DOI: 10.7241/ourd.20123.37

NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

SERUM LEVELS OF INTERLEUKIN-1 (IL-1A, IL-1B) IN PATIENTS WITH ALOPECIA AREATA

STĘŻENIE INTERLEUKINY-1 (IL-1A, IL-1B) U CHORYCH NA ŁYSIENIE PLACKOWATE

Emina Kasumagić-Halilovic, Nermina Ovcina-Kurtovic

Department of Dermatovenereology, Sarajevo University Clinical Center, Sarajevo, Bosnia and Herzegovina

Corresponding author: Emina Kasumagić-Halilovic, MD PhD *kasumagicemina@yahoo.com*

Our Dermatol Online. 2012; 3(3): 161-163

Date of submission: 09.04.2012 / acceptance: 09.05.2012

Conflicts of interest: None

Abstract

Introduction: Alopecia areata (AA) is disease characterized by focally, nonscarring hair loss on the scalp or other parts of the body. It affects 1-2% population of both genders and occurs at all age groups. The etiology is unknown, although most evidence supports the hypothesis that AA is a T-cell-mediated autoimmune disease of the hair follicle and that cytokines play an important role.

Objective: The aim of our study was to evaluate serum concentrations of IL-1α and IL-1β in patients with AA and healthy subjects and also to asses a possible association between these cytokines and duration of the disease.

Methods: Forty six patients with AA and 20 healthy controls were enrolled in the study. Serum concentrations of IL-1α and IL-1β were measured using enzyme-linked immunoassay techniques.

Results: The serum level of IL-1α in patients with AA was significantly higher than that in the control group (4.34±0.86 pg/mL vs 3.66±0.35 pg/mL, respectively). IL-1β levels were greater in patients with AA than in controls (2.35±0.17 pg/mL vs 2.24±0.30, respectively) but the difference was not significant ($p>0.05$). No correlations were found between duration of disease and the serum levels of IL-1α and IL-1β.

Conclusion: Our results have demonstrated the importance of determining IL-1a concentration in serum in patients with AA. This research could contribute to the interpretation of insufficiently well known views of the pathogenesis role and significance of IL-1α in AA.

Streszczenie

Wstęp: Łysienie plackowate to choroba charakteryzująca się ogniskowym, niebliznowaciejącym łysieniem skóry głowy lub też innych okolic ciała. Choroba ta dotyka 1-2% populacji, bez predylekcji płci ani też wieku. Etiologia choroby pozostaje nieznana, jednakże najwięcej dowodów potwierdza hipotezę, że AA jest chorobą autoimmunologiczną mediowaną za pomocą komórek T, zajmującą korzeń włosa oraz że cytokiny pełnią w tym procesie ważną rolę.

Cel: Celem naszego badania było oszacowanie stężenia w surowicy interleukin: IL-1α i IL-1β u pacjentów z AA oraz u osób zdrowych by wykazać możliwe związki pomiędzy tymi cytokinami a długością trwania choroby.

Metody: Do badania zakwalifikowano 46 pacjentów z AA oraz 20 osób zdrowych. Stężenia cytokin IL-1α i IL-1β były mierzone za pomocą techniki EIA.

Wyniki: Poziomy IL-1α u chorych na AA był znacznie wyższy niż ten w grupie kontrolnej (4.34±0.86 pg/mL vs 3.66±0.35 pg/mL, odpowiednio). Poziomy IL-1β były większe u pacjentów z AA niż w grupie kontrolnej (odpowiednio 2.35±0.17 pg/mL vs 2.24±0.30) jednak statystycznie nieistotne ($p>0.05$). Nie znaleziono korelacji pomiędzy trwaniem choroby a poziomami interleukin IL-1α i IL-1β w surowicy krwi.

Wnioski: Nasze wyniki badań dowodzą wagi pomiaru stężenia IL-1a w surowicy krwi osób chorych na AA. To badanie może przyczynić się do nie do końca poznanej roli IL-1α w patogenezie oraz odkryciu pełnego znaczenia w Alopecia Areata.

