

Title: Treatment with Omalizumab in a 16-year-old Caucasian girl with refractory solar urticaria

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Running title: Omalizumab in refractory solar urticaria

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/pai.12413

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To the Editor,

Solar urticaria (SU) is a rare chronic photodermatosis (1). It is considered an Immunoglobulin E (IgE)-mediated condition (1). It is characterized by urticarial skin lesions at the sites photo-exposed usually few minutes after ultraviolet radiation (UV), UV-B and more frequently UV-A, or visible light exposure (1). It is burdened by frequent reduction of patient's quality of life and by the risk of anaphylactic shock after whole-body exposure (1). The treatment of choice consists of sun protection and H₁-antihistamines, and in very severe cases short course(s) of oral steroids, however often SU is unresponsive to them. Other treatment options are: phototherapy, photochemotherapy (psoralene + UV), plasmapheresis, intravenous immunoglobulins, cyclosporine A. Efficacy of these treatments is usually partial or transient. In addition, these treatments may be induce severe unwanted effects, e.g. anaphylaxis, immunosuppression and malignancy (1). Omalizumab is an anti-IgE antibody, approved for severe, difficult asthma: the dose given to patient depending on the levels of total IgE and body weight. Recently, omalizumab was approved for treatment of chronic idiopathic urticaria. On the basis of the pathogenetic mechanism of SU, hypothesized to be IgE-mediated, the use of omalizumab have been attempted and reported recently in a few case of SU with discordant results. A case of SU improved within 4 weeks after the first dose of omalizumab (anti-asthmatic dosage) (2). A case of SU presented a partial improvement of symptoms after the sixth dose (anti-asthmatic dose) and dropped out during the follow-up (3). Two cases of UVA-SU had complete symptoms' control after the first dose and for the entire duration of the treatment. However, one of them interrupted the therapy after six months with relapse of symptoms within some weeks after cessation of treatment (4). In the same way, a patient with SU relapsed some weeks after their last omalizumab subcutaneous injection (5). Finally, two case of failure are also reported (6,7).

We describe herein the case of a 16-year-old Caucasian girl with a 18-month history of solar urticaria (SU) unresponsive to several attempts with conventional therapies but dramatically and fully responsive to omalizumab.

The patient with a poorly disturbing allergic rhinitis to Grass and *Alternaria*, had a quality of life seriously compromised by SU. No food allergy or asthma or other diseases were reported on patient's complete medical background. She, about 15 minutes after a minimal sunlight exposure, presented erythema, followed by intense itch, swelling and hives only in the sun-exposed body's areas. A complete spontaneous resolution occurred after about 30-60 minutes from the stop of sun exposure. Phototest was positive for UVB ($>1.2 \text{ J/cm}^2$), (Figure 1). Negative all tests for investigating other -even if less likely- causes of urticaria and photodermatosis: anti-nuclear antibody (Erythematosus Lupus Systemic); anti-thyroid antibodies; serology for celiac disease; *Helicobacter pylori* fecal antigen; erythrocyte sedimentation rate; liver and renal function panel; white blood cell count; Hepatitis C virus serology, ferritine and heme metabolites (porphyrias, in particular erythropoietic porphyria and porphyria cutanea tarda). In addition, we excluded photodermatosis induced by exogenous chemical agents by phototoxic or photoallergic mechanism because there was no history of oral or topical medications, included drugs potentially correlated to appearance of chronic urticaria such as contraceptives, antibiotics or furosemide.

In this patient, SU was unresponsive to combination of three H₁-antihistamines at standard dose (cetirizine 10 mg/die, desloratidine 5 mg/die and hydroxyine 25 mg/die), and association of H₁-antihistamine at double dose (cetirizine 20 mg/die) with H₂-antihistamine at standard dose (ranitidine 150 mg/die) and anti-leukotriene (montelukast 10 mg) always associated with high-grade sun-blockers. Short courses of prednisone tablets (25 mg daily, over 5 days) were also ineffective and the patient had again urticaria during sunlight exposure. Therefore, due to these failed

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Accepted Article

attempts with conventional therapies we discussed other therapeutic options with the patient and her parents. She and the parents signed an informed consent. Thereafter, she started experimental therapy with omalizumab (Xolair®, Novartis Europharm, United Kingdom, pre-filled syringe). On the basis of her initial serum IgE level (moderately elevated, 228 IU/mL) and her weight (57.7 kg), a calculated dose of 375 mg every 2 weeks of omalizumab was given subcutaneously. Therapeutic response of this patient has been prompt, already at the first administration; and improvement persisted with the maintenance doses. After 6 months, we reduced the dose, in agreement with the recent indication for chronic spontaneous urticarial (300 mg/month in a single dose in the 7th month, 150 mg in 8th and 9th month of treatment) up to suspension. Since the 4th month of omalizumab washout, the patient is in clinical remission. Phototest is negative both for UVA and for UVB at stop therapy and after four months (Figure 2). Currently, the patient is going on follow-up.

This case reports a successful treatment of SU with omalizumab. SU cases are quite uncommon, however the treatment with antihistamines and other drugs is often reported as ineffective (1). Therefore, in our opinion, a treatment with anti-IgE antibody (omalizumab) could contribute to a new therapeutic scenario for SU and throw light on the potential pharmacologic mechanism of omalizumab in this disease. In fact, it is conceivable that omalizumab, depleting IgE, downregulates mast cells activity and reduces mast-cells-depending inflammatory mechanisms (8).

Further studies are needed to identify patients with SU that could be treated earlier and successfully with omalizumab. In addition, randomized controlled trials are awaited in order to identify both effective treatment schedule(s) and doses for eligible patient suffering from solar urticaria unresponsive to conventional treatment.

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FIGURE 1. Before starting omalizumab phototesting demonstrating flare for UV-B (1.2 mJ/cm² within 5 minutes of testing. No reaction occurred to UV-A (>5 mJ/cm²).

FIGURE 2. No reaction occurred to UV-A nor UV-B spectrum after 4 months of treatment wash-out.

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