

Article Type: Letter to the Editor

Successful Omalizumab Treatment of Severe Solar Urticaria in a 6-Year Old Child

A. Levi^{1*}, Y. Tal^{2*}, Z. Dranitzki², M. Shalit² & C. D. Enk³

¹Photodermatosis Clinic and Laser unit, Department of Dermatology, Rabin Medical Center, Petah-Tikva, Israel.

²Allergy and Clinical Immunology Unit, Department of Medicine, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

³Department of Dermatology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

* These authors contributed equally to the manuscript.

Corresponding author: Assi Levi MD, Photodermatosis clinic and Laser unit, department of Dermatology, Rabin Medical Center, Petah-Tikva, Israel, phone- +972-504048730, fax- +97226769036, email: docalevi@gmail.com

Running head: Solar urticaria treatment with omalizumab

Key words: solar urticaria, chronic urticaria, photoprovocation, omalizumab.

Funding sources: none.

Conflict of interest: none.

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.12441

This article is protected by copyright. All rights reserved.

Summary

Solar urticaria is a rare form of inducible urticaria usually occurring minutes after sun exposure. Angioedema might accompany the urticaria in severe cases. Treatment is difficult and often unsatisfactory. Here, we present a 6-year old child with severe solar urticaria and angioedema following short exposures to day light despite continued combination therapy with high dose anti-histamines and leukotriene-receptor antagonists.

The action spectrum was established within the visible light spectrum with a minimal urticaria dose of 30 J/cm^2 . As the child faced a life in darkness unless an effective therapeutic remedy was found, we initiated Omalizumab treatment with cautious dose elevation up to 300 mg every 2 weeks.

At a maintenance dose of 300 mg every four weeks, the child remains in remission one year after initiation of treatment, almost free from urticaria episodes even following prolonged exposure to mid-day summer sun. Repeated photoprovocation with visible light was negative, validating the clinical remission.

To the editor,

Solar urticaria (SU) is a rare photodermatosis classified as a form of inducible urticaria. Clinically, SU is characterized by sudden onset of transient erythema, whealing and pruritus on sun exposed areas, occurring during or minutes after sun exposure (1). It is considered Type I hypersensitivity reaction, and as such it might well be accompanied by other characteristic symptoms and signs, most commonly angioedema (2). The action spectrum (i.e. the light waves which trigger urticaria in an individual patient) for solar urticaria includes ultraviolet A (UVA), visible light (VL) and less frequently UVB. Patients may be sensitive to multiple action spectra and the spectrum might change within a single individual during the course of illness (2).

Patients with action spectra in the UVB and UVA2 spectra often obtain sufficient light protection by using broad-spectrum sunscreens (3). However, sensitization to action spectra in the longer wavelengths often requires complete avoidance from light exposure, which obviously bears a major impact on their quality of life. Therefore, in patients sensitive to UVA1 or VL antihistamines are often prescribed with various degrees of success (4, 5). Leukotriene receptor

antagonists as mono-therapy or in combination with antihistamines can also be beneficial (4, 5). Another accepted treatment modality is UV-hardening in which a patient is gradually exposed to increasing light doses (6) on increasing body surface area. It consists of multiple light exposures for consecutive several days. Other treatments less commonly used with variable efficacy include: cyclosporine A, anti-malaria medications, intravenous immunoglobulins (IVIG) and Omalizumab (7, 8).

Omalizumab is a humanized monoclonal IgG1-kappa antibody against IgE. Omalizumab binds to the C ϵ 3 domain of IgE, forming trimers or hexamers and preventing it from binding to Fc ϵ RI on the surface of mast cells and basophils. Eventually, it down regulates cell surface IgE receptors, thereby preventing IgE-mediated histamine release (9). However, in the case of solar urticaria, the exact nature of the culprit antigen is not entirely clear.

