

LETTER TO THE EDITOR

Adrenergic urticaria successfully treated with omalizumab

Dear Editor,

A 42-year-old woman complained of a 6-month history of 1–4-mm very itchy and erythematous urticarial papules, localized on the extremities and the trunk. Most of the papules were surrounded by a pale halo of vasoconstriction (Figure 1a,b). The flares were accompanied by palpitations and mild dyspnea, and were sometimes exacerbated by coffee intake and emotional stress. Duration of flares was 3–18 h, with lesions leaving no skin marks. Histologically, superficial dermal edema and a mild perivascular mixed infiltrate with few eosinophils were noted. i.d. epinephrine injection (5–20 ng in 0.02 mL saline) on the volar surface of the forearm reproduced the rash (Figure 1c). Tests for dermatographism, cold, and heat urticaria were negative. Cholinergic urticaria was excluded by asking the patient to perform physical exercise and by i.d. injection of 0.02% (0.01 mg) methacholine, both of which were negative. Hence, the diagnosis of adrenergic urticaria was made. H_1 antihistamines even at a two-fold dosage were ineffective, and no up-dosing was advised because the patient referred somnolence. Treatment with s.c. injections of omalizumab, at the dosage of 300 mg every month, was then started with complete resolution in 2 months. Treatment with omalizumab was continued for an additional 4 months. No relapses have been reported at 6-month follow-up.

Adrenergic urticaria is a rare form of stress-induced physical urticaria first described by Shelley and Shelley in 1985. Known triggers include trauma, emotional upset, coffee, chocolate, and ginger. The associated clinical features include wheezing, tachycardia, tachypnea, paresthesias and malaise.¹ Because of the supposed catecholamine-mediated pathogenesis, treatment with oral propranolol, a non-selective β -adrenergic antagonist, is considered the gold standard, at a dosage of 20 up to 40 mg three times a day, but its efficacy is transient. The mechanism of action of propranolol in adrenergic urticaria is not well understood, but the most accredited hypothesis is that it acts centrally to reduce sympathetic drive, which in turn reduces peripheral α -adrenergic receptor activation at mast cell adrenergic receptors, preventing mast cell degranulation.¹ Our patient suffered from moderate asthma treated with montelukast and inhaled corticosteroids; therefore, oral propranolol was avoided. A case of adrenergic urticaria resistant to propranolol was successfully treated with oral clonazepam, as it may diminish the levels of circulating catecholamines.² Finally, a case effectively treated with s.c. monthly injections of dupilumab, has been described.³ Dupilumab may reduce mast cell and basophil activation, preventing the activity of both interleukin (IL)-4 and IL-13. Omalizumab is a recombinant humanized anti-immunoglobulin (Ig)E antibody, which is supposed to reduce the number and function of high-affinity IgE

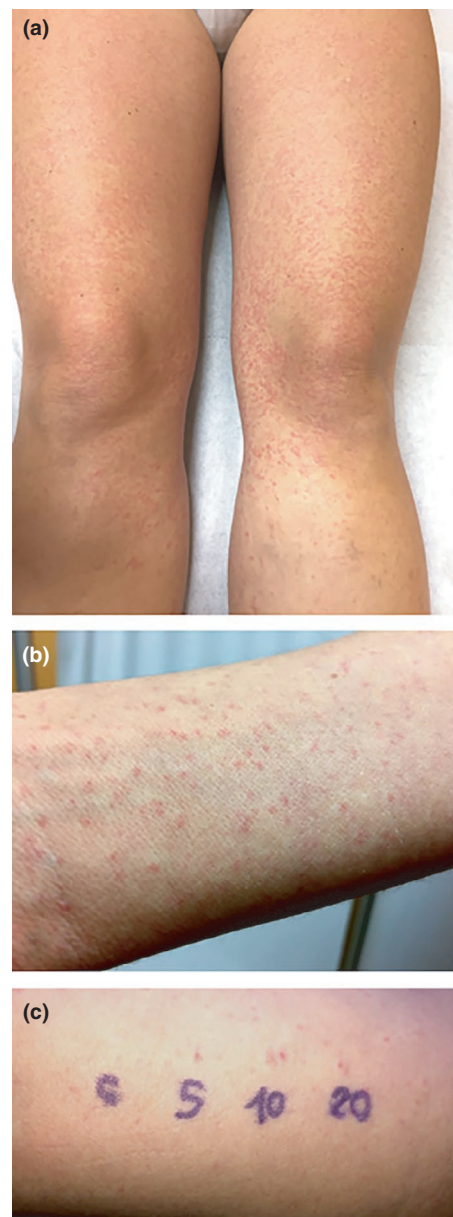


FIGURE 1 Erythematous urticarial papules at the (a) lower extremities and (b) arms. Most of the papules are surrounded by a pale halo of vasoconstriction. (c) i.d. epinephrine injection (5–20 ng in 0.02 mL saline) reproduced the erythematous urticarial papules surrounded by a pale halo of vasoconstriction. In contrast, injection of saline alone (C, control) gave no skin changes. The result of the 10 ng injection was more pronounced

receptors on basophils and mast cells, thus increasing their threshold of activation. A strong body of evidence holds up the use of omalizumab in the treatment of patients affected by chronic spontaneous urticaria.⁴ Omalizumab has been successfully used to treat also inducible chronic urticaria, including chronic cold urticaria, solar urticaria, heat chronic urticaria, delayed-pressure urticaria, dermographia, and vibratory angioedema, as well as cholinergic urticaria, aquagenic urticaria, and contact urticaria, in cases refractory to other therapies.^{4,5} Our case suggests the use of omalizumab also in adrenergic urticaria.

KEYWORDS

adrenergic urticaria, epinephrine, omalizumab, stress-induced physical urticaria, treatment

CONFLICT OF INTEREST

None declared.

ACKNOWLEDGEMENT

None.

Martina Maurelli 
Francesco Bellinato 
Giampiero Girolomoni 

Section of Dermatology and Venereology, Department of
Medicine, University of Verona, Verona, Italy

Correspondence

Martina Maurelli, Section of Dermatology and Venereology,
Department of Medicine, University of Verona, Piazzale A.
Stefani 1, Verona 37126, Italy.
Email: maurelli.martina@gmail.com

ORCID

Martina Maurelli  <https://orcid.org/0000-0001-7492-8010>

Francesco Bellinato  <https://orcid.org/0000-0002-6163-6921>

Giampiero Girolomoni  <https://orcid.org/0000-0001-8548-0493>

REFERENCES

1. Hogan SR, Mandrell J, Eilers D. Adrenergic urticaria: review of the literature and proposed mechanism. *J Am Acad Dermatol.* 2014;70:763–6.
2. Kawakami Y, Gokita M, Fukunaga A, Nishigori C. Refractory case of adrenergic urticaria successfully treated with clonazepam. *J Dermatol.* 2015;42:635–7.
3. Goodman B, Jariwala S. Dupilumab as a novel therapy to treat adrenergic urticaria. *Ann Allergy Asthma Immunol.* 2021;126: 205–6.
4. Maurer M, Metz M, Brehler R, Hillen U, Jakob T, Mahler V, et al. Omalizumab treatment in patients with chronic inducible urticaria: a systematic review of published evidence. *J Allergy Clin Immunol.* 2018;141:638–49.
5. Chicharro P, Rodríguez P, de Argila D. Omalizumab in the treatment of chronic inducible urticaria. *Actas Dermosifiliogr.* 2017;108:423–31.