

Urticaria- bane or boon to treat with omalizumab? A case series

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ABSTRACT

Chronic spontaneous urticaria (CSU) is a condition characterised by the presence of hives with/without angioedema that affects individuals on more days than not for 6 weeks or more. This can be a very debilitating condition affecting the quality of life. Here, we report 3 cases of severe prolonged chronic spontaneous urticaria in 7-year-old, 20-year-old and 25-year-old individuals that went into rapid remission following the treatment with Omalizumab, anti-IgE monoclonal antibody.

Keywords: Antihistamines, Anti-IgE, Monoclonal antibody, Omalizumab, Urticaria.

Urticaria is a dermatological disorder that manifests as raised erythematous lesions that range in size. They are pruritic and typically resolve with no changes to the appearance of the skin. Urticarial lesions may be associated with episodes of ‘angioedema’ [1]. Usually, second-generation antihistamines are the first line of treatment in chronic urticaria [2]. Many a time, pharmacotherapy with antihistamines alone may not be of help. In the majority of the situations, patients continue these medications for a long period of time, with/without desired effect and sometimes, the treating clinician will have to resort to the use of immunosuppressant like Cyclosporine. The treatment may be unresponsive to traditional and increasing doses of anti-histamines. In such cases, Omalizumab, an anti-IgE monoclonal antibody is the treatment option [3]. We report 3 cases of severe chronic spontaneous urticaria that rapidly resolved following treatment with Omalizumab.

CASE SERIES

1st Case: A 7-year-old female patient was referred to the Allergy and Immunology clinic by her Paediatrician. She presented with a two-month history of urticaria with intermittent episodes of angioedema. Her initial symptoms included facial pruritis, periorbital erythema and angioedema involving the upper and lower lips. Within 30 minutes of her first episode of angioedema, she developed widespread urticaria which responded to treatment with antihistamines. The following day, she experienced a recurrence of the symptoms and continued to have almost daily symptoms of urticaria with intermittent episodes of angioedema. These episodes led to her being bullied in school and led to school absenteeism many a time.

She was commenced on alternative anti-histamine by her Paediatrician but continued to develop urticaria and experience swellings of the hands and feet. Her treatment was escalated at

her initial visit to Allergy and Immunology Clinic to fexofenadine 180mg twice a day with an additional 10–20mg of cetirizine. In addition, montelukast, a leukotriene receptor antagonist, was commenced. The number of hives and degree of pruritis were graded using an objective scoring system known as the Urticaria Activity Score 7 (UAS7) that provides a weekly average score out of a maximum score of 40. The patient recorded weekly UAS7 scores of 32, despite treatment with maximum doses of antihistamines and montelukast. Therefore, Anti-IgE therapy with the monoclonal antibody, Omalizumab, was offered. The parents consented for the same and she was started on 300 micrograms of subcutaneous Omalizumab once in 4 weeks.

About 4 weeks after this intervention, her UAS7 score fell to 10 and then to 2–4 after the second dose and she has remained in remission (UAS 7 score 0) for 11 months after about 4 doses of Omalizumab. Initial investigations including full blood count, renal function, liver function and thyroid function tests were all within the normal ranges. She was happy with her remission and it helped her in her academic activities as well.

2nd Case: A 20-year-old male patient was referred to the Allergy and Immunology Clinic by his Ophthalmologist in view

Table 1: Types of Inducible Urticaria

Types	Subtypes	Stimulus
Physical urticaria	Cholinergic urticarial	Rise in body temperature
	Cold urticarial	Upon contact with cold objects
	Vibration urticaria	Contact with a vibrating stimulus
	Pressure urticaria	May be associated with delayed onset of wheals on application of pressure
	Aquagenic urticaria	Contact with water