Only recently omalizumab was approved in Europe, the US and several other countries as an add-on therapy for the treatment of chronic spontaneous urticaria in individuals that are at least 12 years old, with inadequate response to antihistamine treatment. The treatment of solar urticaria with omalizumab is still off-label as well as for other inducible urticarias, and the dosage and effectiveness are unpredictable.

Here, we report a 6-year old child with severe solar urticaria and angioedema who was referred to our clinic due to recurrent episodes of urticaria and angioedema on light exposed skin areas (figure 1) appearing minutes after light exposure. The episodes began approximately 18 months prior to his referral, gradually worsening and eventually occurring indoors as well, following exposure to artificial visible light. Medical history was positive for lactose intolerance, attention deficit hyperactivity disorder (ADHD) and atopic background (allergic rhinitis, mild atopic dermatitis). The patient had unsuccessfully tried broad-spectrum sunscreens and standard dosage of desloratadine (2.5 mg/day) prior his arrival to our clinic. Other sun avoidance measures (i.e. wearing long sleeved shirts and pants and using a hat throughout the entire year) were minimally helpful as the child still experienced urticaria and angioedema.

Physical examination was unremarkable. The patient weighed 24kg. Laboratory tests (CBC, kidney and liver function tests, CRP, ANA, anti Ro, anti La antibodies and porphyrins profile) were within normal range except for elevated IgE (2004 IU/ml). Further evaluation consisted of

photo-provocation with the purpose of inducing an urticarial lesion (figure 2) mimicking the patient's clinical complaint. Photo-provocation was performed as previously described (10). Briefly - 2x2 cm² area of unexposed skin on the back underwent a single exposure to 20 J/cm² of UVA1, 0.03 J/cm² of broad-band UVB and 50 J/cm² of VL. Action spectrum was determined to be within the VL spectrum; the Minimal Urticaria Dose (MUD) was determined as 30 J/cm². The rapidly appearing and disappearing urticaria lesions combined with the positive photo-provocation supported the initial diagnosis of solar urticaria and were not consistent with a diagnosis of other photodermatoses such as polymorphic light eruption.

Treatment was initiated (5) with desloratidine 2.5 mg twice daily, fexofenadine 120 mg twice daily, cetirizine Hcl 5 mg twice daily and montelukast 4 mg once daily. As no improvement was seen, the desloratidine dose was doubled (5mg twice a day) and the night time cetirizine Hcl dose was doubled as well (10mg), which brought a mild subjective improvement. However this improvement was short lived, as urticaria and angioedema ensued and even included a single episode of anaphylaxis which required intramuscular epinephrine administration and hospitalization. Repeated photo-provocation (while the patient is still being treated with the above antihistamines and leukotriene antagonist regimen) remained positive.

UV-hardening was suggested, but the parents rejected the option. They feared that the boy's young age and ADHD would preclude the ability to endure multiple consecutive light exposures. After careful consideration we decided to try treatment with omalizumab.

Followed by an approval from our institution ethics committee for exceptional medical treatments, an initial dose of 75 mg yielded no apparent effect. Gradual dose increment (table 1) up to 300mg twice a month resulted in complete remission. No side effects were noted. Elongating dosing interval to once every 4 weeks maintained remission, although delay of omalizumab administration brought back mild urticaria. Repeated photo-provocation was negative. Ten months after initiation of treatment, he is still on omalizumab, while anti-histamine and leukotriene antagonists are cautiously and gradually decreased. It is of interest to note that no change in atopic symptoms occurred following omalizumab treatment.

Discussion: The exact incidence of SU is unknown, yet it is considered a rare form of both the urticaria and photodermatosis. In most cases symptoms develop in young adulthood, yet pediatric cases have also been documented. Treatment of SU is highly challenging. Patients with

action spectra in the longer wavelengths (UVA1 & VL) often must entirely avoid light exposure. Though often successful (4, 5), our patient failed to respond to high doses of antihistamines combined with a leukotriene antagonist. As UV-hardening was an impractical solution, and as the child faced living in darkness unless an effective therapeutic remedy was found, we considered the best available option to be omalizumab (8).

