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Original Research Article

Serum osteopontin levels in disseminated allergic contact dermatitis

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ABSTRACT

Purpose: The aim of the study was to evaluate serum osteopontin (OPN) concentrations in patients with disseminated form of allergic contact dermatitis (ACD), and to assess the relationship between serum OPN level and disease severity.
Patients and methods: Twenty-four patients with numerous allergic contact dermatitis lesions and twenty-two age- and sex-matched healthy subjects as a control group were enrolled in the study. Serum osteopontin levels were measured in the ACD patients twice: in the acute stage and during disease remission by ELISA.
Results: Serum OPN concentrations were significantly increased in patients with disseminated ACD examined in the acute stage as compared to healthy subjects and ACD patients during remission ($p < 0.01$ and $p < 0.001$, respectively). In the ACD patients with extensive skin lesions (EASI > 10), OPN serum levels were significantly higher than in those with mild disease (EASI < 10).
Conclusions: Acute disseminated ACD is characterized by elevated serum concentrations of osteopontin, with levels depending on ACD severity, which indicates its role in the elicitation phase of allergic contact dermatitis. The possibility of inhibition of OPN activity may create a new therapeutic perspective in severe forms of this troublesome skin disease.

1. Introduction

Allergic contact dermatitis (ACD) is a frequent inflammatory skin disease affecting 15–20% of the general population [1,2]. The development of ACD is attributed to the specific T lymphocyte dependent reaction of delayed hypersensitivity. The reaction consists of 2 phases: the induction of hypersensitivity leading to clone proliferation of antigen-specific effector T lymphocytes and the elicitation phase developing after re-exposure to hapten and resulting in inflammatory skin reaction. The effector cells in contact hypersensitivity reaction are both CD8+ (Tc1) and CD4+ (Th1 and Th17) T lymphocytes. Most commonly ACD skin lesions are limited to the site of contact with allergen and the adjacent area but in some cases may disseminate or even generalize. The mechanisms responsible for development and the course of skin inflammatory reaction in ACD are complex and not fully clarified; the significant role of regulatory T cells has been documented [3,4]. Recently the significance of osteopontin in the development of allergic contact dermatitis has been indicated [5].

Osteopontin (OPN) is an acidic phosphoglycoprotein with diverse biological functions. It is secreted by multiple tissue types and different cells, including immune cells: T and B lymphocytes, dendritic cells and macrophages [6–8]. Two isoforms of osteopontin, i.e. secreted (sOPN) and intracellular (iOPN), have been identified. The functions and the relationship between these isoforms have not been fully explained [9,10]. The contribution of osteopontin to the immune delayed type reactions in infectious, autoimmune and neoplastic diseases has been established [8,11]. Recent investigations have shown the significance of OPN in the immediate and delayed types of allergic reactions [12]. More recent studies have also indicated the role of osteopontin in allergic contact dermatitis. Seier et al. found that osteopontin-deficient mice developed markedly reduced contact hypersensitivity (CHS) reactions and showed that keratinocytes and immune cells i.e. T lymphocytes and dendritic cells secreted great amounts of osteopontin in eczema skin lesions [13]. Osteopontin was strongly

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induced especially in effector T lymphocytes in the skin [13], which may contribute to the clinical course of allergic contact dermatitis. It is unknown if the upregulation of OPN in the skin is accompanied by its increased level in the blood.

The study objective was to evaluate serum osteopontin concentrations in patients with disseminated form of allergic contact dermatitis and to assess relationship between serum OPN level and intensity of skin lesions.

2. Patients and methods

Twenty-four adult patients (10 male and 14 female) with disseminated form of allergic contact dermatitis (ACD) were included in this study. Allergic contact dermatitis was diagnosed on the basis of a detailed history taken before and verified after patch testing as well as on the basis of the clinical picture of skin lesions. The patients with the presence of at least 2 foci of allergic contact dermatitis were enrolled in the study. Severity and extent of skin lesions were assessed using the Eczema Area and Severity Index (EASI) scoring system introduced by Hanifin and Rajka [14] for the estimation of atopic dermatitis lesions and adapted by authors in ACD [15]. The bacterial infection was excluded in all patients on the basis of clinical signs and normal C-reactive protein level. Twenty-two age and sex-matched healthy subjects with negative history of any kind of allergy served as a control group. In patients with allergic contact dermatitis peripheral blood samples were collected twice: in the acute stage, before the beginning of treatment and then during remission of skin lesions. Serum osteopontin (OPN) levels were measured by ELISA (Human Osteopontin ELISA Kit, Quantikine R&D System) according to the manufacturer's instructions. The minimum detectable concentration of OPN ranged from 0.006 to 0.024 ng/ml. Results were presented as a mean of serum OPN levels (in ng/ml) and standard deviation calculated for each group of patients with ACD (exacerbation and remission) and healthy subjects. The data obtained from the study groups were compared with each other and with those of the control group using a paired two-tailed *t*-test and Mann–Whitney test. p value <0.05 was considered to be statistically significant.

