

Correspondence

Increased D-dimer concentration in plasma of patients with severe acute urticaria

DOI: 10.1111/j.1365-2133.2009.09466.x

SIR, Acute urticaria (AU) is a skin disease frequently caused by different factors (drugs, infections, allergens, psychological stress), although the exact aetiology remains unidentified in many cases. The underlying pathophysiology of AU is mast cell activation.¹ The cells release different factors, which exert profibrinolytic and antithrombotic effects.^{2,3} Interestingly, it has been demonstrated that the coagulation cascade is activated in chronic urticaria⁴ and severe exacerbation of the disease is associated with elevated plasma D-dimer concentration.⁵ D-dimer is a useful marker, reflecting a potential activation of both the coagulation and fibrinolytic cascade. Considering that changes in the haemostasis system may contribute to the pathogenesis of some types of urticaria, in the present study we measured plasma concentrations of D-dimer in patients suffering from AU.

The study group consisted of 17 consecutive symptomatic patients (10 women and seven men; the median age was 32 years, range 21–42) with AU. The patients were divided into two groups by disease severity according to the criteria defined by Asero *et al.*⁵ Ten patients with severe AU were virtually covered by wheals (grade 4, very severe). Seven patients with mild/moderate AU had 1–10 small (< 3 cm in diameter) wheals (grade 1, slight) to 10–50 small wheals or 1–10 large wheals (grade 2, moderate). Five patients suffered from AU caused by nonsteroidal anti-inflammatory drugs; three patients had AU presumably in the course of acute respiratory tract infection; one suffered from AU and concomitant urinary tract infection treated with antibiotics (amoxicillin). In the remaining eight, the reasons for AU were unidentified. No patient had a history of chronic urticaria. The patients had not taken anti-urticarial drugs. Blood for analysis was taken within 24 h from the onset of symptoms. The control group consisted of 30 healthy subjects (23 women and seven men; the median age was 31 years, range 19–40), also described previously.⁶

Plasma D-dimer level was measured by enzyme-linked immunosorbent assay, following standard procedures (Asserachrom[®] D-Di kit; Diagnostica Stago, Asnieres sur Seine, France).

Data were determined as medians and interquartile ranges. Kruskal–Wallis variance analysis was used for screening differences between the groups. The Mann–Whitney

U-test was used to compare data between patient groups and healthy controls. The correlation coefficient was obtained using the Spearman test. P-values < 0.05 were considered significant.

D-dimer concentration was significantly higher in patients with severe AU compared with patients with mild/moderate AU and healthy subjects [2.6 (2.2–4.5) vs. 0.17 (0.05–0.18) and 0.14 (0.08–0.22) $\mu\text{g mL}^{-1}$, respectively; $P < 0.001$]. The values of plasma concentration of D-dimer were above the normal laboratory norms (< 0.5 $\mu\text{g mL}^{-1}$) in all patients with severe AU. There were no significant differences in plasma D-dimer concentration between patients with mild/moderate AU and the controls. In addition, in all subjects of the two groups D-dimer concentration was within normal laboratory range (< 0.5 $\mu\text{g mL}^{-1}$). There was no significant correlation between disease severity and plasma D-dimer concentration.

Data regarding the behaviour of the haemostasis system in AU are very scarce.⁷ In the present study, we found significantly elevated plasma concentration of D-dimer in patients with severe AU compared with patients with mild AU and healthy subjects. These data indicate that severe AU is accompanied by increased plasma fibrin turnover. D-dimer is a degradation product of cross-linked fibrin and its elevated concentration reflects increased fibrin formation, followed by degradation.⁸ Interestingly, fibrin degradation products exert pharmacological activity⁹ and enhance histamine action as well as other mediators of the inflammatory response.¹⁰ We did not observe any significant association between AU severity and plasma D-dimer concentration. Therefore, further studies are required to establish whether raised D-dimer or other factors of the coagulation and fibrinolysis cascade are an epiphenomenon or are actively involved in the pathophysiology of AU. Interestingly, Asero *et al.*⁵ suggested that activation of the coagulation cascade might contribute to the pathomechanism of chronic urticaria.

Taken together, it seems that in the course of acute severe urticaria enhanced fibrinolytic activity in the peripheral blood occurs, as expressed by increased plasma D-dimer concentration. The results noted above supplement some earlier observations made in the case of patients suffering from chronic urticaria⁵ and indicate that higher plasma D-dimer concentration is a common phenomenon shown in severe urticaria of both acute and chronic course. Further studies are needed to establish if D-dimer testing may be a prognostic factor in AU or used to identify candidates for anticoagulant therapy.

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Key words: acute urticaria, D-dimer, fibrinolysis

Conflicts of interest: none declared.