

CORRESPONDENCE

Efficacy of omalizumab for extracutaneous symptoms of chronic spontaneous urticaria

The anti-IgE antibody, omalizumab, is an effective treatment for cutaneous symptoms of chronic spontaneous urticaria (CSU) [1]. As some CSU patients exhibit extracutaneous symptoms (CSU+) [2], we studied the evolution of extracutaneous symptoms in CSU+ patients treated with omalizumab. We retrospectively collected data from all CSU+ patients treated with omalizumab and followed in the Department of Clinical Immunology of Grenoble-Alpes University Hospital, France.

Since 2014, 137 patients were treated with omalizumab, among whom 19 presented extracutaneous symptoms. Thirteen of them were included in this study. Informed consent from all patients was collected. The median age of our patient cohort was 43 years (range: 17-77). The majority of patients were women (65.2%). The median age at the appearance of the first symptoms was 26 years (range: 6-68) and the age at diagnosis was 38 years (range: 13-72). The major debilitating symptoms pretherapy were angioedema (92%), wheals (100%), gastro-intestinal (GI) symptoms (abdominal cramps, diarrhea, nausea) (77%) and fatigue (54%). Other symptoms were postural orthostatic tachycardia syndrome (POTS) (n=6), arthralgias (n=4), wheezing (n=4), headache (n=3), bone pain (n=1), anaphylaxis (n=1) and keratoconjunctivitis (n=1). All patients simultaneously received H1-antihistamines (92%), H2-antihistamines (31%) or treatment with anti-leukotrienes (15%). Among them, three (25%) were treated with a median dose of 300 mg/three weeks, eight (69%) received a dose of 300 mg/month and two (17%) a dose of 300 mg/fortnight. The injections were mainly (75%) delivered at home. The median age at first injection was 40 years (range: 14-75).

For our collected data, we noticed improvements that appeared one month post-treatment (range: 1-9) (table 1). Patients noticed notable improvement in POTS (100%), GI symptoms (77%), arthralgias (50%), and headache (67%). The patients also noticed improvement in cutaneous CSU symptoms (such as angioedema, wheals and fatigue) (83%). Omalizumab was given during a median period of 18 months (range: 5-51) with no serious adverse events. The commonest side effects included transient asthenia (54%), fainting attack (16%) and arthralgia (8%). One patient (8%) exhibited exacerbation after the first injections. No long-term side effects were observed.

CSU is defined as daily pruritic wheals, angioedema, or both, for six weeks or more, without an identifiable trigger. The international EAACI/GA2LEN/EDF/WAO urticaria

Table 1. Efficacy and safety of omalizumab in CSU+ patients (n=13).

Parameters	Data analysis CSU+
Efficacy	
Improvement (n [%])	13 (100)
Median time between improvement (months, range)	1 (1-9)
Type of improvement	
Cutaneous	
AE (n [%])	11 (91)
Median time between improvement (months, range)	2 (1-9)
Asymptomatic	3 (25)
Urticaria (n [%])	13 (100)
Median time between improvement (months, range)	1 (0-9)
Asymptomatic	4 (33)
Extracutaneous	
POTS (n [%])	6 (100)
Median time between improvement (months, range)	1 (1-2)
Asymptomatic	1 (17)
GI symptoms (n [%])	7 (77) ^b
Median time between improvement (months, range)	3.5 (1-9) ^b
Asymptomatic	2 (22)
Fatigue (n [%])	5 (83) ^b
Median time between improvement (months, range)	4.5 (0-9) ^b
Asymptomatic	1
Anaphylaxis	NA
Arthralgias	2 (50)
Median time between improvement (months, range)	9 ^b
Bladder infiltration	0 (0)
Bone pain	1 (100)
Headache	2 (67)
Stabilization (n [%])	0 (0)
Worsening (n [%])	0 (0)
Safety	
Patients with adverse events (n [%])	7 (58)
Local side effect	0 (0)
Fainting attacks	2 (16)
Asthenia	6 (54)
Arthralgias	1 (8)
Patients with worsened intensity of symptoms between 1 (8)	
0 and 24 hours after start of treatment (n [%])	
Number of injections followed by symptom worsening	1
Patients with at least possible related adverse events	0

