Increased Serum Level of P-Selectin in Patients with Lichen Planus

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Lichenplanus (LP) is a common, pruritic and inflammatory disease of the skin, hair follicles and mucous membranes. Immunologic mechanisms, especially cell-mediated immunity, play a major role in triggering the clinical expression of the disease. P-selectin is an adhesion molecule present within endothelial cells and mediates endothelial-leukocyte interactions. Therefore, it is considered that P-selectin plays an important role in LP. The aim of our study is to research the relation between P-selectin and LP.

Serum P-selectin levels were determined with the enzyme-linked immunosorbent sandwich assay method in sera from 40 LP patients and 40 healthy controls.

The serum levels of P-selectin were statistically significantly higher in the patients than in healthy controls ($p<0.05$), in female patients (39.32±11.34 pg/ml) than in male patients (31.93±9.83 pg/ml) ($p<0.01$), and in the patients with eruptive form (40.27 ± 9.32 pg/ml) than in those with the localised (32.83 ± 9.93 pg/ml) and hypertrophic (31.72 ± 8.39 pg/ml) forms (both $p<0.01$).

In conclusion, we found a meaningful relation between LP and serum P-selectin levels.

**Key Words:** Lichen planus, P-selectin

**INTRODUCTION**

Lichen planus (LP) is a common, pruritic and inflammatory disease of the skin, hair follicles and mucous membranes. There are several suggested mechanisms in the etiopathogenesis of LP and immunologic mechanisms certainly mediate its development. Leukocytes mediated (cell-mediated) immunity plays the major role in triggering the clinical expression of the disease.¹⁻³ P-selectin (GMP-140) is an adhesion molecule present within endothelial cells that is rapidly translocated to the cell membrane upon activation, where it mediates endothelial-leukocyte interactions.⁴ It is therefore thought that P-selectin plays an important role in LP which has an inflammatory process in its pathogenesis. The aim of our study is to research the relation between P-selectin and LP.

**MATERIALS AND METHODS**

The subjects of our study comprised; a healthy control group and a patient group. All subjects visited our clinic between September 2001 and November 2002. LP was diagnosed both clinically and histopathologically. The patients with systemic disease such as heart disease and hepatic disorder were excluded from the study. There were 40 patients (26 females, 14 males, 22-58 years of age, mean: 51.2 ± 10.4 years) and 40 controls (24 females, 16 males, 22-58 years of age, mean: 49.7 ± 10.8 years) in the study. Most of the subjects were between 30-40 years of age. There were no statistical differences in age or sex between patients and controls ($p>0.05$). The duration of the disease in these patients varied from 2 to 60 months (mean: 16.04 ± 20.8 months). On dermatological examination, all 40 patients (100%) had lesions located on the skin, 29 (72.5%) on the skin alone, and 11 (27.5%) on the skin and oral mucosa. Skin lesions were located on different areas including the trunk, extremities, face and genital region. There was oral involvement in 12 patients; in 8 (66.64%) the lesions were...
located on the buccal mucosa bilaterally and in 4 (33.32%) on the dorsum of the tongue. Reticular, papular, and plaque lesions were seen in these patients. Clinical data on patients are presented in Table 1.

For studying P-selectin, 5 ml of venous blood for human P-selectin assay were collected from each subject in vacutainers without additive, allowed to clot for 30 minutes at room temperature, and centrifuged at 3000 rpm for 5 minutes. The serum aliquots were stored immediately at -80°C until analysis. Serum P-selectin levels were assayed by the enzyme-linked immunosorbent sandwich assay method using a commercial kit (Bendermed Systems Diagnostic, Austria, Kit no: BMS 219/2). The lower limit of detection for P-selectin was 1.3 ng/ml, the-intra and-inter-assay co-efficients of variations were 2.4 and 5.5%, respectively. All results were evaluated with Mann-Whitney-U test.

RESULTS

The mean values of P-selectin serum levels detected in LP patients and healthy controls are presented in Table 2. The serum levels of P-selectin were statistically significantly higher in the patients than in healthy controls \( p<0.05 \) and in female patients \( (39.32 \pm 11.34 \text{ pg/ml}) \) than in male patients \( (31.93 \pm 9.83 \text{ pg/ml}, p<0.01) \).

In terms of oral involvement, the mean serum level of P-selectin in the patients with oral involvement \( (35.83 \pm 7.2 \text{ pg/ml}) \) was slightly higher than that in the patients without oral involvement \( (33.77 \pm 8.4 \text{ pg/ml}) \) but the difference was not significant \( (p>0.05) \).

