Renal Involvement in Psoriasis

O.		Kaftan ^a
B.		Kaftan ^c
M.F.		Toppare ^b
M.		Ekşioğlu ^c

Departments of ^aInternal Medicine and ^bPediatrics, Turkish Health and Therapy Foundation Medical Center Hospital, and ^cDepartment of Dermatology, Ankara Hospital, Ankara, Turkey

Key Words

Psoriasis
Kidney dysfunction
 β_2 -Microglobulin
Microvasculature

Dr. Mete F. Toppare, Alaçam Sok. No 12/12, Çankaya 06690 Ankara (Turkey)

In psoriasis, the presence of intercellular adhesion molecule 1, endothelial leukocyte adhesion molecule and angiogenic factor in the dermal papillary vascular endothelium predicts microvascular involvement [1]; however, evidence of systemic vascular involvement is still scarce. In psoriatic patients with diffuse involvement, renal impairment and cardiovascular diseases are reported to occur [2]. We have recently studied the renal functions of psoriatic patients with moderately extensive skin involvement in search of kidney dysfunction.

Thirty-five patients with histologically documented psoriasis were enrolled as the patient group after informed consent had been obtained. The duration of the disease, the disease severity (%) and the ESI score (erythema, squame, inflammation) were recorded. A group of healthy and age-matched controls (n = 36) was also included. Serum albumin, blood urea nitrogen (BUN), serum creatinine, routine urinalysis, urine creatinine, creatinine clearance, urine microalbumin and urine β_2 -microglobulin were quantitatively determined in the patient and control groups. All the subjects in both groups underwent renal ultrasonographic examination.

Urine β_2 -microglobulin was determined by a solid-phase immuno-radiometric assay (Coat-A-Count IRMA). The assay was based on monoclonal and polyclonal anti- β_2 -microglobulin antibodies: one I25-I-labeled anti- β_2 -microglobulin monoclonal antibody in liquid phase and one polyclonal anti- β_2 -microglobulin antibody immobilized to the wall of a polystyrene tube. The pH of urine was adjusted to 7 adding 1.0 M NaOH. The samples were then stored at -20 °C for a period of not more than 4 weeks until analysis. Urine microalbumin was determined by a competitive radioimmunoassay in which I2T-labeled albumin competes with albumin in the patient sample for antibody sites. The procedure has a detection limit of approximately 0.3 µg/ml.

The general characteristics of the groups are given in table 1. All the measured parameters of renal functions with the exception of β_2 -microglobulin (p = 0.047) were similar. Multiple regression analysis revealed that no factor significantly affected the β_2 -microglobulin levels;

however, disseminated skin lesions significantly affected micro-albumin excretion ($p = 0.001$). There were correlations between cre-

Table 1. General characteristics of the study population and controls

atinine clearance and β_2 -microglobulin ($p = 0.047$) and between urinary microalbumin and the ESI score of the patients ($p = 0.014$). Duration of the disease did not have any effect on urinary β_2 -microglobulin or albumin excretion. All renal ultrasonograms were normal in the controls and in the study group.

Urinary albumin excretion in small amounts is accepted to be due to glomerular endothelial dysfunction. The amounts exceeding 30 mg/24 h reflect widespread vascular damage [3]. Although all our cases had urinary albumin levels below pathological limits, it is not clear why the mean level in the patient group was somewhat elevated compared to controls.

To the best of our knowledge, this is the first report on urinary excretion of β_2 -microglobulin in psoriasis. β_2 -Microglobulin was first isolated in 1968 from the urine of patients with Wilson's disease and was subsequently found to be elevated in cadmium poisoning [4]. It has since been identified as the light chain of the HLA-A, -B and -C major histocompatibility complex antigens. In structure and amino acid sequence, it resembles the CH3 region of IgG, though it is antigenically distinct. β_2 -Microglobulin occurs on the surface of nucleated cells – particularly abundantly on lymphocytes and monocytes – and on many tumor cell lines. It has been reported to be elevated in urine in several conditions like rheumatoid arthritis [5] and Kawasaki disease [6]. Rates higher than 370 $\mu\text{g}/24\text{ h}$ are interpreted as evidence of tubular dysfunction [7]. Though in the present study, there was a significant difference between the patient and control groups, the results were still within normal limits which is evidence against renal tubular involvement, and the lack of microalbuminuria is evidence

KARGER

E-Mail karger@karger.ch Fax+ 41 61 306 12 34

© 1996 S.KargerAG, Basel 1018-8665/96/1922-0189 \$ 10.00/0

against renal glomerular involvement in psoriatic patients with moderate skin involvement.

Although β_2 -microglobulin excretion is somewhat related to urine flow rate, and the effect of urinary flow upon the excretion rates of the various low-molecular-mass proteins has to be considered as a preanalytical factor when used as indicators of tubular dysfunction [8], the creatinine clearance was within normal limits in all the subjects, hence this could not be a significant affecting factor. The present study suggests that no occult deterioration of renal function could be attributed to psoriasis.

References

Barker JNWN: The pathophysiology of psoriasis. *Lancet* 1991 ;338: 227-230.

Ena P, Madeddu P, Glorioso N, Cerimele D, Rappelli A: High prevalence of cardiovascular diseases and enhanced activity of the renin angiotensin system in psoriatic patients. *ActaCardiol* 1985;15:199-205.

