



Clinical Features of Patients with Chronic Urticaria and the Results of the Skin Prick Tests

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ABSTRACT

Objective: Chronic urticaria (CU), which is mostly idiopathic, may also be a sign of an allergic or systemic disease. A variety of diseases and allergens that accompany CU have been reported in various studies. The aim of this study was to investigate the factors that play a role in the etiology of CU.

Materials and Methods: The demographic and clinical data from 302 patients – aged over 18 years - who were being monitored for CU were recorded. Several tests were performed to analyze comorbidities such as infection, malignancy, and autoimmune and rheumatic diseases. Skin Prick Test (SPT) results and questionnaires were reviewed.

Results: Two hundred and thirteen out of the 302 patients with a mean age of 40.26 ± 14.3 years were females. The duration of CU was 43.30 ± 62.60 months and 42.9% of the patients had comorbidities. The most common disease was autoimmune thyroiditis (13.9%). Fifty-five percent of the patients were sensitive to inhalant allergens, and 5% exhibited allergen positivity for food. The most common allergens were house (43.7%) dust mites. Allergen positivity was 37.2% in those with comorbidities, while it was 62.8% in those without any comorbidities and this relationship was statistically significant ($p < 0.05$).

Conclusion: This study showed that there was an association between house dust mite and CU dust sensitivity. House dust mite sensitivity may trigger CU.

Keywords: Chronic urticaria, skin prick test, etiology

INTRODUCTION

Chronic urticaria (CU) is a relapsing vascular skin reaction that manifests itself with itch, rash and swelling, lasting more than six weeks (1-3). Urticaria lesions are plaques that tend to merge. Urticaria may occur in association with angioedema. While the disease is usually self-restricting, it can become a life-threatening condition due to asphyxia in the case of anaphylaxis and laryngeal edema (4-6). Recurrent attacks may disturb the patient's physical appearance, cause anxiety and effect the quality of life (6-9).

CU has a prevalence of 0.1-3% and it is observed more frequently in middle-aged women (1-6). Although CU

is mostly idiopathic, occupational and environmental allergens, drugs, infections, food and food additives, parasites, autoimmune diseases, endocrine and malignant diseases, stress and physical stimulants can play a role in the etiology (1-6). The variety of comorbidities and allergens have drawn the attention of researchers and numerous studies have been carried out on the subject. As CU constitutes a heterogenous disease group, all examinations for the determination of the etiology should be completed before concluding that the disease is idiopathic (1-9).

In our study, we hypothesized that various allergens are associated with CU and aimed to determine allergen sensitivities of our CU patients.

MATERIALS and METHODS

SPT results and questionnaires of 302 CU patients -aged over 18 years- were reviewed retrospectively. The approval was obtained from Celal Bayar University Medical School ethics committee.

Patients were diagnosed with CU after reviewing their history and physical examination. Questionnaire included, patient demographic (name, last name, sex, occupation and address) and clinical features (chronic disease, use of drugs and herbal products, dietary habits, duration of complaints, and their relation to physical factors such as cold, heat, pressure, light and exercise). Hemogram, sedimentation rate, biochemistry tests, hepatitis markers, serologic tests (C3, C4, ANA), thyroid function tests and autoantibodies, chest and sinus x-Rays, urine test, and stool parasite exams were performed. Further examinations (thyroid and abdominal ultrasound, anti DNA and other autoantibodies, computed tomography, gastrointestinal system endoscopy, provocation tests) were performed when required. All patients underwent SPT to detect inhalant and food allergen sensitivities. An informed consent form was obtained from all patients before performing SPT.

Vegetation and environmental factors were taken into account while determining the allergen panel. SPT was performed with 55 allergen extracts such as house dust mites (*Dermatophagoides farinea*, *Dermatophagoides preterynisnus*), animal epithelia, (cat, dog, cockroach), meadow pollens, tree pollens (olea, mix tree), weed pollens (artemisia, plantago, parietaria), latex, and food allergen extracts (wheat, walnuts, peanut, hazelnut, corn, rice, milk,

egg yolk, egg white, soy, fish, beef, meat, chicken, cacao, tomatoe, orange, grape, banana, peache, carrot, potatoe) (Allergopharma, Germany).

The SPSS 15.0 program was used for the statistical analysis of the study. In descriptive statistics, percentage (%), and median ± standard deviation values were used for categorical variants, and the chi-square and t-tests were used for comparisons. P<0.05 was accepted as statistically significant.

