Observational retrospective cohort study of 549 patients with chronic spontaneous urticaria

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Introduction

Chronic Spontaneous Urticaria (CSU) is a cutaneous disease with a considerable clinical variability in activity, duration, comorbidities and response to the treatment. It is by far the most common subtype of all forms of non-acute urticaria. At any single time, 0.5-1% of the population is suffering from CSU. CSU may persist for several years (usually between 1 and 5 years) and the detrimental effect of CSU on quality of life is similar to that of severe coronary artery disease.[1]

Some clinical parameters of patients with CSU have been linked to greater severity and worse prognosis of the disease such as a high Urticaria Activity Score (UAS) at the beginning of the disease, the presence of angioedema, a concomitant inducible urticaria or the positivity of the autologous serum skin test (ASST).[2]

The identification of different CSU phenotypes that allow us to predict the severity of the disease and the refractoriness to antihistamines is still an unmet need.

Objectives

The main objective of this study was therefore to describe clinical features, management behaviour and disease course of CSU by studying a large cohort of 549 patients.

Patients and methods

This is a single-center observational retrospective study. All the clinical data were collected from the clinical history and introduced systematically in specialized software for urticaria. This tool was created specifically for the management of the patients with urticaria.

Results

The medical records of 1056 patients were reviewed and 997 patients diagnosed with urticaria were analysed. Of those 997 patients, 55.0% (n=549) suffered from CSU. (Figure 1)

The mean age was 51.5 ± 15.8 years (mean ± SD) and 402 patients were females (73.2). Eighty-nine patients presented associated angioedema (16.2%) and 111 (20.2%), a concomitant CIndU.

The most frequent CIndU observed was dermographic urticaria (74.7%) followed by delayed pressure urticaria (33.2%).

Twenty-five per cent of patients suffered more than one episode of chronic urticaria during their life. The most frequent triggers reported were drugs (non-steroidal anti-inflammatory drugs and acetylsalicylic acid) followed by stressful life events and intense emotions.

The weekly average (UAS7) at the baseline visit was 20.1 ± 13.2, so most of the patients showed a moderate CSU according to the health states proposed by Stull et al.[3]

A more active disease was observed in patients with combined CIndU (significantly higher UAS3w: 53.9 ± 28.0 vs 33.5 ±35.1, p<0.05). (Figure 2)

Personal history of atopy was reported in 19.1% of CSU patients and it was more frequent also in patients with concomitant CIndU (27.9% vs 16.9%, p <0.05). Thyroid impairment was observed in 15.5%. This percentage is higher than reported in the general population, with an estimated prevalence of 11% according to an European meta-analysis[4], and it was even higher in those patients without CIndU associated (18.0% vs 5.4%, p <0.05).

Extended diagnostic procedures were performed in most of the patients according to and the last *European guidelines* published.[5] The vast majority of patients showed some alteration in the complementary tests (86.7%). The most important findings are in agreement with the previous published data and are summarized in table 1.[6] The ASST was performed in 64.5% of our patients (n=354) resulting positive in 54.9% (n=192).

Focusing on the treatment, 12.4% of these patients still received treatment after 5 years of follow up. This percentage was higher when CIndU was associated (19.8% vs 15.1%). Three hundred and eighty-two patients (77.0 %) were refractory to licensed doses of second-generation H1-antihistamines, 33.7% (n=174) of them needed to increase the dose to achieve disease control, 9.5% (n=49) required treatment with cyclosporine A and 2.1%, with omalizumab (n=11) (n = 516). (Figure 3)

Figure 1. Study population

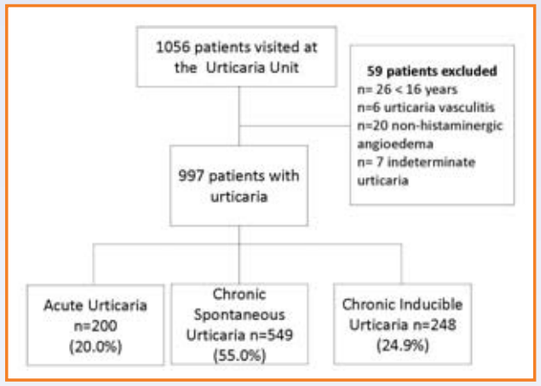

Figure 2. Activity of the disease (average UAS7) and classification according to the health states

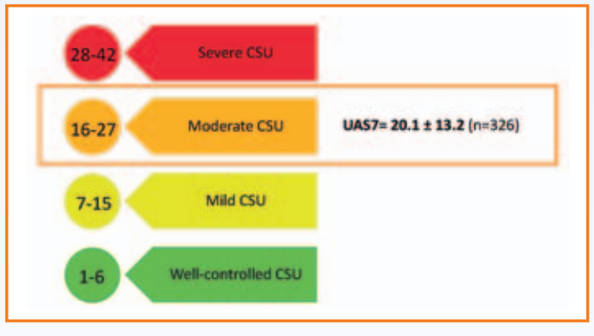

Figure 3. Distribution of patients according to the last line of treatment that controls the disease

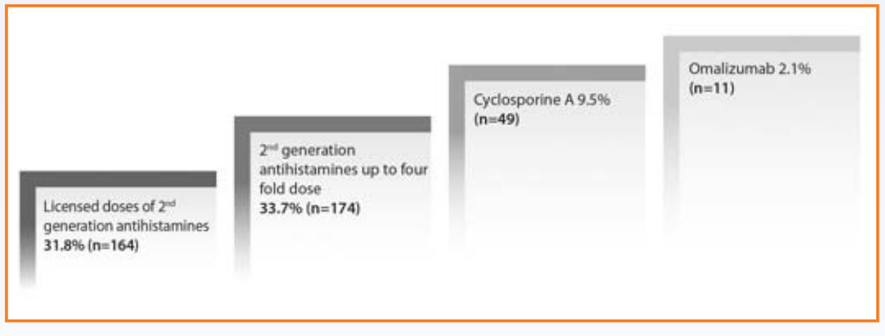

Table 1. Main results of the complementary tests

Variables	All patients n (%)		CSU without CindU n (%)	CSU + CindU n (%)
Phosphatase alkaline (UI/L)	129/405 (31.9)	H*= 129 L* = 0	106/324 (32.7)	23/81 (28.4)
Anti TPO[1] (U/ml)	77/378 (20.4)		65/296 (22.0)	12/82 (14.6)
Anti TG[2] (U/ml)	46/373 (12.3)		40/291 (13.7)	6/82 (7.3)
ANA[3] (1/>40)	48/166 (31.0)		41/122 (33.6)	7/33 (21.2)
IgE[4] (kU/L)	185/418 (44.3)		141/330 (42.7)	44/88 (50.0)
DD[5] (ng/ml)	29/92 (31.5)		21/69 (30.4)	8/23 (34.8)

*Range level of the parameters H: higher, L: Lower

[1]Anti-TPO: anti-thyroid peroxidase antibodies, [2]Anti-TG: anti-thyroglobulin antibodies, [3]Antinuclear antibodies, [4]Immunoglobulin E, [5]D- Dimer

Discussion and conclusions

Detailed analysis of these 549 patients with CSU allows us to define different clinical features. Patients with CSU and CIndU presented more long-lasting and active diseases. These patients also presented more atopy but less thyroid diseases. More than 75 % of patients did not obtained a complete control of the disease with licensed doses of antihistamines. The management of patients with CSU is always a challenge. This first approach to our data allow us to define at least two phenotypes of CSU that show different prognosis, 1)CSU alone and 2)CSU with an associated CIndU.

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