3. Results

The demographic and clinical characteristics of the study and control groups are presented in Tables 1 and 2. The duration time of the skin lesions was 3.9 weeks on average (range 1–9). On examination, all patients had multiple typical eczema areas of inflammatory lesions showing undefined borders, with the presence of papules, vesicles and erosions. The mean eruption score in the study patients was 11.2 ± 6.6 (range 2.4–32.6). The mean serum secreted osteopontin levels in patients with allergic contact dermatitis examined in the acute stage of disease amounted to 61.46 ± 57.59 (range: 6.75–300.0) ng/ml and were significantly higher ($p < 0.001$) than in patients with remission (mean 35.11 ± 28.54; range: 5.5–137 ng/ml) and healthy subjects (mean 27.64 ± 14.13 ng/ml; range: 9.5–50), ($p < 0.01$), (Fig. 1). Comparison of the mean serum sOPN levels between ACD groups differing in the intensity of skin lesions showed significantly higher values in the group of patients with EASI > 10 scores as compared to those with mild changes ($p < 0.05$), (Fig. 2). In patients with skin lesions lasting less than 2 weeks, sOPN concentrations were increased in comparison with those having longer duration, the difference being close to the value of significance ($p = 0.07$), (Fig. 3).

Table 1
Demographic data of patients with allergic contact dermatitis and control group.

	ACD patients, n – 24	Control group, n – 22	p value
Age (years)			$p = 0.4293$
Mean ± SD	47.2 ± 16.8	43.7 ± 12.4	
Range	19–71	24–74	
Sex (% of men)	10/24 (41.7%)	9/22 (40.9%)	$p = 0.6217$

$p < 0.05$ – statistically significant.

Table 2
Duration and severity of the skin lesions in ACD patients.

Duration of lesions (weeks)	
Mean ± SD	3.9 ± 3.1
Range	1–9
EASI[a] score	
Mean ± SD	11.2 ± 6.6
Range	2.4–32.6

[a] Eczema area and severity index.

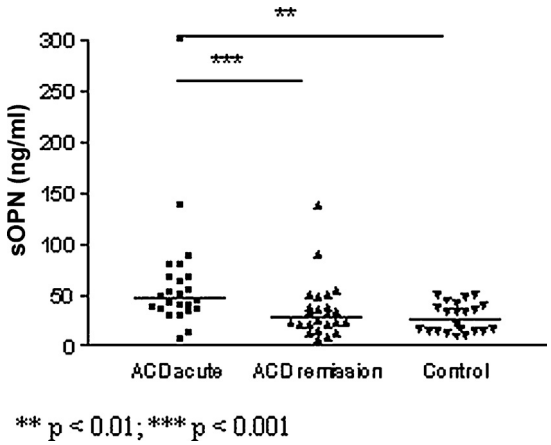

Fig. 1. By ELISA method the ACD patients have elevated OPN serum levels during acute stage of disease as compared with healthy persons and patients in remission ($p < 0.01$ and $p < 0.001$, respectively).

4. Discussion

The role of osteopontin in allergic contact dermatitis has been investigated mainly in the murine model of contact hypersensitivity reaction (CHS). The foremost study revealed the increased OPN expression during the sensitization phase of allergic contact dermatitis both in the skin and in the regional lymph nodes, occurring after hapten application (5). Further investigations showed a stimulating effect of secreted OPN on Langerhans and dendritic cell migration from epidermis to draining lymph nodes

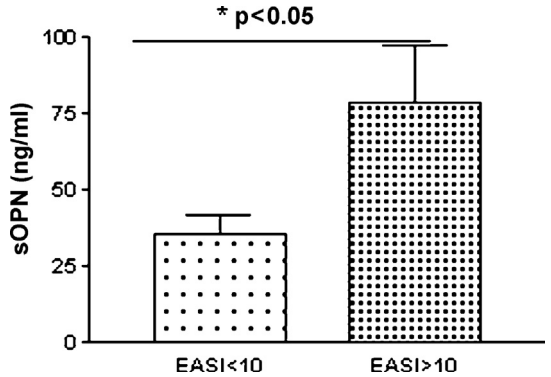

Fig. 2. Serum OPN levels are significantly higher in ACD patients with extensive skin lesions (EASI > 10) than in those with mild eczema (EASI < 10).