Key words: alopecia areata; cytokines; interleukin-1a; interleukin-1β

Słowa klucze: łysienie plackowate; cytokiny; interleukina-1a; interleukina-1β

Introduction

Alopecia areata (AA) is heterogeneous disease characterized by nonscarring hair loss on the scalp or other parts of the body. It affects 1-2% population of both genders and occurs at all age groups [1]. A wide range of clinical presentation can occur-from a single patch of hair loss to complete loss of hair on the scalp (alopecia totalis-AT) or the entire body (alopecia universalis-AU). The course of AA is usually characterized by phases of acute hair loss followed by spontaneous hair regrowth. However, in severe forms hair loss can persist for many years or even life. Although the etiopathogenesis of the disease is not clear, several studies have shown that within the cascade of pathogenesis of AA, cytokines play a crucial role.

It is also considered that a disequelibrium in the production of cytokines, with a relative excess of proinflammatory, versus antiinflammatory cytokines may be involved in the persistence of AA lesions [2-4]. Hair loss may occur because proinflammatory cytokines interfere with the hair cycle, leading to premature arrest of hair cycling with cessation of hair growth [5]. This concept may explain typical clinical features of AA such as a progression pattern in centrifugal waves [6] and spontaneous hair regrowth in concentric rings [7], suggesting the presence of soluble mediators within affected areas of the scalp. Interleukin 1 (IL-1) is a multifunctional proinflammatory cytokine, which has been implicated in the pathogenesis of several chronic inflammatory disorders with an autoimmune component. There are two forms of IL-1: IL-1α and IL-β. Both forms of IL-1 bind to the same receptor and therefore also show similar if not identical biological activities. Studies have shown that IL-1 is a very potent inducer of hair loss and a significant human hair growth inhibitor in vitro [8,9].
Literature data on serum IL-1 in patients with AA are very limited. Therefore, the aim of our study was to evaluate serum concentrations of IL-1α and IL-1β in patients with AA and healthy subjects and also to asses a possible association between these cytokines and duration of the disease.

Methods

The study included 46 patients (29 females and 17 males, median age 36.5, ranging from 5 to 69 years) who presented to the Dermatological Clinic with complaints of hair loss and were diagnosed with AA. Patients with any scalp disorders such as irreversible alopecia, trichotillomania and scalp psoriasis were excluded from the study. The patients who had received any treatment within previous 3 months were excluded from the study, as well as patients with any diseases based on the immune pathomechanism, which could influence serum concentrations of IL-1.

According to the duration of disease, patients were divided into 3 groups:
1. Duration for 6 months or less,
2. Duration of greater than 6 months, but less than 12 months,
3. Duration for year or longer.

The control group consist of 20 generally healthy people (11 females and 9 males, age range 6-63, median age 32.6 years). They did not have any scalp lesions in their personal history or on clinical examination. All subjects gave their informed consent in accordance with the requirements of the Institutional Ethics Committee.
Serum concentrations of IL-1α and IL-1β were measured by an enzyme-linked immunosorbent assay (ELISA) technique, using Quantikine Human IL-1α and IL-1β Immunoassay (R&D Systems, Minneapolis, USA). Briefly, a microplate was coated with a monoclonal antibody that was specific for the cytokines, and standards and samples were pipetted into the wells. After washing, an enzyme-linked polyclonal antibody that was specific for the cytokines was added. The reaction was revealed by addition of the substrate solution. The color development was stopped and the intensity of the color was measured at 450 nm with a photometar (Rider Biotek Elx800).

The data are expressed as mean±standard deviation. The test distribution was done by Kolmogorov-Smirnov test, and comparisons were performed by T-test. The data were considered statistically significant if p values were less than 0.05. Statistical analyses were done by the SPSS software.

Results

In our study, the mean serum IL-1α level in AA patients was 4.34±0.86 pg/mL (mean±SD), with 20% of variation and range 3.40 to 7.10 pg/mL (Tabl. I). Patients with shorter duration of the disease had higher concentration of IL-1α, but not significantly (p>0.05). Correlation between the duration of the AA and concentration of IL-1α: r = +0.273; ρ(rho)=0.097; 95%C.I. (-0.160; 0.343); p>0.05; n.s. Among controls, IL-1α mean is 3.66 pg/mL, with 9% of variation, standard deviation was ±0.35 and range 2.60 to 4.30 pg/mL. Statistical analysis showed significant differences between IL-1α values of patients with AA and healthy controls (p=0.006).
The mean serum level IL-1β in AA patients was 2.35±0.17 pg/mL (mean±SD), with 7% of variation and range 2.10 to 2.60 pg/mL. There was no correlation between the duration of AA and serum IL-1β concentration: r =0.196; ρ(rho)=0.177; 95%C.I. (-0.080; 0.413); p>0.05; n.s. Among controls, IL-1β mean is 2.24 pg/mL, with 13% of variation, standard deviation was ±0.30 and range 1.90 to 3.20 pg/mL. IL-1β levels were greater in patients with AA than controls, but the difference was not significant (p=0.3137).

