

Correspondence

No alteration of circulating testosterone concentration in patients with chronic urticaria with positive response to autologous serum skin test

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MADAM, The aetiology of chronic urticaria (CU) is unclear, but in many cases an autoreactive pathogenesis is proposed, which may be associated with presence of autoantibodies against both IgE and the high-affinity IgE receptor. An autologous serum skin test (ASST) is commonly used in clinical practice to assess autoreactivity, and a positive result suggests an auto-immune basis for the disease. Patients with CU with a positive ASST are more likely to have associated HLA-DR4. In addition, they have a longer disease course and their urticarial lesions may be less responsive to treatment with antihistamines than those with a negative ASST.^{1,2} A correct endocrine balance may be crucial for immune homeostasis. Naturally occurring sex hormones may predispose to and modulate the course of autoimmune diseases.³ Interestingly, it has been suggested that mast cells are regulated by the neuroimmunoendocrine system and that dysfunction of the system might be involved in the pathogenesis of CU (reviewed⁴). It has been demonstrated that testosterone modulates the immune response and exerts anti-inflammatory effects. In humans, the lack of testosterone may result in the enhancement of cellular and humoral immunity.⁵ In addition, this hormone may retard the progress of autoimmunity.⁶ A growing body of evidence suggests that mast cell function is regulated by testosterone.⁷ Interestingly, the synthetic derivative of testosterone, stanozolol, was effective in the treatment of urticaria.⁸ However, it is unclear whether endogenous sex hormones may contribute to pathogenesis of CU.⁴ In the present study, we investigated whether there are differences in serum concentration of total testosterone

between patients with CU with positive reactivity to ASST and healthy subjects.

The study group consisted of 68 patients (24 men and 44 women; median age 37 years, range 24–50, and 34 years, range 19–44, respectively) with CU, all identified causes of urticaria having been excluded by appropriate investigation. All the patients showed a positive response to ASST. Blood tests did not reveal the presence of thyroid antibodies. Their disease was characterized by recurrent hives occurring at least four times a week for more than 6 weeks. Daily urticarial activity was measured by assessment of weals and pruritus on a scale of 0–3 (sum of scores: 0–6) according to Zuberbier *et al.*² The patients had not taken systemic steroids for more than 12 weeks preceding the study. All other therapy (antihistamines) had been discontinued at least 3 days before the study. The control group consisted of 75 healthy subjects (29 men and 46 women; median age 37 years, range 24–51, and 35 years, range 18–44, respectively).

Blood samples were obtained in the morning (08:00–09:00 h). Serum concentration of total testosterone was measured by automated electrochemiluminescence immunoassay (ECLIA; Roche Diagnostics, Mannheim, Germany). In women the samples were taken during the early to midfollicular phase of the menstrual cycle.

Data were delivered as medians and interquartile ranges. The Mann–Whitney U-test was used to compare data between the patient groups and the healthy controls. Correlation was analysed by the Spearman test. $P < 0.05$ was considered significant.

As shown in Table 1, the serum concentration of testosterone did not differ significantly between patients with CU of both sexes and the control subjects. There was no correlation between hormone concentration and disease activity.

In our earlier studies we observed a decline in the circulating concentration of dehydroepiandrosterone sulphate (DHEA-S) in patients with CU, suggesting that the lowered DHEA-S concen-

Table 1 Serum concentration of total testosterone [median (interquartile range)] in patients with chronic urticaria (CU) with positive autologous serum skin test (ASST+) and in healthy controls

Testosterone (ng dL ⁻¹)			
Healthy controls		CU/ASST+ patients	
Women (n = 46)	Men (n = 29)	Women (n = 44)	Men (n = 24)
54.01 (33.44–72.23)	436.0 (191.2–967.0)	39.87* (22.45–58.47)	418.75** (353.35–521.25)

* $P = 0.12$, female controls vs. women with CU; ** $P = 0.76$, male controls vs. men with CU (Mann–Whitney U-test).

tration is a phenomenon that accompanies the disease, plausibly secondary to psychological disturbances.⁹

Dehydroepiandrosterone and DHEA-S are precursors to testosterone and oestrogens. Testosterone is the most potent androgen which is secreted in women by the adrenal gland and the ovarian stroma. Because androgens are known to exert immunosuppressive properties and protect from autoimmune diseases, we hypothesized that there would be a lower testosterone level in patients with CU with a positive ASST, similarly to other diseases associated with autoreactive phenomena. To our knowledge, this is the first report of testosterone behaviour in CU. The men and women with CU with a positive ASST had a serum total testosterone concentration similar to healthy subjects. In contrast, some changes in concentrations of androgens have been demonstrated in patients with immune-mediated diseases.¹⁰ It may be that urticarial inflammation or distress does not influence basal testosterone secretion or that such changes may be too small to be measured; thus, only specific examination of the hypothalamic-pituitary-endocrine gland axis may reveal some alterations.

In conclusion, CU with positive ASST is not accompanied by changes in circulating testosterone concentration.

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Conflicts of interest: none declared.