Long-term follow-up of patients treated with dupilumab for chronic spontaneous urticaria: A case report

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Abstract

Several therapeutic strategies have been established to achieve maximal remission and improve quality of life in patients with chronic spontaneous urticaria. We previously reported dupilumab as a novel therapy for antihistamine-refractory chronic spontaneous urticaria patients who failed to respond to administration of omalizumab at increased doses for longer durations. This is the first case series to report data on the long-term duration of chronic spontaneous urticaria remission after discontinuation of dupilumab in patients who were able to obtain controlled chronic spontaneous urticaria. Six patients diagnosed with chronic spontaneous urticaria, who failed to respond to antihistamines and prolonged therapy with omalizumab at increased doses, were followed in this study for up to 34 months following initiation of dupilumab therapy. By demonstrating the maintenance of chronic spontaneous urticaria remission with dupilumab following discontinuation of therapy, in 67% of the patients, over an observation period up to 22 months, this case series highlights dupilumab's potential disease-modifying efficacy in patients affected by this disease.

Keywords

Chronic spontaneous urticaria, dupilumab, type 2 inflammatory pathway

Introduction

Several therapeutic strategies have been established to achieve maximal remission and improve quality of life in patients with chronic spontaneous urticaria (CSU). Omalizumab, a monoclonal anti-IgE antibody, has been previously shown to be effective in patients with CSU where first- and second-line therapies have been unsuccessful.[1] However, there is more evidence suggesting that omalizumab cannot achieve well-controlled CSU in a significant percentage of these patients.[2]

We previously reported dupilumab as a novel therapy for antihistamine-refractory CSU patients who failed to respond to administration of omalizumab at increased doses for longer durations.[3] This included six patients with CSU (three females and three males, average age of 36 years) who all failed to respond to long durations (at least 6 months, up to 38 months) of omalizumab (dosed 300–600 mg monthly) who then subsequently responded to dupilumab within 3 months of initiation, as measured by Urticaria Activity Score summed over 7 days (UAS7). Herein, we report the long-term follow-up of these patients. To our knowledge, this is the first case series to report data on the long-term duration

of CSU remission after discontinuation of dupilumab in patients who were able to obtain controlled CSU.

Case report

Six patients (three females, three males, average age of 36 years) were followed in this study, for up to 34 months. Written consent was obtained prior to initiation of this study for data collection and case report publishing. CSU disease activity was assessed using UAS7. The cohort demonstrated an initial mean UAS of 37.4 (standard deviation, 4.04). Of these six patients, one remained uncontrolled despite dupilumab and was given omalizumab as an add-on therapy 9 months after initiating dupilumab. Another patient was unable to afford to continue dupilumab and had a lapse of

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receiving dupilumab for 18 months and was restarted on dupilumab through compassionate access. CSU remission was therefore not achieved in these two patients. The other four patients presented in our original paper, however, showed that UAS remained zero, at 14–22 months of follow-up since discontinuation of dupilumab.

Discussion

Our initial case series highlighted dupilumab's potential role in controlling disease activity in CSU as the pathophysiology of CSU involves type 2 inflammatory pathways. These follow-up data report the absence of disease activity long after discontinuation of therapy, suggesting dupilumab's potential disease-modifying efficacy in patients impacted by this disease.[4] Dupilumab's mechanism of action is widely reported in the current literature as it inhibits interleukin (IL)-4 and IL-13 signalling through their shared IL-4a receptor subunit blockade and indirect downstream affects that arise as a consequence of activation of IL-4 and IL-13 such as cell trafficking and recruitment of mast cells and other components of type 2 inflammation. The Th2 cytokines IL-4 and IL-13 promote isotype class switching to IgE and IgG and act on mast cells, eosinophils, and basophils, all of which have been identified to play a role in the pathogenesis of this disease.[5]

In conclusion, this case series demonstrates CSU remission with dupilumab following discontinuation of therapy, in 67% of the patients, over an observation period up to 22 months. Evidence of benefit lasting long after discontinuation of this therapy suggests that discontinuation of dupilumab can be safe and a cost-efficient and effective therapy that accomplishes clinical resolution in many patients while limiting unnecessary exposure and costs of requiring maintenance biologic and other therapies. Further long-term follow-up studies can enhance our current understanding of the potential for disease modification.

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