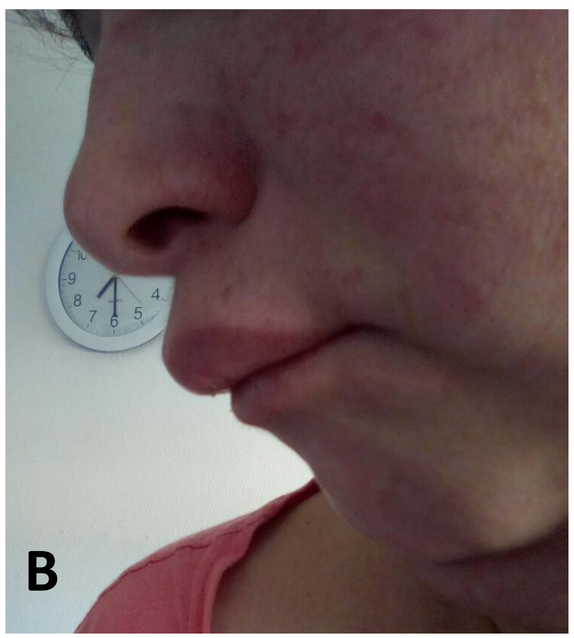
Histaminergic angioedema and belimumab : a report of two cases

Noureddine J, Trefond L, Smets P, Tollis E, Olagne L, Aumaître O, André M
Internal Medicine Department, Gabriel Montpied University Hospital of Clermont-Ferrand

Belimumab is a third-line treatment of systemic lupus erythematosus (SLE. We here report two cases of patient with a history of histaminergic angioedema who presented a new episode after an injection of Belimumab.

A 38-year-old woman with a history of SLE with cutaneous, articular, pericardial and renal involvement, and prior episodes of angioedema of the lips and tongue (without C1 inhibitor deficiency or anti-C1q antibodies) presented a cutaneous and articular flare. Intravenous Belimumab 10mg/kg and Prednisone 10 mg/d were added to her treatment. Two days later, she noticed a painless right periorbital oedema (A) quickly followed by an oedema of the upper lip (B) without dyspnea. It disappeared within a few hours after taking Ebastine. She had no C1 inhibitor deficiency, no anti-C1q antibodies ; serum tryptase was normal. Belimumab treatment was not resumed.

1. Wallace D, Navarra S, Petri M, Gallacher A, Thomas M, Furie R, et al. Safety profile of belimumab: pooled data from placebo-controlled phase 2 and 3 studies in patients with systemic lupus erythematosus. Lupus. févr 2013;22(2):144-154.



A 49-year-old woman with a history of spontaneously regressive oedema of the face and SLE (cutaneous, and articular involvement) presented a pericarditis with cutaneous and articular flare. Intravenous Belimumab 10mg/kg and corticosteroids were added to her treatment. Four days after the 4th Belimumab perfusion, she presented an oedema of the face and neck with dyspnea, dysphagia, dysphonia and nausea. She was treated with intravenous Dexchlorpheniramine with good response within a few hours. She had no C1 inhibitor deficiency, no anti-C1q antibodies, normal serum tryptase. Long-term Cetirizine was introduced and Belimumab cures were continued, with no recurrence.

We here report two cases of face angioedema after an injection of Belimumab. Clinical and biological data orient towards a histaminergic mechanism. These patients had prior angioedemas but less severe and without relapse for several years. Angioedemas or urticarial lesions are possible in SLE : classic urticaria, bradykinic angioedemas with C1 inhibitor deficiency, neutrophilic urticaria with rarely angioedemas.

Histaminergic angioedema associated with Belimumab has not been previously described. Phase 3 trials reported mainly immediate anaphylactic reactions after injection; in their study of two phase 2 and 3 trials, Wallace et al reported one case of angioedema 39 days after the 8th course of Belimumab (1).

These cases suggest a histamine-releasing property of Belimumab, that could justifiy a particular surveillance or a systematic antihistamine associated treatment.