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Benefit from Reslizumab Treatment in a Patient with Chronic Spontaneous Urticaria and Cold Urticaria

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Running Head: Reslizumab in urticaria

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Dear Editor,

Chronic urticaria (CU) is a group of common and debilitating conditions containing both chronic spontaneous urticaria (CSU) and chronic inducible urticarias (CIndU) including cold urticaria (ColdU) [1]. While antihistamines and omalizumab are effective treatments for both CSU and ColdU [2], many patients show insufficient response to either or both of these treatments [3], and additional and better therapies are needed [4].

Reslizumab is a humanized monoclonal anti-interleukin 5 (IL-5) antibody licensed for the treatment of severe eosinophilic asthma. IL-5 is the major cytokine responsible for the recruitment, activation and survival of eosinophils, which play a crucial role in causing tissue and subsequent airway hyperresponsiveness in asthma [5]. Previously, we demonstrated that eosinophil numbers are increased in the skin of CSU patients [6]. Recently, we reported that treatment with mepolizumab, another monoclonal antibody against IL-5, can result in the rapid remission of CSU [7].

Here, we report the case of a 43 year-old woman with severe non-allergic refractory eosinophilic asthma (non-smoker, IgE 136 kU/l, skin prick test negative to pollen, mites and other common aeroallergens, eosinophils 540/ μ l, FEV₁ 75% predicted, asthma control test (ACT) 15 points, four asthma exacerbations in the last year, therapy including prednisolone 50 – 25 mg/day, LAMA and LABA) who was successfully treated for her asthma with reslizumab. Our patient experienced a rapid improvement of her asthma following the first infusion of reslizumab (300 mg). The FEV₁ increased to 91%, ACT to 20 points, prednisolone was reduced to 15 mg 7 days later, cough and night symptoms diminished in the first 10 days.

In addition to her asthma, our patient had ColdU and CSU with recurrent angioedema but without wheals for 23 years. She first became aware of her ColdU because of a severe systemic reaction and widespread whealing after swimming in a cold Swedish lake. Subsequent provocation testing confirmed ColdU. Despite her attempts to avoid cold exposure, she experienced cold-induced symptoms approximately weekly each winter.

Together with her ColdU, our patient also started to experience episodes of recurrent angioedema without wheals, the least common of the three phenotypes of CSU. Her swellings affected her lips, eyes, cheeks, hands and feet and lasted for up to one day. They were accompanied by a burning painful sensation. The frequency of these swelling episodes over the years varied from once to twice per month with a gradual increase over the last years. Retrospective assessment of her CU, both ColdU and CSU, before reslizumab treatment by the urticaria control test (UCT) showed uncontrolled disease with a UCT score of 6. In this 4-item validated instrument with a 0 to 16 scoring range, a score of <12 indicates uncontrolled and $\geq$ 12 indicates well controlled disease [8-10].

Immediately following reslizumab injection, our patient experienced substantial sustained improvement of her urticaria symptoms, both CSU and ColdU. Four weeks after the first injection, her UCT score was 16, indicating complete disease control. This score has been maintained over the last four months of treatment with reslizumab 300 mg / month.

To our knowledge this is the first case of reslizumab treatment of a CU patient. Before reslizumab treatment, the patient's poorly controlled urticaria symptoms and her need to avoid cold exposure impacted greatly on her quality of life.

In conclusion, our observation that the anti-IL-5 antibody, reslizumab, effectively reduces the symptoms of CSU and ColdU suggests an axial role of eosinophils in these conditions. While a mechanism cannot be concluded, we speculate that eosinophils contribute to the development of wheals and angioedema or induce tissue hyperresponsiveness thereby reducing the threshold for symptom development.

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