

Report

Markers of systemic inflammation in delayed pressure urticaria

Alicja Kasperska-Zajac¹, MD, PhD, Tatiana Jasinska², MD, PhD, Alicja Grzanka³, MD, PhD, and Agata Kowalik-Sztylec¹, MD

¹Clinical Department of Internal Diseases, Allergology and Clinical Immunology, Medical University of Silesia, Katowice, ²Department of Dermatology, Regional Specialised Hospital, Bytom, Poland, and ³Department of Internal Diseases, Dermatology and Allergology, Medical University of Silesia, Katowice, Poland

Correspondence

Dr Alicja Kasperska-Zajac, MD, PhD
Clinical Department of Internal Diseases
Allergology and Clinical Immunology
ul. Ceglana 35
40-925 Katowice, Poland
E-mail: kasperska@plusnet.pl

Conflict of interest: The authors have no conflict of interest.

doi: 10.1111/j.1365-4632.2011.05330.x

Delayed pressure urticaria (DPU) is characterized by deep dermal wheals and inflammatory infiltration consisting mainly of eosinophils. The inflammatory process is associated by a variety of mediators produced by mast cells and migrating leukocytes.^{1,2} Among these, interleukin-6 (IL-6) needs special attention, due to several reasons. Firstly, IL-6 activity has been significantly higher in lesional skin in DPU.² Secondly, IL-6 is a multifunctional cytokine produced by a wide range of cells and may contribute to initiation and extension of the inflammatory process.³ Thirdly, IL-6 is the main cytokine responsible for regulation of acute phase protein synthesis, including C-reactive protein (CRP); both are markers of systemic inflammation.^{4,5} Elevated circulating levels of IL-6^{6,7} and CRP^{7,8} have been demonstrated in chronic urticaria. In addition, it has been suggested that CRP and IL-6 may be useful markers of the disease activity.^{7,8} There is no information available to describe the behavior of the biomarkers of systemic inflammation in DPU. Therefore, the objective of this study was to determine the circulating levels of IL-6 and CRP in patients with DPU.

Eight symptomatic patients (five men and three women) of age range 28–43 years (mean 37 years) with

Abstract

Background We have previously reported, increased plasma IL-6 concentration in chronic urticaria. In addition, it has been suggested that IL-6 and C-reactive protein (CRP) may be useful markers of the disease activity.

Aim The aim of this study was to evaluate whether a systemic inflammation is present in delayed pressure urticaria (DPU).

Methods Plasma IL-6 and serum CRP concentrations, biomarkers of acute phase response, were measured in DPU, and the healthy subjects matched by age, gender, and BMI using ELISA method.

Results DPU patients showed significantly higher plasma IL-6 and serum CRP concentrations than the healthy subjects.

Conclusions Similarly to the known locally increased IL-6 activity in DPU lesions, the elevated circulating levels of IL-6 and CRP have been currently found in DPU. This indicates that the disease induces a systemic inflammatory process, termed the acute phase response.

pure DPU (without concomitant spontaneous chronic urticaria) were enrolled into the study, their clinical characteristics described previously.⁹ Briefly, three patients suffered from severe DPU, urticarial lesions still elicited even under slight pressure; five patients suffered from milder DPU. Less extensive urticarial lesions were observed mainly in two areas: the feet and the hands. At least three weeks before the examination, the patients ceased to take corticosteroids (except for one patient). The antihistamines were withdrawn two days before the study. Infection foci were excluded by appropriate examinations.

The control group consisted of 20 non-smoking healthy subjects compared by age, sex, and body mass index. Plasma IL-6 concentration was determined in plasma (ELISA; R&D Systems, Minneapolis, MN, USA). The turbidimetric latex agglutination method (BioSystems SA, Barcelona, Spain) was used to determine CRP concentrations.

The comparisons between groups were performed by Mann–Whitney's *U*-test. The correlation coefficient was obtained by Spearman test. *P*-values lower than 0.05 were considered significant.

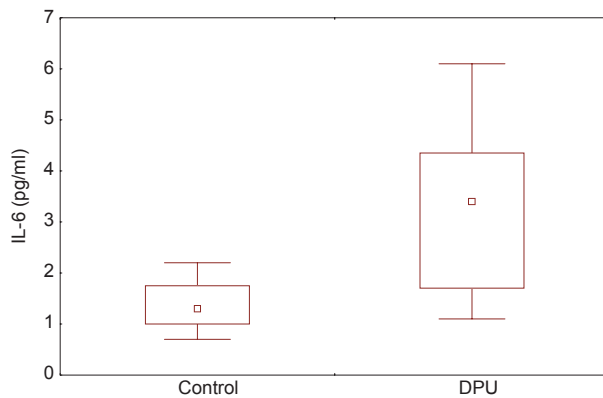


Figure 1 Plasma IL-6 concentration was significantly higher in patients with DPU compared with controls ($P = 0.0026$)

