

Chronic spontaneous urticaria in autoimmune connective tissue diseases

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Abstract

Objective Chronic spontaneous urticaria is one of the most troubling symptoms in autoimmune connective tissue diseases (ACTDs). Our aim is to better characterize the association between chronic spontaneous urticaria and ACTDs.

Methods A retrospective study of patients seen at ACTDs clinic at Massachusetts General Hospital.

Results Of the 41 patients who fit our criteria, 58% had no underlying ACTDs, 22% had systemic lupus erythematosus (SLE), and only 4% had other types of ACTDs.

Conclusion Chronic spontaneous urticaria is a frequent condition in SLE. We did not find a strong association between other ACTDs and chronic spontaneous urticaria.

Key words

Chronic urticaria, autoimmune, connective tissue, lupus, hives.

Introduction

Urticaria is a common skin condition with complex pathogenesis, characterized by cutaneous wheals (hives), angioedema, or both. The prevalence of urticaria is about 9%.¹ It has a significant impact on the quality of life of affected patients¹. It's often divided into acute or chronic based on the disease duration of less or more than 6 weeks, respectively. Chronic urticaria is subclassified into chronic inducible urticaria or chronic spontaneous urticaria.² Chronic inducible urticaria characterized by the appearance of recurrent wheals for more than 6 weeks in duration as a response to specific triggers. Triggers include both physical (cold & heat urticaria, delayed pressure urticaria, solar urticaria, vibratory urticaria, and symptomatic

dermographism) and non-physical triggers (contact, aquagenic, and cholinergic urticaria). Chronic spontaneous urticaria is a condition which persists for more than 6 weeks in the absence of an identifiable provoking factor.

Autoimmune hyperthyroidism diseases such as rheumatoid arthritis, hyperthyroidism, celiac disease, and type I diabetes mellitus have been linked to chronic spontaneous urticaria.^{1,2} However, there is very limited data on other rare connective tissue diseases including systemic sclerosis, dermatomyositis, mixed and undifferentiated connective tissue diseases.

Autoimmune connective tissue diseases (ACTDs) are relatively rare group of disorders characterized by immune dysregulation, multisystem involvement, and autoantibodies. The most common is systemic lupus erythematosus (SLE), dermatomyositis (DM), systemic sclerosis (SSc), Sjogren's syndrome (SJO), undifferentiated connective tissue disease

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(UCTD), and mixed connective tissue disease (MCTD). Usually, they present with characteristic signs and symptoms. Skin manifestations are common in ACTDs including chronic spontaneous urticaria. There are few studies of chronic spontaneous urticaria in ACTDs and most of them on SLE. However very little is known about chronic spontaneous urticaria in other less common ACTDs. We performed this study to know more about the frequency and characteristics of chronic spontaneous urticaria in different ACTDs.

Methods

This study was performed to characterize the association between chronic spontaneous urticaria and ACTDs of patients who were evaluated and treated at a specialty ACTDs clinic.

We performed a retrospective chart review of all patients seen at the ACTDs clinic, formerly known as Rheumatology-Dermatology clinic, at Massachusetts General Hospital, Boston, MA, USA between Nov 2012 and Nov 2017. The study was reviewed and approved by Partners IRB. The chart review was performed by the author.

Presence and frequency of chronic spontaneous urticaria was extracted from patient HPI and physical examination, and underlying cause and management of urticaria from the assessment and plan. Patients included in the study were those referred to our ACTDs combined clinic because of a rash and specific or un-specific autoimmune disease symptoms, and or patients with known ACTDs who presented with a new rash. Patients were evaluated simultaneously by a board-certified rheumatologist and a board-certified dermatologist specifically trained in this area. Acute urticaria, chronic inducible urticaria, viral urticarial rash and urticarial drug

eruption were excluded. We included only chronic spontaneous urticaria based on clinical presentation. Skin biopsy was performed only in few selected cases where histopathology was needed to confirm the diagnosis.