	Alopecia areata	Control group
Number of patients	46	20
Age (year; mean±SD)	36.5±16.5	32.6±16.1
IL-1α (mean±SD)	4.34±0.86	3.66±0.35
IL-1β (mean±SD)	2.35±0.17	2.24±0.30

Table I. Characteristics of all patients in the study

Discussion

Although the pathogenesis of AA is still poorly understood, a perifollicular, peribulbar and perivascular accumulation of T lymphocytes provide evidence that an immune process is involved, interfering with the hair cycle and leading to reversible hair loss. Recent progress in the understanding of AA has shown that the regulation of local and systemic cytokines play an important role in its pathogenesis [9,10]. In their study, Harmon and Nevis investigated the effects of IL-1α on hair follicle growth and hair fiber production in vitro [11]. They found that incubation with IL-1α resulted in a significant inhibition of DNA synthesis, rapid antiprolliferative effect on hair follicle and inhibition of hair fiber growth.

These observations suggest that IL-1 may play a role in the pathogenesis of AA through direct inhibitory effects on the hair follicle, in addition to its putative proinflammatory role mediated by stimulation of cells of the immune/inflammatory system. Additionally, experiments in cultured human hair follicles by Hoffmann et al. showed that IL-1β completely abrogated hair growth [12]. In vivo studies have shown that IL-1α protects hair follicle from the cytotoxic effects of chemotherapy agents and it has been suggested that this protection may occur as a result of inhibition of hair follicle matrix cell division by IL-1α [13,14]. In vitro studies have shown that IL-1α along with IL-1β and TNF-α, causes vacuolation of matrix cells within the follicle bulb and a decrease in the size of the matrix, as well as disorganization of follicular melanocytes and abnormal differentiation and keratinization of the precortal cells and the inner root sheath [15]. These changes in hair follicle morphology are similar to those reported in AA and suggest that IL-1α and IL-1β may play an important part in the pathophysiology of inflammatory hair disease. Tarlow et al. demonstrated an association between the severity of AA and the frequency of allele 2 of a 5 allele polymorphism in intron 2 of the interleukin 1 receptor antagonist gene [16]. IL-1 gene polymorphysms may be responsible for exaggerated release of IL-1, leading to rapid and more progressive disease. This allele is also associated with severity in other chronic inflammatory autoimmune disorders including systemic lupus erythematosus and psoriasis [17].

In addition, increased serum levels of IL-1α in patients with AA compared with normal controls has been reported, further suggesting a role for this cytokine. The results presented in our study demonstrated that the mean serum levels of IL-1α were significantly elevated in AA patients in comparison to healthy subjects (4.34±0.86 pg/mL vs 3.66±0.35 pg/mL, respectively). Patients with shorter duration of the disease had higher concentration of IL-1α, but not significantly. These results are consistent with a clinical study performed by Teraki et al. [18]. They also recorded a significant increase in serum IL-1α in patients with AA, and there was an inverse correlation between disease duration and the serum levels of IL-1α. After that, Barahmani et al. analyzed serum cytokine profiles in 269 patients with AA and found it that increased IL-1α levels is associated with AA and atopy [19].

A limited number of studies in the literature have evaluated the serum levels of IL-1β in patients with AA. In the study of Nada et al. serum levels of IL-1β in patients with AA did not differ from that in controls [20].

The importance of serum cytokines in dermatology is increasing dramatically. We think that the high serum levels of IL-1α indicate the activation of the immune system in AA and may have a patophysiological role in the disease. Further investigation are required to clarify the pathogenetic role and clinical significance of IL-1, and these findings may provide important clues to assist in the development of new therapeutic strategies for patients with AA.

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