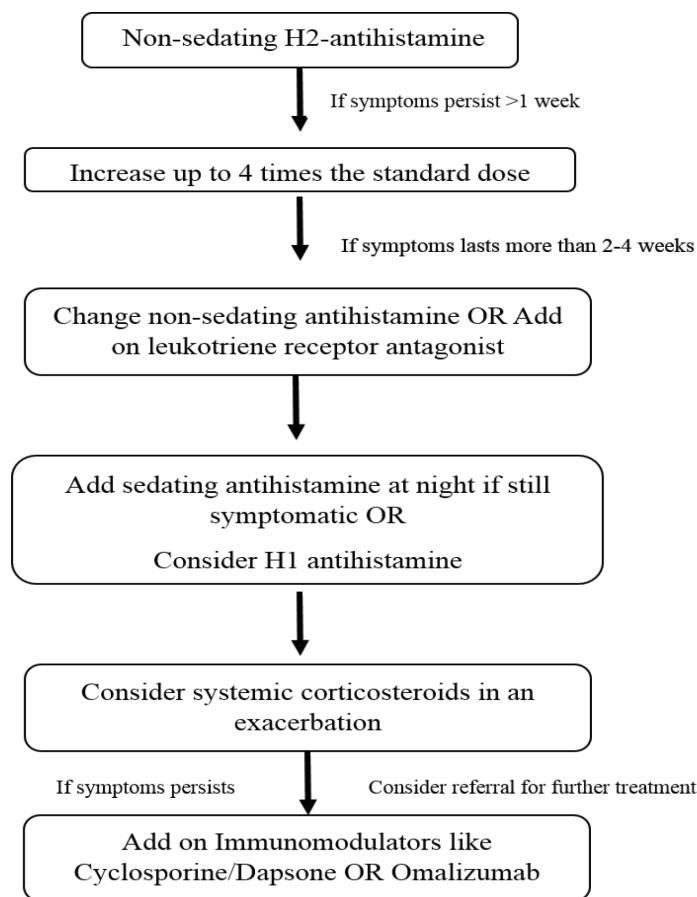


Figure 1: Algorithm for treatment of chronic urticaria.

of persisting allergic rhinoconjunctivitis of 1-year in spite of optimal local treatment with eye formulations. Incidentally, he also had a history of urticaria of 6-month duration along with the presenting complaints. He was being treated with an oral antihistamine for his urticaria by his general practitioner (GP), with recurrence of his symptoms. He was escalated to oral fexofenadine 180mg twice daily and montelukast 10mg, once daily at his initial visit to Allergy and Immunology clinic. UAS7 was used to grade the number of hives and degree of pruritis as was done in the earlier patient. The patient recorded weekly UAS7 score of 30, in spite of higher doses of antihistamines. Hence, the decision to start therapy with Omalizumab was mutually taken after due discussion with the patient and his family. He was started on 300 micrograms of subcutaneous Omalizumab once in 4 weeks.

After about 6-8 weeks into this therapy, his UAS7 score decreased to about 10 and then to 0 after the third dose and has remained in remission for a year, after a total of 6 doses of Omalizumab. His allergic rhinoconjunctivitis symptoms have also improved concurrently.

3rd Case: A 25-year-old male patient was referred to the Allergy and Immunology Clinic by his dermatologist with a history of chronic urticaria since last few months. He was treated with oral antihistamines, with increased dose, for a few weeks, with relapse of symptoms. In view of the severity of symptoms, the decision of starting Omalizumab was taken after discussion

with the patient. In spite of 3-4 doses of 300mcg subcutaneous Omalizumab, the patient had minimal relief. Hence, we re-visited the history with the patient. Upon review, the patient mentioned that he had pigeons at his home. On advice to avoid the same, the patient got better within a few weeks. This is to emphasise that medical history and examination is of utmost importance, to be considered at each step of the treatment if there are no desired results with appropriate medical management.

DISCUSSION

Urticaria is a heterogeneous, common group of disorders characterised by the appearance of fleeting wheals, lasting for 1-24 hours and/or angioedema lasting for up to 72 hours. The prevalence in children is estimated to be around 3-8% with chronic urticaria being less common. Acute urticaria typically lasts less than 24 hours and is usually self-limiting. It is mainly seen in association with infections in children. Acute urticaria can also occur in combination with other systemic symptoms as part of an allergic reaction upon exposure to certain foods (milk, eggs, nuts, peanut), drugs like penicillins, stinging insect venom (wasp, honey bee) or skin contact with an allergen. Symptoms can be treated with non-sedating anti-histamines if very bothersome.

Chronic spontaneous urticaria (CSU) is defined as daily or almost daily urticaria for at least 6 weeks [1]. In up to 50% of patients, urticaria may be associated with episodes of angioedema [2]. Chronic urticaria (CU) is rarely caused by allergies and is not a life-threatening condition. These features are the result of degranulation of mast cells with the release of granule contents, predominantly histamine.

Resolution of symptoms occurs in approximately 80% patients within 1 year of onset of symptoms but can persist beyond five years in about 10 % of patients [4,5]. It often lasts less than 5-10 years. Quality of life is often severely affected [6, 7]. In Inducible forms of Chronic Urticaria, avoidance of the trigger is preferred, though it may not be feasible all the time.

Patients often present to their GP and are referred for further assessment and management by Immunologists, Allergists or Dermatologists when first-line treatment with antihistamines fail to control the symptoms. The mainstay of treatment is high dose antihistamines and leukotriene receptor antagonists [1]. In recent years, the anti-IgE monoclonal antibody therapy, Omalizumab, has been used as an effective treatment for patients who fail to respond to first-line therapy. The algorithm for the treatment of chronic urticaria [8] is given in Fig. 1.

As highlighted in our case series, patients with recalcitrant chronic urticaria to antihistamine went into remission soon after initiation of therapy with Omalizumab. They are continued to follow up periodically, to assess the quality of life and relapse of urticaria. Only a single patient, had mild relapse of symptoms about 10 months of cessation of therapy with Omalizumab, which was treated with second-generation antihistamines for three days and has been better since.

CONCLUSION

There is definitely a need for more clinical data from our country in the setting of treatment of Chronic Urticaria to streamline the use of biologicals like Omalizumab. Clinicians should recognise the potential role of Omalizumab in treating such chronic urticaria cases. There should be a low threshold to consider this option for treatment in cases of resistance to treatment with anti-histamines.

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