CSU+: chronic spontaneous urticaria with extracutaneous symptoms; GI: gastrointestinal, POTS: postural orthostatic tachycardia syndrome. data missing for two patients. data missing for one patient. data missing for three patients

guidelines advise second-generation H1-antihistamines as first-line therapy [3]. When H1-antihistamines are ineffective, as was the case in all our patients, omalizumab therapy should be considered. With this therapy, cutaneous CSU

doi: 10.1684/ajd.2020.3717

symptoms, like angioedema and wheals, may significantly and rapidly improve [3, 4], as was the case in our study. Staubach *et al.* [4] also reported an improvement in quality of life with this therapy. Except for fatigue, the efficacy of omalizumab on extracutaneous CSU symptoms is still unknown. These symptoms are, however, not uncommon. Indeed, Doong *et al.* [2] reported a cohort of 155 patients, of whom 103 had systemic complaints, such as joint pain, headache, fatigue, wheezing or GI complaints. In our cohort, patients reported reduced fatigue under omalizumab therapy, as described previously in the literature (reported time to improvement: four months) [4]. Omalizumab also seems to be effective for other symptoms, especially GI symptoms. Our study also shows an association between CSU and POTS, which has not been extensively described previously in the literature [5]. Indeed, we reported improvements in most POTS cases, which has not been previously described.

Overall, this study demonstrates that treatment of CSU+ patients with omalizumab leads to rapid improvement (table 1), and these results are in line with previous studies [4, 6]. Moreover, we reported few side effects associated with omalizumab which is also in line with other studies [4, 6-8].

In several previous reports, off-label dosing periods during monthly administration of omalizumab were suspected and increased dosing intervals have been reported to be more effective [9]. In this study, we also adapted interval dosing based on symptom recurrence; following dose interval decrease, no increase in side effects was found and improvement was observed.

Despite some limitations of our study (in particular, its retrospective nature and the non-objective criteria for improvement), we consider omalizumab as a safe and effective therapy for extracutaneous symptoms of CSU. ■

Disclosures. Financial support: none. Conflicts of interest: none.

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doi:10.1684/ejd.2020.3717

Dasatinib-induced panniculitis in a patient with chronic myeloid leukaemia

Dasatinib is an oral tyrosine kinase inhibitor (TKI) used in the treatment of chronic myeloid leukaemia (CML) and Philadelphia chromosome-positive acute lymphoblastic leukaemia (Ph+ ALL). The development of TKIs, including imatinib, dasatinib, nilotinib, and ponatinib, has markedly improved the prognosis of patients with CML [1]. However, TKIs are associated with various cutaneous adverse reactions, including maculopapular rash, xerosis, alopecia, and keratosis pilaris [2]. Herein, we report a case of panniculitis that developed during long-term treatment of CML with dasatinib.

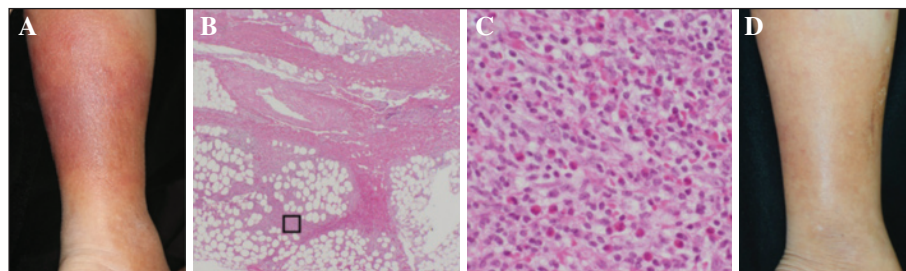


Figure 1. A) Dark red erythema and oedema on the left lower leg. B) Histopathology showing numerous inflammatory cells involving both the septa and lobules of the subcutaneous fat (haematoxylin and eosin; original magnification: $\times 20$). C) Higher magnification of the area marked with a black square in (B), showing that inflammatory cells are mainly composed of lymphocytes and scattered eosinophils and histiocytes (original magnification: $\times 400$). D) Marked improvement of the left lower leg one week after discontinuation of dasatinib.