The natural history of chronic urticaria in childhood: A prospective study

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Background: There are few prospective studies on the natural course of chronic urticaria (CU) in children.

Objective: We sought to examine the natural history of CU in children and to identify predictors for remission.

Methods: Children 4 to 15 years of age with CU were investigated with a complete blood cell count, erythrocyte sedimentation rate, antinuclear antibody titer, complement CH_{50} level, thyroid studies, autologous serum skin test, skin-prick tests, food challenges, and stool examination for parasites. They were considered to be in remission if symptoms did not recur for at least 12 months without medication.

Results: In all, 92 children (53.3% female) with CU were recruited and followed up for a median duration of 4.3 years (range 2.5-5.8 years). Chronic autoimmune urticaria (CAU) was identified in 40% of the patients. Food allergy was found in 8.7% and parasitic infestations in 5.4%. Remission rates at 1, 3, and 5 years after the onset of CU symptoms were 18.5%, 54%, and 67.7%, respectively. The remission rate did not differ in CAU compared with non-CAU. No predictor of CU remission was identified.

Limitations: The basophil histamine release assay was not performed.

Conclusion: Children with CU have a favorable outcome. CAU did not have an intractable course. (J Am Acad Dermatol 2014;71:663-8.)

Key words: autologous serum skin test; autoreactivity; children; chronic spontaneous urticaria; chronic urticaria; food allergy; natural course; remission.

Chronic urticaria (CU) is defined as urticarial episodes lasting for 6 weeks or longer.[1] The major subgroups of CU are chronic spontaneous urticaria (CSU), urticarial vasculitis, and physical urticaria.[2,3] Disorders identified as possible causes of CSU include food allergies, connective tissue diseases, chronic infections, and parasitic infestation.[2,4-6] In recent studies more than 30% of adults and children with CSU had autoantibodies to the α-subunit of high-affinity IgE receptor (FcεRIα) and/or anti-IgE antibodies.[5,7-14] These patients were classified as having chronic autoimmune urticaria (CAU). The presence of autoantibodies may be screened for by performing the autologous serum skin test (ASST) or by an

Abbreviations used:

ANA:	antinuclear antibody
ASST:	autologous serum skin test
CAU:	chronic autoimmune urticaria
CSU:	chronic spontaneous urticaria
CU:	chronic urticaria
SPT:	skin-prick test

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in vitro basophil histamine release assay.[15] The ASST has relatively high sensitivity, moderate specificity, and a high negative predictive value compared with the basophil histamine release assay.[14,16,17] It is also a practical test to assess autoreactivity in patients with CU especially where the basophil histamine release assay is not available.[14] This autoreactivity may indicate mast cell activating autoantibodies in patients with CSU who have positive ASST.[16]

In adults, there are associations between CAU and autoimmune diseases such as thyroid disease, rheumatoid arthritis, celiac disease, type 1 diabetes mellitus, and an increased frequency of autoimmune markers such as rheumatoid factor and antinuclear antibody (ANA).[18-22] Approximately 14% of adults and 4% of children with CSU have positive antithyroid antibodies.[1,5,18-20] A cause for CSU is not identified in approximately 60% of patients.[1]

Studies of the natural history of CU show that 30% to 50% of adults achieve remission 1 to 3 years after the onset of symptoms.[23-27] The objectives of this prospective study were to investigate the natural course of CU in children and to identify predictors of disease remission.

CAPSULE SUMMARY

- There are few prospective studies on the natural course of chronic urticaria in children.
- In this study of children aged 4 to 15 years, remission rates at 1, 3, and 5 years after the onset of symptoms were 18.5%, 54%, and 67.7%, respectively. There was no identified predictor of remission.
- Chronic urticaria has a favorable outcome in children.

METHODS

Patients

The study was approved by the institutional review board of Siriraj Hospital in Bangkok, Thailand. It was performed in the pediatric allergy clinic, from March 2003 to March 2009. Children 4 to 15 years of age with daily or almost daily urticaria lasting for 6 weeks or longer were asked to participate. Informed consent was obtained from the parents. Exclusion criteria included isolated physical urticaria and other urticaria subtypes (including aquagenic, cholinergic, and exercise-induced urticaria), inability to attend for follow-up, pregnancy, and underlying conditions such as cardiovascular, hepatobiliary, and renal disease.

Investigations

All patients underwent a complete history, physical examination, and the following laboratory tests: complete blood cell count, erythrocyte sedimentation rate, ANA, CH_{50}, free-T4, thyroid-stimulating hormone, antithyroglobulin antibody, antimicrosomal antibody, and stool examination for parasites. A skin biopsy specimen was obtained if there were clinical features of vasculitis and connective tissue disease such as fever, arthralgia, raised erythrocyte sedimentation rate, painful skin lesions, and lesions lasting more than 24 hours or with residual purpura or petechiae.

Skin-test procedure

Skin-prick tests (SPT) to foods and ASST were performed in all patients. SPT with commercial food extracts (cow's milk, soy, egg white, chicken, pork, beef, mixed fish, shrimp, crab, clam, oyster, peanut, and wheat from Center Laboratory, Port Washington, NY) were performed with 10 mg/mL of histamine phosphate and glycerinated saline as positive and negative controls. Oral antihistamines were discontinued for 7 days or longer before SPT. The SPT result was considered positive if the mean wheal diameter was 3 mm or greater compared with the negative control.

The ASST was performed using an intradermal skin test with 0.05 mL of sterile, fresh autologous serum. Histamine (10 μg/mL) and 0.9% sterile saline were used as positive and negative controls.[11] Wheal and flare reactions were recorded after 30 minutes. A wheal diameter of 1.5 mm or greater compared with that elicited by a control saline solution was considered positive.

Food-challenge procedure

Open food challenges to suspected foods were done in patients who had a positive SPT finding. The patients were asked to avoid all foods that elicited a positive SPT result and discontinue oral antihistamines for 7 days or longer before food challenges. Patients with asthma were asymptomatic and had forced expiratory volume in 1 second greater than 70% of predicted value. The food challenge was administered in the fasting state, beginning with a dose of 500 mg of lyophilized food. The dose was doubled every 15 minutes. A maximum dose of 10 g of lyophilized food was used, followed by open feeding.[28] Vital signs and any symptoms or signs were recorded every 15 minutes. Emergency resuscitation equipment and drugs were available.