, infiltrate of leukocytes and eosinophils, extended into the lower epidermis	DIF: IgG and IgA along BMZ LSCM: IgG below laminin-5 and above collagen IV, Immunoblotting and ELISA: negative	not made	Prednisone: 40 mg/d, sulfasalazine: 1.0 g 3 times daily	4 Weeks
Narbutt et al.(6) 2015/poland	F/41	ulcerative colitis	**Type of lesions :** Blisters filled with purulent content, which later evolved into hypertrophic tumors **Localization :** the submammarial folds and abdominal skin	None	Acanthotic hyperplasia with the formation of intra-epidermal vesicles with eosinophils and neutrophils Intense infiltration of inflammatory cells in the dermis	DIF: IgG and IgA along BMZ LSCM: IgG below laminin-5 and above collagen IV	Neg	Prednisone: 60 mg/d	3 Months
Jakubowska *et al.*(2) *2018/poland*	M/45	Arsenic derivatives	**Type of lesions :** pustules and vegetating erosions **Localization :** axillae inguinal area, and inner areas of the upper thighs	Erosive lesions located on the **oral mucosa** and **nasopharyngeal areas.** nodular lesions on the **conjunctivae** of both eyes	Sub-epidermal blisters, Acanthosis, papillomatosis, pseudocarcinomatous hyperplasia Infiltrate of leukocytes and eosinophils	IgG anti-BMZ 1:10	Prednisone: 60 mg/d and Dapson: 100 mg/d	4 Weeks	
Current case 2020/ morroco	M/26	Chronic canabism and tabagism	**Type of lesions :** vegetating without pustules erosions **Localization** : scalp, the nape , the ears pavilion, the neckline and the right elbow	**oral mucosa:** Erosive lesions and vegetating lesion of the tongue **conjunctival mucous** :bilateral hyperemia with synechiae in the left eye diffuse hemorrhagic erosion in the nasal and genital mucosa	Sub-epidermal blisters, Acanthosis, hyperplasia in the epidermis, Infiltrates of eosinophils in the dermis. Linear IgG and C3 at basement membrane zone	Neg	Prednisone: 60 mg/d and Dapson: 150 mg/d Rituximab 1g IV on day 1 and day 14	One year	

Three cases, including ours, presented solitary or bilateral synechial conjunctival lesions and one case presented the particular type of nodular lesions as the first case of pyogenic granuloma of conjunctivae in a course of MMP [2]. Two biopsies were performed in all patients, including ours: a biopsy of the oral mucosa and a skin biopsy, except for Jakubowska et al., [2] who performed a conjunctival biopsy, revealing the pyogenic granuloma.

Histopathologically, all cases showed subepidermal blisters and eosinophilic infiltration along the BMZ, suggesting pemphigoid, and epidermal hyperplasia reflecting vegetating lesions, which are the same as those in pemphigoid vegetans. Direct immunofluorescence revealed IgG and C3 deposits along the BMZ in skin and mucosal biopsies in all cases. Our department does not provide confocal microscopy or ELISA tests. Indirect immunofluorescence was positive in only 1 in 5 patients (20%), which is the same as in common vegetative pemphigoid (Table 1).

Interestingly, both of the Polish patients presented with ulcerative colitis, although the pathogenic relationship between mucocutaneous and intestinal conditions was unclear [8]. In the latter case [2], unconventional medicine containing arsenic compounds was the most likely provocative factor for vegetating lesions on the skin and pyogenic granulomas on the conjunctivas, since the patient began taking arsenic five months beforehand.

MMP may be induced by infections and drugs [10,11], including medications [12,13]. In the present case, the patient's chronic cannabis use might have been the trigger for the CPV. Another argument in favor of this hypothesis is the patient's young age.

Corticosteroid therapy was the treatment of choice for all the authors, with the dose varying from 0.5 to 1 mg/kg/day. Dapsone at a dose of 100 mg a day was added in the case of three patients, including ours, and Salazopyrine in one patient in combination with corticosteroid therapy.

We have reported the first case of vegetative cicatricial pemphigoid treated with a bolus of corticosteroid therapy and rituximab without a relapse after a one-year monitoring period (Table 1).

CONCLUSION

Although cicatricial pemphigoid vegetans is a very uncommon subunit of mucous membrane pemphigoid, it is important to consider it when faced with severe synechial mucosal damage associated with vegetative cutaneous lesions. It may affect young individuals as well; in these cases, it is important to look for the induced forms. The severe forms may be treated by targeted therapy with rituximab.

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.

REFERENCES

1. Murrell DF, Marinovic B, Caux F, Prost C, Ahmed R, Wozniak K, et al. Definitions and outcome measures for mucous membrane pemphigoid: Recommendations of an international panel of experts. J Am Acad Dermatol. 2015;72:168-74.
2. Jakubowska B, Kowalewski C, Ishii N, Hashimoto T, Wozniak K. Vegetating erosive cutaneous lesions and pyogenic granuloma in the course of mucous membrane pemphigoid: A case report and review of literature. Int Wound J. 2018;15:909-13.
3. Reeves GMB, Lloyd M, Rajlawat BP, Barker GL, Field EA, Kaye SB. Ocular and oral grading of mucous membrane pemphigoid. Graefes Arch Clin Exp Ophthalmol. 2012;250:611-8.
4. Chan LS, Ahmed AR, Anhalt GJ, Bernauer W, Cooper KD, Elder MJ, et al. The first international consensus on mucous membrane pemphigoid: Definition, diagnostic criteria, pathogenic factors, medical treatment, and prognostic indicators. Arch Dermatol. 2002;138:370-9.
5. Winkelmann RK, Su WP. Pemphigoid vegetans. Arch Dermatol. 1979;115:446-8.
6. Kuokkanen K, Helin H. Pemphigoid vegetans. Report of a case. Arch Dermatol. 1981;117:56-7.
7. Al-Najjar A, Reilly GD, Bleehen SS. Pemphigoid vegetans: A case report. Acta Derm Venereol. 1984;64:450-2.
8. Wolff K, Rappersberger K, Steiner A, Konrad K. Vegetating cicatricial pemphigoid. A new subset of the cicatricial pemphigoid spectrum. Arch Dermatol Res. 1987;279 Suppl:S30-7.
9. Narbutt J, Ciepłowska K, Drewnik A, Olejniczak-Staruch I, Słowik-Rylska M, Kowalewski C, et al. Cicatricial pemphigoid vegetans in a Polish woman. Int J Dermatol. 2015;54:e317-9.
10. Kanahara SM, Agrawal A. Drug-induced bullous pemphigoid. J Gen Intern Med. 2016;31:1393-4.
11. Stavropoulos PG, Soura E, Antoniou C. Drug-induced pemphigoid: A review of the literature. J Eur Acad Dermatol Venereol. 2014;28:1133-40.
12. Thorne JE, Anhalt GJ, Jabs DA. Mucous membrane pemphigoid and pseudopemphigoid. Ophthalmology. 2004;111:45-52.
13. Cozzani E, Di Zenzo G, Cioni M, Javor S, Altieri M, Anselmi L, et al. Is gliclazide a new antidiabetic drug implicated in the pathogenesis of ocular mucous membrane pemphigoid? Eur J Dermatol. 2018;28:396-7.

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