RESULTS

Two hundred thirteen (70.5%) patients were female and the mean age was 40.26±14.37. Age distribution was as follows: 24.8% in the 18-28 years age group, 23.2% in 29-38, 24.5% in 39-48, 14.9% in 49-58, 8.9% in 59-68, and 3.6% in 68 and older. Average disease duration was 43.30±62.60 months (2 months to 40 years) (Table I).

The results concerning the etiology of CU are presented in Table II. 42.7% of the patients had comorbidities. Percentile distribution of comorbidities was 13.9% autoimmune thyroiditis, 7% atopic disease, 6.6% drug allergy, 6% parasitic disease, 5.3% infection, 5% iron deficiency, and 1.7% connective tissue disease. Examination of the allergic etiology revealed a rate of 55% inhalant allergen and 5% food allergen sensitivity. Allergen distribution was 43.7% for house dust mites, 29.8% for meadow pollens, 22.5% for tree pollens, 7.3% for weed pollens, 3% for latex, and 2% for fungal mixture. A total of 36 patients (12%) had physical urticaria (Table II).

The examination of the relationship between demographic features and presence of allergen sensitivity

Table I. Demographic and disease features of patients with CU.

Features	(n:302)	(%)	
Age (years)	18-28	75	24.8
	29-38	70	23.2
	39-48	74	24.5
	49 -58	45	14.9
	59-68	27	8.9
	69 years and older	11	3.6
median±SD (min-max) 40.26±14.37 (18-79)			
Sex	Female	213	70.5
	Male	89	29.5
Duration of Urticaria (month)		median ±SD (min-max) 43.30±62.60 (2 months-40 years)	

CU: Chronic urticaria, SD: Standard deviation.

showed allergen sensitivity in 74.4% of females and 25.6% of males, which was statistically significant ($p < 0.05$) (Table III).

When the relationship between age groups and allergen sensitivity was examined, allergen sensitivity was observed to be higher in young and middle-aged individuals, and this result was statistically significant ($p < 0.05$).

Table II. Comorbidities of patients with CU.

Features	(n)	(%)
Presence of Comorbidities	129	42.7
Autoimmune Thyroiditis	42	13.9
Atopic Disease	21	7
Drug Allergy	20	6.6
Parasitic Disease	18	6
Infection	16	5.3
Iron Deficiency	15	5
Vitamin B Deficiency	5	1.7
Connective Tissue Disease	5	1.7
Inhalant Allergen Sensitivity	166	55
House Dust Mite	132	43.7
Meadow Pollen	90	29.8
Tree Pollen	68	22.5
Weed Pollen	22	7.3
Animal Epithelia	9	3
Latex	9	3
Fungal Mixture	6	2
Food Allergen	15	5
Physical Urticaria	36	12

CU: Chronic urticaria.

DISCUSSION

CU may be idiopathic as well as a sign for an allergic or systemic disease. Regional differences in prevalence and etiologic factors attract the attention to the role of provoking factors in these diseases.

CU is more prevalent in middle-aged women, lasting 3 to 5 years. Most of our patients were female (the M/F ratio was 2.4) and the mean age was 40.26 ± 14.37 years. Our patient profile was consistent with the literature (1,6,10-12).

Almost half of the patients (42.7%) had comorbidities and autoimmune thyroiditis was the most frequently observed comorbidity. Despite differing opinions, many studies have reported the role of autoimmunity in CU etiology and it has also been reported in many studies that autoimmune thyroid disease is observed at a rate of 12-36.6% (12-16). Autoimmune comorbidity was also observed, albeit at low rates, in our patients.

The prevalences of allergic rhinitis, allergic asthma, or atopic dermatitis were not increased in our patients. A total of 21 patients had history of atopic disease (7%). Drug allergy prevalence was 6.6%. Inquiry of the types of drugs revealed high rates of ACE inhibitor, non-steroidal anti-inflammatory drug and myorelaxant use. These medications are frequently reported in studies that focus on urticaria and drug allergies and are known to be CU provokers (1-9, 17-20).

Prevalence of parasitic diseases was 6% in our study (18 patients). Twelve patients had *Blastocytis hominis* while 4 had *Giardia lamblia*, and 2 of them had *Ascaris*. In

Table III. The relationship between SPT positivity and sociodemographic features of the patients with CU.