To date, there are only 10 reported cases of omalizumab treatment for solar urticaria with heterogeneous results varying from complete remissions (6 cases) to no response (2 cases). All these cases consisted of patients older than 16 years, none of which had elevated IgE levels.

In light of the EU guidelines enabling only children older than 6 years old with severe allergic asthma (as opposed to urticaria) to receive omalizumab, we carefully initiated omalizumab treatment with ultimate success. Prior to this treatment, the patient sustained severe restrictions and was denied the ability to partake in normal childhood activities. Fortunately, omalizumab treatment brought complete remission (also supported by objective negative photo-provocation results) which enabled the child to resume his normal childhood. As for now, duration of treatment is still unknown.

Sincerely

A. Levi¹, Y. Tal², Z. Dranitzki², M. Shalit² & C. D. Enk³

¹Photodermatosis Clinic and Laser unit, Department of Dermatology, Rabin Medical Center, Petah-Tikva, Israel.

²Allergy and Clinical Immunology Unit, Department of Medicine, Hadassah-Hebrew University Medical Center, Jerusalem, Israel

³Department of Dermatology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

References

1. Dice JP. Physical urticaria. *Immunol Allergy Clin North Am*. 2004;24:225-46
2. Ng JC, Foley PA, Crouch RH, Baker CS. Changes of photosensitivity and action spectrum with time in solar urticaria. *Photodermatol Photoimmunol Photomed*. 2002; 18:191- 195.
3. Faurschou A, Wulf HC. Synergistic effect of broad-spectrum sunscreens and antihistamines in the control of idiopathic solar urticaria. *Arch Dermatol*. 2008;144:765-9.
4. Grundmann SA, Ständer S, Luger TA, Beissert S. Antihistamine combination treatment for solar urticaria. *Br J Dermatol*. 2008;158:1384-6.
5. Levi A, Enk CD. Treatment of solar urticaria using antihistamine and leukotriene receptor antagonist combinations tailored to disease severity. *Photodermatol Photoimmunol Photomed*. 2015 Jun 6. doi: 10.1111/phpp.12186. [Epub ahead of print]
6. Masuoka E, Fukunaga A, Kishigami K, Jimbo H, Nishioka M, Uchimura Y, Taguchi K, Ohgou N, Nishigori C. Successful and long-lasting treatment of solar urticaria with ultraviolet A rush hardening therapy. *Br J Dermatol*. 2012;167:198-201.
7. Güzelbey O, Ardelean E, Magerl M, Zuberbier T, Maurer M, Metz M. Successful treatment of solar urticaria with anti-immunoglobulin E therapy. *Allergy*. 2008 ;63:1563-5.
8. Boushey HA Jr. Experiences with monoclonal antibody therapy for allergic asthma. *J Allergy Clin Immunol*. 2001 ;108:S77-83.
9. Chang TW, Chen C, Lin CJ, Metz M, Church MK, Maurer M. The potential pharmacologic mechanisms of omalizumab in patients with chronic spontaneous urticaria. *J Allergy Clin Immunol*. 2015 ;135:337-342.
10. Hölzle E, Plewig G, Lehmann P. Photodermatoses--diagnostic procedures and their interpretation. *Photodermatol*. 1987;4:109-14.

Table 1: Omalizumab dosage and clinical response

Omalizumab dosage	Clinical response	Duration of treatment
75mg (A single dose)	None	Dose increment two weeks after treatment due to lack of response
150mg (A single dose)	Minimal	Dose increment two weeks after treatment due to minimal response (improvement in angioedema severity)
225mg (A single dose)	Partial	Dose increment two weeks after treatment due to partial response (fewer attacks and of shorter duration)
300mg twice a month	Complete remission	3 months
300mg once a month	Complete remission	10 months

Figure legend

Figure 1: an angioedema triggered by indoor artificial visible light.

Figure 2: A positive photoprovocation for visible light.



