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Recurrent oedema of the uvula in a patient with chronic spontaneous urticaria successfully treated with omalizumab

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ABSTRACT

Uvula oedema is a condition characterized by a sensation of a foreign body in the oropharynx and difficulty to speak; sometimes, if associated with glottis oedema, difficulty to breathe and dysphonia are also present. Urticaria is a disease characterized by itching wheals on the skin, and sometimes angioedema. Chronic urticaria is spontaneous when the etiology is unknown. Chronic urticaria may be disabling and difficult to treat, with a negative impact on the patient's quality of life. Omalizumab administration is suggested for refractory patients as add-on therapy to the antihistamines, in a third line. In Italy, omalizumab may be used for the treatment of spontaneous chronic urticaria in patients older than 12 years, refractory to antihistamines, with UAS >3 and UAS7 > 16. We describe a case of a 62-year-old woman had had recurring uvula oedema and chronic urticaria, not responder to antihistamines and oral corticosteroids. After 6 months of treatment with omalizumab and antihistamines, no urticaria recurrence was reported and no new episodes of angioedema had occurred. Our experience showed that omalizumab might be effective in patients with recurrent uvula oedema associated with urticaria.

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KEYWORDS

Uvula oedema; chronic spontaneous urticaria; CSU; omalizumab

Introduction

Uvula oedema is a condition characterized by a sensation of a foreign body in the oropharynx and difficulty to speak; sometimes, when glottis oedema is concomitantly diagnosed, difficulty to breathe and dysphonia are also present. It may be associated with urticaria/angioedema and anaphylaxis (1). Only a few studies have been published about pathophysiology and therapy of uvula oedema. It was reported that the risk of oedema might be increased by some anatomical features, such as a long uvula and by exposure to some factors, such as drugs, cannabis or cocaine abuse, or related to the presence of allergy, respiratory tract infections, and trauma (2).

Urticaria is a disease characterized by itching wheals, and sometimes angioedema. According to EAACI/GA²LEN/EDF/WAO (European Academy of Allergy and Clinical Immunology, Global Allergy and Asthma European Network, European Dermatology Forum, World Allergy Organization) guidelines, urticaria is considered chronic when it lasts longer than 6 weeks (3). Chronic urticaria is spontaneous when the etiology is unknown. Chronic urticaria may be disabling and difficult to treat, with a bad impact on the patient's quality of life. A first line therapy with second generation antihistamine drugs is recommended for chronic urticaria, titrating the dosage up to fourfold the usual dose (second line treatment). Omalizumab administration is suggested for refractory patients as add-on therapy to the antihistamines, in a third line treatment (3). According to Italian regulatory, omalizumab may be used for the treatment of spontaneous chronic urticaria in patients older than 12 years, refractory to antihistamines, with UAS >3 and UAS7 > 16.

Patient and methods

A 62-year-old woman had recurring uvula oedema for 3 years, with 4 or 5 episodes/year, and chronic urticaria in the last year, before arriving at our center. During these episodes, difficulty to breathe and dysphagia were reported. The patient received antihistamines and oral corticosteroids, at home, with unsatisfactory benefit; otolaryngologist had visited the patient; she was referred to an emergency division on some episodes. Additional drugs were not administered. The patient did not report individual or familial atopy. The physical examination did not show abnormal factors. The patient has no clinical history of additional chronic diseases nor was she taking other drugs.

Results

Blood analysis was performed: complete blood count, erythrocyte sedimentation rate, C reactive protein, functional thyroid markers, liver enzymes, immunoglobulins, C3, C4, C1 inhibitor, C1q, anti-nuclear antigen, and anti-DNA antibodies. Allergy tests were executed to rule out a secondary urticaria: prick test for airborne or food allergens and patch test with the SIDAPA (Società Italiana di Dermatologia Allergologica Professionale) series antigens. Blood analysis results were within the normal values and allergy tests were negative.

Rupatadine 10 mg twice a day for 20 days was prescribed and the clinic diary for UAS determination was given to the patient. At control visit, UAS was 4 and UAS7 was 20. Chronic spontaneous urticaria with uvula angioedema was diagnosed, and, due to unsatisfactory control and intolerable symptoms of

urticaria, omalizumab 300 mg every 4 weeks was added to rupatadine 10 mg/day. After the first injection of omalizumab, urticaria regression was observed, with UAS = 0 and UAS7 = 0. After 6 months of treatment with omalizumab and antihistamines, no urticaria recurrence was reported and no new episodes of angioedema had occurred. Antihistamine and omalizumab treatments were discontinued.

No new urticaria or uvula oedema episodes were reported one year after treatment with omalizumab.

Discussion

Oedema of the uvula etiology is unknown in most cases, and idiopathic oedema recurs more often than secondary oedema (2,4). Uvula oedema is considered a localized type of angioedema, resistant to antihistamines and corticosteroids. Angioedema may have several localizations and may be either associated with urticaria or not. Different mediators, such as histamine or bradykinin, have a role in different forms of angioedema, but all of them increase vessel permeability. Angioedema mediated by bradykinin is usually not associated with urticaria (5). Three hereditary types and four acquired types of angioedema without urticaria were identified by a recently published consensus report: idiopathic histaminergic AE (IHAAE), idiopathic non-histaminergic AE (InH-AAE), acquired AE related to angiotensin-converting enzymes inhibitors (ACEi-AAE) and AAE with C1-inhibitor deficiency (C1-INH-AAE) (6). Several physiopathological mechanisms and therapeutic approaches were described (6). Idiopathic angioedema is often mediated by histamine, whose release usually follows to mastocyte degranulation, and is often associated to urticaria (7). It was also reported that angioedema is more frequent in patients with spontaneous chronic urticaria resistant to antihistamines, than in cases that may be controlled by antihistamines (59% vs. 29%, $p < .001$) (8).

Chronic urticaria and IH-AAE are thought to belong to the same clinical entity; the clinical characteristics of IH-AAE have been described as similar to those of chronic urticaria (6,9). In our patient, the angioedema came first, followed by urticaria, in two years. Although a histamine-mediated mechanism would be presumable for both diseases, it is not possible to assume if the symptoms pathophysiology is common. Efficacy of omalizumab in chronic urticaria associated with angioedema was demonstrated by clinical studies. A significantly greater mean proportion of angioedema-free days, from weeks 4 to 12, with 300 mg of omalizumab versus placebo, has been reported in three clinical trials: ASTERIA I (96.1% vs. 88.2%, $p < .001$), ASTERIA II (95.5% vs. 89.2%, $p < .001$), and GLACIAL (91.0% vs. 88.1%, $p < .001$) (10). Other studies have shown that omalizumab can be effective in antihistamine-resistant angioedema, when its mechanism of action is not fully understood; this might be the case here (11–14).

Conclusion

Our experience showed that omalizumab might be effective in patients with recurrent uvula oedema associated with urticaria.

Patient consent

The patient gave consent to the inclusion of material pertaining to herself into this article, she acknowledged that she cannot be identified via the paper; the authors fully anonymized patient's material.

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Disclosure statement

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