Features		SPT Negative (%)	SPT Positive (%)	P
Sex	Female	65.4	74.4	0.08
	Male	34.6	25.6	
Comorbidity	Present	50	37.2	0.026*
	Absent	50	62.8	
Age (years)	18-28	18.5	29.7	0.034*
	29-38	26.2	20.9	
	39-48	23.8	25	
	49-58	14.6	15.1	
	59-68	13.1	5.8	
	68 years and older	3.8	3.5	

* $P < 0.05$.

a study by Giacometti et al. that evaluated the relationship between parasitic infections and cutaneous allergy, the comorbidity of allergic dermal diseases (chronic urticaria, atopic eczema or itch of unknown cause) in patients with *Giardia lamblia* was observed to be significant (21). In our study, the rate of *Blastocystis hominis*, which is a known comorbidity in CU patients, was found to be significantly high. Prevalence of parasitic diseases in CU patients has been observed at various levels in studies carried out on the subject (21-22).

The results concerning the co-morbidity of CU with chronic infections is variable. Prevalence of chronic infections was 5.3% (16 patient) in our patients and 9 patients had *helicobacter pylori* (HP) gastritis, 4 had chronic B hepatitis, 2 had chronic sinusitis, and one patient had chronic hepatitis C. Although the prevalence of infectious diseases was not considerably high, the HP prevalence attracts attention. There are several studies that have reported the prevalence of HP in CU and its provoking role (23-26).

Vitamins and minerals play important role on the immune system. Studies on vitamin and mineral deficiencies have found them at increased rates in allergic diseases. Of the patients 5% (15 patients) had iron deficiency anemia, and 1.7% (5 patients) had vitamin B12 deficiency. Iron deficiency anemia is known to lead to a number of diseases and pruritus. We did not encounter a study that investigated the effect of iron deficiency on CU, while there are studies on vitamin B12 deficiency. In some of these studies, low vitamin B12 level is referred as an autoimmune condition independent of HP gastritis (27-28).

Physical factors such as UV light, heat, cold, pressure, light, exercise and water can provoke urticaria. The prevalence of physical urticaria was 12% in our patients and dermatographism (23 patients) was the most common type. A physical urticaria diagnosis was determined through a review of patient history, physical examination, and provocation tests if required. As avoiding the provoking factors alleviates the symptoms rapidly, physical provoking factors should be inquired in patients with CU. It is emphasized in the literature that physical urticaria constitutes an important part of the CU and must be investigated (1-6, 29).

Atopy is the tendency to develop a type 1 sensitivity reaction against environmental allergens in individuals with a genetic predisposition. Atopic individuals produce

specific IgE antibodies against the frequently encountered allergens. Inhalant and food allergens can cause urticaria and angioedema in sensitive individuals by entering through respiratory, digestive or dermal routes. Numerous studies have demonstrated inhalant and food allergen positivity in patients with CU (30-40).

The Aegean region has a rich flora and humid climate, that increase the allergen load of the region. Inhalant allergen positivity was found to be 55% in our patients. (43.7% house dust mites, 29.8% meadow pollens, 22.5% tree pollens, 7.3% weed pollens, 3% animal epithelia, 3% latex, and 2% fungi). The most common sensitivity was against house dust mites, which are common environmental allergens with strong immunogenic properties and frequently cause sensitivity in atopic patients. CU was observed in a number of studies where house dust mite sensitivity was observed frequently (30-35). Meadow and tree pollen sensitivities were also highly prevalent amongst our patients. Other inhalant allergens in CU are encountered with variable prevalence in the literature, and none at the same rate as house dust mites (30-35).

Prevalence of food allergy was 5% (15 patients) where 5 of our patients were sensitive to peanut allergen, and 3 to peanuts, 3 to wheat flour, 2 to corn flour, 1 to cacao, and 1 to tomato. SPT results of these patients were compatible with food allergy history. Food additives and biologic amines are reported more often in association with allergic reactions these days. Recent studies point to this phenomenon, emphasizing the prevalence of these allergens in CU (36-40).

Allergen sensitivity was higher in young and middle-aged patients. The association between allergen positivity and age was statistically significant ($P < 0.05$). Skin test positivity was higher among young age groups, with a gradual decline as the age progresses (41-42). Our results are compatible with this. There was no relation between allergen sensitivity and gender.

Patients without comorbidities had higher rates of allergen sensitivity. While allergen positivity was 37.2% in those with comorbidities, it was 62.8% in those without. This result was striking and statistically significant ($p < 0.05$). Most of the comorbidities in patients with CU were Th1 type comorbidities. This may be related to hygiene hypothesis and Th1/Th2 balance which are thought to play important role in etiopathogenesis of allergic diseases (43,44).

House dust mite and meadow pollen allergen sensitivity in patients with CU show that these may be provoking factors in CU. It is known that treatment is more successful and drug use is decreased if the triggering factors are determined and avoided in CU. All examinations should therefore be performed before deciding that CU is idiopathic in a particular patient. As all allergens can not be demonstrated by testing, triggers can be identified by asking patients to keep a diary.

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