Results

A total of 734 patients were evaluated at our ACTDs clinic between Nov. 2012 to Nov. 2017. The total sample age ranges from 16 to 94 year with a mean age of 51 years, and 80% of the sample was female. Only 41 patients with chronic spontaneous urticaria fit our criteria, of whom 10 patients (24%) were males and 31 patients (76%) were females, with an age range between 21-85 years, and average of 46 years. Of the 41 patients with chronic spontaneous urticaria, rheumatologists referred 28 patients (64%), and dermatologists referred 9 patients (20%), and the remaining 16% were referred by primary physicians. Of the 41 patients, 24 patients (58%) had no underlying ACTDs, 9 patients (22%) had systemic lupus erythematosus (SLE), 4 patients (10%) had psoriasis, 2 patients (5%) had rheumatoid arthritis (RA), one patient (2%) had MCTD, and one patient (2%) had UCTD (**Table 1**).

Table 1 Showing the number of patients with autoimmune connective tissue diseases (ACTDs) who presented with chronic spontaneous urticaria at our clinic. SLE, Systemic lupus erythematosus; DM, Dermatomyositis; SJO, Sjogren's syndrome;

Table 1

<i>ACTDs</i>	<i>Total number of patients</i>	<i>With chronic spontaneous urticaria</i>
SLE	77	9
DM	42	0
SJO	33	0
SSc	32	0
MCTD	16	1
UCTD	14	1

SSc, Systemic sclerosis; MCTD, Mixed connective tissue disease; UCTD, Undifferentiated connective tissue disease; DLE, Discoid lupus erythematosus.

Discussion

A total of 734 patients evaluated, of whom 214 patients had ACTDs. The most common condition was SLE, but a significant number of other ACTDs were also seen. Most of the cases were referred by Rheumatologists (64%). Dermatologists referred 20%, while Primary care physicians referred 16% of the cases. Chronic spontaneous urticaria found in only 5% of all ACTDs. There is little know about the frequency of chronic spontaneous urticaria in ACTDs, and majority of studies were on SLE. A large Israeli population study of over 12,778 subjects given a diagnosis of chronic urticaria by either allergy or dermatology specialists during 17 years in a large health maintenance organization found that female patients with chronic spontaneous urticaria demonstrated a significantly higher incidence of rheumatoid arthritis, Sjogren's syndrome, celiac disease, type I diabetes, and systemic lupus erythematosus than patients without chronic spontaneous urticarial.³ A systematic review of the prevalence of chronic spontaneous urticaria in SLE was investigated by 42 independent studies and comorbidity in adult patients reportedly ranged from 0% to 21.9%. In children with SLE, chronic spontaneous urticaria was reported in 0–1.2%.⁴ We evaluated 77 patients with SLE and found chronic spontaneous urticaria in 9 (12%) of all SLE patients. Our study supports the above studies that chronic spontaneous urticaria is frequent in SLE patients.

MCTD is a connective tissue disorder characterized by the presence of high titers of ribonucleoprotein autoantibody and clinical

features of SLE, systemic sclerosis, rheumatoid arthritis, and polymyositis. Only one patient out of our 16 patients with MCTD had chronic spontaneous urticaria. Patients who have characteristic features of systemic ACTD, but do not meet the criteria for classification of a particular ACTD are often considered to have UCTD. We evaluated 14 patients with true UCTD, of which only one patient presented with chronic spontaneous urticaria.

Finally, at our ACTDs clinic, we evaluated 33 patients with SJO, 42 patients with DM, 32 patients with SSc. None of them had chronic spontaneous urticaria. Up to our knowledge, there are no studies specifically described chronic spontaneous urticaria in SJO, DM, or SSc.

Conclusion

Chronic spontaneous urticaria is a frequent troubling condition in SLE. Data about chronic spontaneous urticaria in ACTDs are minimal. Although our sample size is relatively small given the rarity of these disorders, we did not find any strong association between other ACTDs and chronic spontaneous urticaria. We set out this study to increase the awareness for non-dermatologists and dermatologists alike in identifying this type of urticaria in ACTDs. Larger longitudinal studies are needed to better characterize chronic spontaneous urticaria in ACTDs.

Limitations of our study include that our data is mainly based on chart review, which may not accurately document urticaria and differentiate different subtypes of urticaria.

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