



Letter

Short-term omalizumab treatment in an adolescent with cutaneous mastocytosis

Omalizumab is a recombinant humanized monoclonal antibody that blocks the binding of IgE to the FcεRI receptor on the surface of mast cells (MCs) and basophils, reducing receptor expression¹ and the release of mediators.² It is approved for patients 12 years or older with moderate to severe persistent allergic asthma that is inadequately controlled with inhaled corticosteroids. However, successful anti-IgE therapy with omalizumab has been documented in some conditions, such as chronic urticaria,³ idiopathic anaphylaxis,⁴ and mastocytosis,⁵ among others.

We report the case of a girl residing on the south coast of Spain who was diagnosed as having mastocytosis at birth by a skin biopsy that confirmed massive MC infiltration (Figure 1). Extensive cutaneous involvement did not change during the follow-up, and during this period the patient presented with occasional pruritus and erythema, although she did not require any therapy to control these symptoms. However, at 7 years of age, she presented with daily pruritus and diarrhea as symptoms due to release of the MC mediators. At that time she was referred to our center, and her serum basal tryptase level was determined for first time (15.4 ng/mL); furthermore, scheduled oral disodium cromoglycate and H₁- and H₂-antihistamines were prescribed and the symptoms improved. Afterward, she developed several bronchospasm attacks treated at the emergency room; an allergological workup was performed, and she was diagnosed as having allergic asthma caused by dust mites. She began therapy with twice-daily inhaled fluticasone furoate, 250 μg, and the asthma was controlled. She remained stable until 12 years of age, when she presented with almost daily unprovoked generalized urticaria sometimes associated with facial swelling and unprovoked anaphylactic episodes manifested with urticaria, shortness of breath, and wheezing despite the scheduled antimedator and bronchodilator therapies prescribed. Of interest, she did not present with isolated bronchospasm crisis in this period. Several times she required attention at the emergency department, and treatment with parenteral H₁-antihistamines, corticosteroids (methylprednisolone, 1 mg/kg), and inhaled epinephrine was administered. Subsequently, the doses of the scheduled antimedator therapy were increased; moreover, inhaled long-acting β₂-agonist (salmeterol, 50 μg twice daily) and inhaled and oral corticosteroids in an attempt to follow decreasing courses (fluticasone furoate, 500 μg twice daily, and prednisone, 1 mg/kg daily, as the highest dose, respectively) were also added. From this moment on, she had no more anaphylactic episodes; however, the urticaria was refractory to this therapy after 3 months of treatment, even when she was taking the highest doses of prednisone.

Clinical workup did not reveal any environmental exposure, food ingestion, drug administration, insect stings, exercise, or any other identifiable allergens as elicitors of these symptoms; in

addition, a complete routine peripheral blood cell count, as well as routine biochemical analysis and thyroid function tests, revealed normal values; abnormalities were not found in a stool analysis with microscopic examination and culture. The allergic workup revealed a serum basal tryptase level of 8.57 ng/mL; a total IgE level of 508 kU/L; a specific IgE level to *Alternaria alternata*, *Aspergillus fumigatus*, *Cladosporium herbarum*, *Anisakis*, *Ascaris*, and *Echinococcus* less than 0.1 KU/L; and a specific IgE level to *Dermatophagoides pteronyssinus* of 56.9 kU/L. Skin prick tests were not performed because use of H₁-antihistamines and corticosteroids therapies could not be discontinued because of the severity of the MC-mediator related symptoms. The spirometry test revealed normal results, although the test was performed while the patient was using inhaled long-acting β₂-agonist (salmeterol, 50 μg twice daily) and oral and inhaled corticosteroids (fluticasone furoate, 500 μg twice daily). A subsequent skin biopsy was performed when the patient was 12 years of age, and the results revealed a remarkable decrease in MC infiltration compared with the previous biopsy result (Figure 1), although cutaneous mastocytosis involvement persisted. The systemic involvement was not ruled out because the parents of the patient refused their consent to perform a bone marrow study. The patient was diagnosed as having mastocytosis in the skin presenting with unprovoked severe symptoms (such as generalized urticaria and anaphylaxis) secondary to mast cell activation. The patient weighed 76 kg, a dose of 450 mg of omalizumab every 4 weeks was prescribed, and she was given a total of 3 doses. Forty-eight hours after the first injection the patient became completely asymptomatic, so progressive and total discontinuation of the antimedator and bronchodilator therapies was achieved in 2 months, and the absence of symptoms persisted after 12 months of follow-up.

