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Dupilumab as a rescue therapy for a chronic urticaria patient who showed secondary failure to omalizumab

Chronic urticaria (CU) is a mast cell (MC)-driven disease characterized by the development of wheals, angioedema, or both for more than 6 weeks. Although current management guidelines recommend a stepwise approach, beginning with antihistamine therapy and gradually increasing its dosage,¹ some patients remain refractory to the usual treatment guidelines. It has been postulated that MC-degranulating signals involving immunoglobulin-E (IgE) autoantibodies may be implicated in patients with CU.^{2,3} Patients with refractory CU are experiencing complete remission for the first time, thanks to the use of omalizumab, an IgG monoclonal antibody that inhibits IgE binding to the high-affinity IgE receptors on MCs. However, few studies to date have mentioned the options available to patients who develop secondary failure to omalizumab after a positive initial response. Herein, we describe a patient with CU who developed tolerance to omalizumab and demonstrated a favorable response to dupilumab.

A 44-year-old man presented with episodes of pruritic wheals and papules over his trunk and extremities, as well as occasional episodes of angioedema occurring over 6 weeks. Therefore, a diagnosis of CU was made. Laboratory investigations showed elevated IgE levels (732 IU/ml) and were negative for autoimmune, thyroid, and paraneoplastic workups. Over the next 6 months, antihistamines (H1 Receptor blockers), ciclosporin, and phototherapy were all attempted as therapeutic modalities, without improvement. The patient experienced symptomatic relief upon administration of systemic steroids but had to discontinue the treatment due to severe weight gain. His urticaria activity score over 7 days (UAS7) was graded as severe, at 42 points. Due to the refractory nature of his illness, omalizumab therapy was initiated at 300 mg per month, which led to marked clinical improvement after just 1 month of treatment (UAS7: 7). However, severe pruritus and wheals recurred around the time the third injection was administered, and complete loss of efficacy was noted by the fifth injection (UAS7: 42). Hence, omalizumab was discontinued due to what was classified as secondary failure, and severe flare-ups of the patient's illness persisted. Owing to his favorable response to anti-IgE therapy, a decision was made to initiate dupilumab, a monoclonal antibody with actions against interleukin 4 (IL-4) and interleukin 13 (IL-13) (600-mg subcutaneous loading dose, followed by 300 mg every 2 weeks thereafter). Significant clinical improvement was noted in symptoms such as pruritus, wheals, and

angioedema, after the very first dose itself (UAS7: 0). IgE levels normalized (8.2 IU/ml) on subsequent laboratory investigations. Most importantly, the patient's quality of life improved drastically. His condition remained stable for the next 24 months while on maintenance dupilumab treatment.

CU is a multifactorial, refractory disease. The pathophysiology of CU remains poorly described, with IgE and non-IgE-mediated release of histamine being attributed as the two main causes of the disease. The role of IgE in CU is congruent with reports on patient responsiveness to omalizumab.² In cases of CU refractory to omalizumab, dupilumab has been used with varying degrees of success⁴; however, the best treatment protocol for treating patients with CU is still under investigation. While the reason for the secondary failure of omalizumab in this patient remains unclear, his initial favorable response to omalizumab confirms that IgE does play a crucial role. Taken together, for CU patients who develop secondary failure to omalizumab, dupilumab represents a logical rescue treatment. It effectively blocks (IL-4) and (IL-13) signaling pathways that are crucial in initiating and driving the class-switching of B-cell immunoglobulins toward IgE,⁵ giving the patient a chance to experience better quality of life.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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