Deckert T, Rasmussen BF, Borch-Johnsen K, Jensen T, Kofoed-Enevoldsen A: Albuminuria reflects widespread vascular damage. *Diabetologia* 1989;32:219-226.

Nishijo M, Nakagawa H, Morikawa Y, Tabata M, Senma M, Kitagawa Y, Kawano S, Ishizaki M, Sugita N, Nismi M: Prognostic factors of renal dysfunction induced by environmental cadmium pollution. *Environ Res* 1994;64:112-121.

Saito M, Uechi Y, Nakabayashi K, Kitamoto K, Nagasawa T: Clinical significance of microalbuminuria in patients with rheumatoid arthritis. *Nippon Jinzo Gakkai Shi* 1993;35:815-821.

Ohta K, Seno A, Shitane N, Kato E, Yachie A, Seki H, Miyawaki T, Taniguchi N: Increased levels of urinary interleukin-6 in Kawasaki disease. *Eur J Pediatr* 1993;152:647-649.

Piscator M: Early detection of tubular dysfunction. *Kidney Int* 1991;34 (suppl):15-17.

Jung K, Pergande M, Porstmann B, Porstmann T: Diuresis-dependent excretions of low-molecular mass proteins in urine: Beta2 microglobulin, lysozyme, and ribonuclease. *Scand J Clin Lab Invest* 1988;48:33-37.

Dermatology 1996; 192:190

Mast Cells in Psoriasis

S.O. Özdamar, D. Seçkin, B. Kandemir, A.Y. Turanlı

Departments of

Pathology and

11 Dermatology, Ondokuz Mayıs University School of Medicine, Samsun, Turkey

Key Words

Psoriasis · Mast cells ■ Toluidin blue · Immunohistochemistry

Recent studies have shown that mast cells may play a role in the pathogenesis of psoriasis [1].

Toluidin blue reaction is the conventional method used for investigation of mast cells. Lysozyme (muramidase), α -antitrypsin (AAT), and CD68 antibodies are well-defined markers of histiocyte and monocyte lineage and these antibodies may react with mast cells.

The study included 20 patients with psoriasis vulgaris and 20 controls. The biopsy specimens for controls were obtained from healthy skin tissue of patients with basal cell carcinoma after excision. Lesional psoriatic skin and control specimens were fixed in 10% buffered formalin and embedded in paraffin wax. Sections were cut at 5 μ m and stained with 0.001% toluidin blue (pH 4.00); immunostaining was performed with the previously described streptavidin biotin peroxidase method [2]. The following antibodies were used: CD68 (KPl, monoclonal, mouse), AAT (polyclonal, rabbit), and lysozyme (polyclonal, rabbit) (Biogenex Laboratories, San Ramon, USA). The number of reactive cells was counted in 10 high power fields (HPF) (5 subepidermal, 3 middermal, 2 deep-dermal zones) (Nikon Optiphot-2 microscope, $\times$ 10 ocular, $\times$ 40 objective; 1 HPF = 0.125 mm²) [3]. Results are expressed as mean $\pm$ SEM. Student's t test was performed for statistical analysis.

The number of mast cells with positive toluidin blue reaction was significantly higher in lesional psoriatic skin (8.27 ± 0.66) than in controls (3.11 ± 0.41) ($p < 0.05$). The number of cells with positive CD68, AAT, and lysozyme staining was not significantly different between psoriasis and controls (table 1).

Table 1. Number of cells positive with CD68, AAT and lysozyme (mean $\pm$ SEM) (1 HPF = 0.125 mm²)

	CD68(KPl)	AAT	Lysozyme	Toluidin blue
Psoriasis	1.80 $\pm$ 0.18	2.08 $\pm$ 0.33	2.02 $\pm$ 0.47	8.27 $\pm$ 0.66
Control	1.96 $\pm$ 0.36	1.75 $\pm$ 0.16	1.52 $\pm$ 0.19	3.11 $\pm$ 0.41
	> 0.05	> 0.05	> 0.05	< 0.05

This study showed increased mast cells in psoriasis, and thus confirms previous reports [1, 4]. To our knowledge lysozyme, AAT and CD68 (KPl) antibodies have not been previously studied in

psoriasis and our investigation shows that the use of these antibodies does not reveal any difference between psoriasis and normal skin tissue.

There is different staining of mast cells with toluidin blue reaction and lysozyme, AAT, and CD68 (KPI) in psoriasis; the cause and significance of this difference remain to be defined by further studies.

References

Harvima IT, Naukkarinen A, Harvima RJ, Aalto M-L, Neittaanmaki H, Horsmanheimo M: Quantitative enzyme-histochemical analysis of tryp-tase- and chymase-containing mast cells in psoriatic skin. Arch Dermatol Res 1990;282:428-433.

Taylor CR, Cote RJ: Immunomicroscopy: A Diagnostic Tool for the Surgical Pathologist, ed 2. Philadelphia. Saunders, 1994, pp 34-106.

Wilkinson B, Jones A, Kossard S: Mast cell quantitation by image analysis in adult mastocytosis and inflammatory skin disorders. J Cutan Pathol 1992;19:366-370.

Schubert C, Christophers E: Mast cells and macrophages in early relapsing psoriasis. Arch Dermatol Res 1985;277:352-358.

Dr. Sükrü Özdamar, Ondokuz Mayıs University School of Medicine. Department of Pathology, Kurupelit, TR-55139 Samsun (Turkey)

19() Dermatology 1996;192:189-190

Letters to Dermatology