There were no statistically significant differences in the levels of serum P-selectin between patients with localised and hypertrophic forms \( (p>0.05) \). However, the levels were statistically significantly higher in the patients with eruptive form \( (40.27 \pm 9.32 \text{ pg/ml}) \) than in those with localised \( (32.83 \pm 9.93 \text{ pg/ml}) \) and hypertrophic \( (31.72 \pm 8.39 \text{ pg/ml}) \) forms, (both \( p<0.01 \)).

DISCUSSION

It has been suggested that T-cell mediated autoimmune reaction is involved in LP pathogenesis. In LP histopathology, the hydropic degeneration of the basal cell layer and the broad sub-epithelial band of predominantly activated T cells are most

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prominent. The migration of T cells at sites of inflammation requires various T cell surface adhesion receptors and molecules that mediate binding to keratinocytes and other resident cells of the mucosa and skin as well as to the extracellular matrix proteins, collagen, fibronectin and laminin. There is some evidence that the characteristic histopathological alterations in LP depend on a T cell mediated immune response caused by antigenic modification in the skin and mucosa. Cell surface adhesion receptors and molecules are crucially involved in the migration of T cells and in the interactions of activated T cells during immune response. On the other hand, the typical histopathologic alterations in LP are due to a multiplicity of cell-cell and cell-matrix interactions regulated by cytokines that induce adhesion molecule expression and by localized changes of the avidity state of adhesion receptors. Recent studies have demonstrated the crucial involvement of adhesion molecules in LP pathogenesis.\textsuperscript{26-8}

The selectins belong to an identified family of cell surface glycoproteins that play important roles as adhesion molecules and appear to be the initial adhesion molecules that influence the properties of leukocytes at the initiation of the inflammatory process.\textsuperscript{9} Localization of neutrophils to inflammatory sites involves a series of precisely regulated events ultimately leading to their emigration from the circulation to the tissues. Rolling of neutrophils along the lining of post capillary venules might represent the first event bringing in close contact neutrophils and endothelial cells during an inflammatory reaction. This initial interaction of neutrophils with the blood vessels is probably necessary before a more complete attachment and extravascular migration can occur. Some recent studies indicate that adhesion molecules present on both neutrophils and endothelium participate in the rolling process.\textsuperscript{10}

P-selectin, previously known as platelet activation dependent granule-external membrane protein (P ADGEM) or granule membrane protein -140 (GMP-140) is a member of the selectin family of cell surface adhesion molecules which mediate the interaction of leukocytes with the endothelial lining of blood vessels.\textsuperscript{11,15} P-selectin, a glycoprotein, is located in alpha granules of platelets and Weibel-Palade bodies of endothelial cells, and is translocated within seconds or minutes to the cell surface without the need for new protein synthesis after the factor triggering inflammation. P-selectin mediates the interaction of granulocytes with platelets and stimulated endothelium in the region of tissue injury leading to platelet-leukocyte binding and granulocytes from endothelium-mediated fibrin deposition during inflammation.\textsuperscript{9,14-16} P-selectin plays an essential role in leukocyte rolling in vivo and therefore may be a key participant of the inflammatory response. It is believed to participate in transient neutrophil attachment to endothelium. Therefore, P-selectin plays an important role in the inflammatory process.\textsuperscript{10} LP has also an inflammatory component so that its pathogenesis is related to P-selectin.

In our study, we found a meaningful relation between LP and serum p-selectin levels. There were statistically significant differences between female and male patients in terms of the serum P-selectin levels. Probably, this difference is due to the fact that eruptive forms of females were more excessive than those of males in this study. The serum levels of P-selectin of both the male and female patients with eruptive form were statistically significantly higher than those with localised form. These results may show that statistically meaningful differences between female and male patients in terms of the levels of serum P-selectin are related to clinical subtypes. In conclusion, we don't think that there is a real difference between male and female patients with LP.

In addition to LP, P-selectin was increased in a lot of immunological diseases such as Behcet's disease,\textsuperscript{17} systemic lupus erythematosus,\textsuperscript{18} autoimmune rheumatologic diseases\textsuperscript{19} and scleroderma.\textsuperscript{20}

LP has many different clinical forms with different natural courses, so to perform broad and randomized studies on LP is difficult. Furthermore, no standardized methods exist to evaluate the severity of the disease, there are no consensual criteria of improvement or cure and the course of the disease is varies from one patient to another and according to the clinical form. Therefore, we evaluated our patients according to clinical forms, rather than according to clinical forms of disease, sex and oral involvement because there is not any knowledge about these issues.
According to the only previous study about LP and P-selectin in the literature, performed by Regezi JA, increased staining for P-selectin was shown histopathologically in one or more of the microvascular compartments in patients with LP.21 Interestingly, our study is only second study in the literature about P-selectin in LP, and is the first about the serum levels of P-selectin in LP.

REFERENCES