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Prolactin and Dehydroepiandrosterone Sulfate: Are They Related to the Severity of Chronic Urticaria?

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Background and Aims. Elevated prolactin and reduced dehydroepiandrosterone sulfate (DHEA-S) levels are associated with autoimmune diseases. A limited number of studies have investigated these hormones in chronic urticaria (CU). The autologous serum skin test (ASST) reaction has also been linked to autoimmune diseases, and a positive reaction is usually associated with a more severe disease. We aimed to compare serum prolactin and DHEA-S levels between female CU patients with positive and negative ASST reactions and healthy controls.

Methods. The study included 30 female CU patients with a positive ASST reaction, 30 female CU patients with a negative ASST reaction, and 30 healthy female controls. All identifiable causes of urticaria were excluded. Serum prolactin and DHEA-S levels were measured in all subjects.

Results. Prolactin was significantly higher among ASST positive patients than among ASST negative patients and controls but did not differ between ASST negative patients or controls. Higher prolactin levels were associated with increasing disease severity among ASST positive patients. DHEA-S levels did not differ between ASST positive or negative patients but were significantly lower among both patient subgroups than controls. DHEA-S levels did not differ according to the severity of disease among either of the patient subgroups. DHEA-S levels did not correlate with prolactin among any group.

Conclusion. We demonstrate for the first time a possible role for prolactin in ASST-positive CU patients and its association with disease severity. We recommend larger prospective studies to assess changes in prolactin and DHEA-S levels after complete disease remission.

Key Words: Autoimmune disease, Autologous serum skin test, Chronic urticaria, Dehydroepiandrosterone sulfate, Prolactin.

Introduction

Chronic urticaria (CU) is defined as the occurrence of daily, or almost daily, wheals and itching with or without angioedema for at least 6 weeks (1). It is characterized by the activation of autoimmune and inflammatory processes (2). Up to 45% of patients with CU exhibit autoreactivity characterized by an immediate wheal and flare response to an intradermal injection of autologous serum (autologous serum skin test, ASST) (3). A positive ASST reaction has been associated with various autoimmune diseases including rheumatoid arthritis (RA) (4), autoimmune thyroiditis, celiac disease (5), type 1 diabetes, and Graves' disease (6) and with markers of autoimmunity such as antinuclear antibodies, rheumatoid factor, and antithyroid antibodies (7).

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Prolactin is a peptide hormone secreted by lactotroph cells in the anterior pituitary gland. In addition to its well-known lactogenic and mammotrophic functions, prolactin is a common mediator of the neuroendocrine-immune network (8). Its immunostimulatory effects may be mediated by inhibition of apoptosis and increased antibody production (9). Elevated prolactin levels have been associated with various autoimmune diseases and have been observed in patients with systemic lupus erythematosus (SLE), RA, multiple sclerosis and Sjögren's syndrome (10).

Dehydroepiandrosterone (DHEA) and its sulfated metabolite (DHEA-S) are the major androgens secreted by the adrenal glands and are precursors for synthesis of androgens and estrogens (11). Circulating DHEA and DHEA-S possess anti-inflammatory, anti-proliferative and immunomodulatory properties and have been shown to decrease in various chronic inflammatory and immune-mediated diseases. Their deficiency has been observed among patients with SLE, RA, autoimmune thyroiditis and other immune inflammatory disorders (12−14).

Only very limited information is available on the status of these hormones in patients with CU. In the present study we aimed to evaluate serum concentrations of prolactin and DHEA-S among 30 female patients with CU and a positive ASST reaction as compared to 30 female patients with CU and a negative ASST reaction and 30 healthy female controls.

Materials and Methods

The current case-control study was conducted from April 2011−December 2011 and included 30 female patients with CU and a positive ASST reaction (mean age 30.1 ± 6.7 years) and 30 female patients with CU and a negative ASST reaction (mean age 28.7 ± 7.4 years). All patients were recruited from the Allergy and Clinical Immunology outpatient clinic at Ain Shams University Hospital and were symptomatic at the time of their enrollment. CU was diagnosed based on the appearance of continuous or recurrent hives with or without angioedema for more than 6 weeks (15). In all patients, identifiable causes of urticaria were previously excluded by history, clinical examination and appropriate investigations. These investigations included a complete and differential blood cell count, erythrocyte sedimentation rate, C-reactive protein, tests for infectious diseases and hepatitis virus markers, skin prick test for allergy, antinuclear antibodies, C3, C4, thyroid hormones (free T3, free T4, thyroid-stimulating hormone) and thyroid antibodies, including anti-thyroglobulin and anti-thyroid peroxidase antibodies (16). Further exclusion criteria were physical urticaria, subjects who had been on systemic steroid therapy within 6 months prior to recruitment, subjects who had been receiving antihistamines or any other therapies for urticaria within 10 days before recruitment, pregnant or lactating females, and females with any past history of contraception. Disease duration was comparable between both groups [median (interquartile range): 6 (3,9) years among ASST-positive patients and 6 (3,7) years among ASST-negative patients, $p = 0.736$]. In addition, the study also included 30 apparently healthy female controls who were not pregnant or lactating and who had negative ASST reactions (mean age 29.1 ± 7.5 years). None of the controls had received any medications for at least 4 weeks before recruitment. A written informed consent was obtained from all study participants prior to conducting the study, and the study was approved by the Research Ethics Committee of Ain Shams University.

Grading of Disease Severity

This was assessed according to the number of wheals present at the time when blood samples were collected, as follows: 1−10 small (<3 cm in diameter) wheals = grade 1 (slight); 10−50 small wheals or 1−10 large wheals = grade 2 (moderate); >50 small wheals or >10 large wheals = grade 3 (severe); virtually covered with wheals = grade 4 (very severe) (17).

Autologous Serum Skin Test Procedure

ASST was performed for all patients with chronic urticaria and for all healthy controls according to the method by Sabroe et al. A positive test was defined as a serum-induced wheal response with a diameter of 1.5 mm or more than that of the saline-induced response (18).

Hormonal Assays

Morning fasting blood samples were obtained from all patients and controls for measurement of serum prolactin and DHEA-S levels. Prolactin concentrations in serum were measured by a microplate immunoenzymometric assay (Monobind Inc., Lake Forest, CA) according to the manufacturer's instructions. According to this kit, normal prolactin levels in serum among healthy adult females were 1.2−19.5 ng/mL. DHEA-S levels in serum were measured by enzyme immunoassay (DIAsource ImmunoAssays SA, Nivelles, Belgium) according to the manufacturer's instructions. According to this kit, normal DHEA-S levels in serum among healthy adult females <50 years of age were 0.40−2.17 μg/mL.

Statistical Analysis

Data analysis was performed using the SPSS program, v.12. Data were expressed as mean ± standard deviation (SD) for parametric data and as median and interquartile range (IQR) for nonparametric data, respectively. Parametric data were analyzed using one-way analysis of variance (ANOVA) for the comparison of three groups. Nonparametric data were analyzed using the Mann-Whitney U and