Previous series have found that 11% of pediatric patients with mastocytosis present with severe (even life-threatening) MC-related symptoms, more frequently within the first 18 months after disease onset; moreover, increased serum basal tryptase levels identified patients at risk of severe MC-related symptoms.⁶ In addition, a frequency ranging from 6% to 9% of anaphylaxis in pediatric patients with mastocytosis was previously described,^{7,8} accompanied with an extent of skin lesions of more than 45% and elevated tryptase levels in these children.⁸

We describe a patient with mastocytosis with cutaneous involvement who presented with an atypical evolution indicating an age-related worsening of MC release mediator symptoms and a decrease in serum tryptase levels and skin MC infiltration as assessed by skin biopsy. The efficacy of omalizumab in the treatment of unprovoked anaphylaxis in atopic patients with mastocytosis was previously reported⁵; however, to the best of our knowledge, this is the first case of mastocytosis successfully treated with short-term courses of omalizumab, resulting in a rapid, complete, and long-term remission of severe MC mediator-related symptoms.

Disclosures: Authors have nothing to disclose.

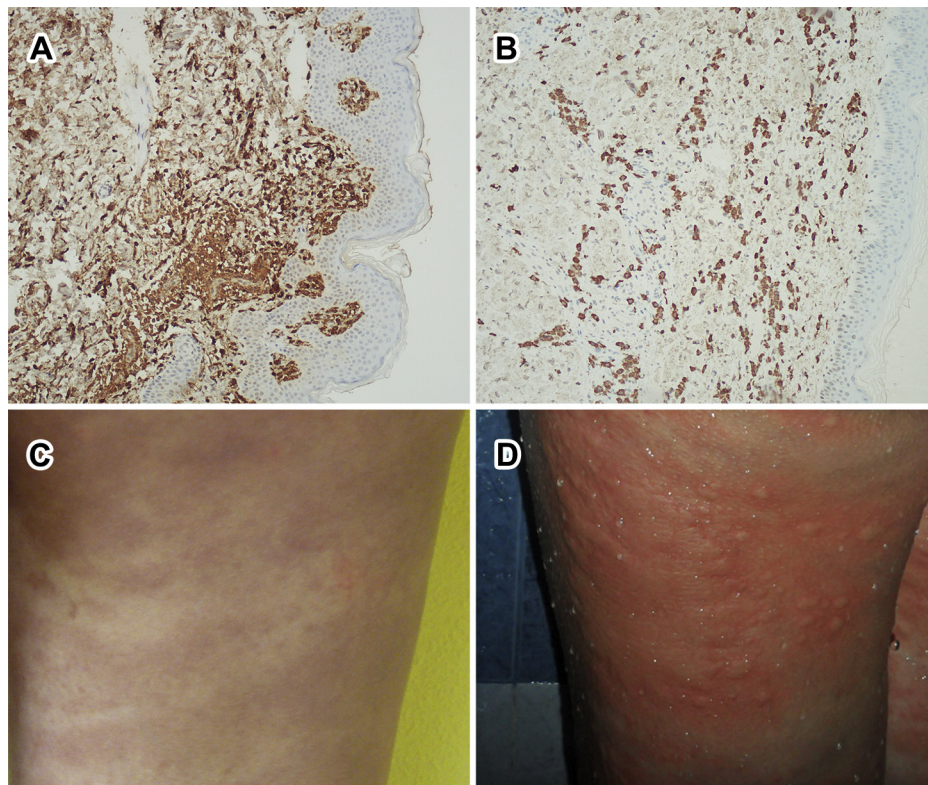


Figure 1. A, Skin biopsy specimen at birth with massive mast cell infiltration (tryptase, original magnification $\times 100$). B, Skin biopsy specimen at 12 years of age (tryptase, original magnification $\times 100$) shows a remarkable decrease of mast cell infiltration. C, Extensive cutaneous mastocytosis involvement. D, Hives.

In addition, the long-term efficacy of short-term omalizumab treatment in chronic urticaria and the rapid onset of action in severe MC mediator release symptoms in mastocytosis patients treated with omalizumab were also described,^{5,9,10} although all of these cases needed maintenance treatment with omalizumab to control the MC mediator release symptoms.

This case highlights some important points regarding omalizumab treatment, such as the rapid and long-term efficiency of this monoclonal antibody to control severe or even life-threatening MC-related symptoms in mastocytosis patients, as well as the use of short courses of this drug and the discontinuation of other therapies, both aspects of great interest if we consider that we were treating an adolescent. However, further studies and reports to confirm the efficiency of this short-term treatment with omalizumab in mastocytosis are required.

Acknowledgments

Drs Matito, Álvarez-Twose, Mollejo, Sánchez-Muñoz, and Escribano and Mr Morgado are members of the Spanish Network on Mastocytosis (REMA).

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