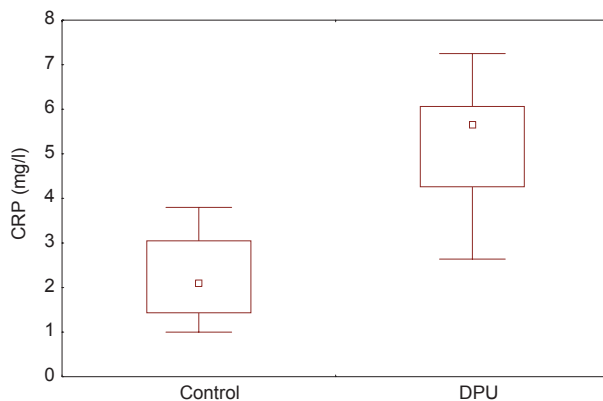


Figure 2 Serum CRP concentration was significantly higher in patients with DPU compared with controls ($P = 0.0003$)

Plasma IL-6 concentration was significantly higher in patients with DPU compared with the healthy subjects (Fig. 1). Also, serum CRP concentration was significantly higher in patients with DPU compared with the controls (Fig. 2). However, in two out of eight (25%) patients, serum CRP concentration remained within the normal range. There was a significant correlation between CRP and IL-6 concentration in patients with DPU ($r = 0.994$; $P < 0.001$). This is not surprising because CRP is produced mainly by hepatocytes under the control of IL-6.^{4,5} No statistical comparison was performed between the severe DPU and milder DPU groups, as both included too few patients (three and five, respectively). Therefore, no conclusions could be drawn to relate IL-6 concentration

to CRP scores upon the disease activity. The so-called pure DPU is very rare (about 94% of patients with DPU suffer from concomitant chronic urticaria).¹⁰ Exclusion of patients suffering from DPU concomitant with chronic urticaria would hamper interpretation of the results, as patients with chronic urticaria showed both increased IL-6^{6,7} and CRP^{7,8} concentrations. So far, cellular sources of IL-6 in DPU have not been established, while mast cells and infiltrating inflammatory cells might contribute to the release of IL-6.²

Because elevated circulating levels of IL-6 and CRP have been currently found in DPU, it indicates that the disease is accompanied by a systemic inflammation. Whether the elevated levels of the proteins contribute to the pathogenesis of DPU needs to be determined.

References

- 1 Czarnetzki BM, Meentken J, Kolde G, Bröcker EB. Morphology of the cellular infiltrate in delayed pressure urticaria. *J Am Acad Dermatol* 1985; 12: 253–259.
- 2 Lawlor F, Bird C, Camp RD, et al. Increased interleukin 6, but reduced interleukin 1, in delayed pressure urticaria. *Br J Dermatol* 1993; 128: 500–503.
- 3 Sehgal PB. Interleukin-6: molecular pathophysiology. *J Invest Dermatol* 1990; 94: 2S–6S.
- 4 Genest J. C-reactive protein: risk factor, biomarker and/or therapeutic target? *Can J Cardiol* 2010; 26(Suppl. A): 41A–44A.
- 5 Pepys MB, Hirschfield GM. C-reactive protein: a critical update. *J Clin Invest* 2003; 111: 1805–1812.
- 6 Kasperska-Zajac A, Brzoza Z, Rogala B. Plasma concentration of interleukin 6 (IL-6), and its relationship with circulating concentration of dehydroepiandrosterone sulfate (DHEA-S) in patients with chronic idiopathic urticaria. *Cytokine* 2007; 39: 142–146.
- 7 Kasperska-Zajac A, Sztylec J, Machura E, Jop G. Plasma IL-6 concentration correlates with clinical disease activity and serum C-reactive protein concentration in chronic urticaria patients. *Clin Exp Allergy* 2011; 41: 1386–1391.
- 8 Takahagi S, Mihara S, Iwamoto K, et al. Coagulation/fibrinolysis and inflammation markers are associated with disease activity in patients with chronic urticaria. *Allergy* 2010; 65: 649–656.
- 9 Kasperska-Zajac A, Jasinska T. Analysis of plasma D-dimer concentration in patients with delayed pressure urticaria. *J Eur Acad Dermatol Venereol* 2011; 25: 232–234.
- 10 Sussman GL, Harvey RP, Schocket AL. Delayed pressure urticaria. *J Allergy Clin Immunol* 1982; 70: 337–342.