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LETTER TO THE EDITOR

Efficacy of Omalizumab in a Patient with Angioedema Clinically Resembling a Hereditary Angioedema

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Dear Editor:

A 20-year-old man was referred to our allergy and immunology department with complaints of recurring angioedema attacks, lasting 48～96 h, on his lips, eyes, and face, as well as swelling of the extremities and testicles during the last 1 year. Regular use of antihistamine and steroid drugs was generally ineffective against the frequency and severity of the angioedema attacks. He experienced recurrent abdominal pain attacks during the evaluation period. He was hospitalized in another center with a prediagnosis of familial Mediterranean fever; however, that diagnosis was excluded later. Urticarial lesions were not observed during the angioedema attacks. He did not have a history of drug or food allergy, and no specific family history for angioedema was reported. A detailed evaluation for arthritis and rheumatologic disorder was done but no specific findings were found. Furthermore, rheumatologic markers were negative (IRB No. 1491-21-16/1539). Routine laboratory tests for the management of chronic urticaria-angioedema and for anti-nuclear antibody, rheumatoid factor, anti-cyclic citrullinated peptide antibodies, C3, and C4 were within the reference limits. The total immunoglobulin E (IgE) value was 213 IU/ml, and the C4 levels during the attacks were normal. However, C1 esterase inhibitor was measured to be 28.3 mg/dl (reference, 32～39 mg/dl), and hereditary angioedema (HAE) was clinically considered. Danazol treatment up to 400～600 mg/day was started; however, no significant benefit was observed. As the 1,000 U C1 esterase inhibitor administered during the attacks (Cetor, 500 U; Sanquin, Amsterdam, The Netherlands) was ineffective, the diagnosis of HAE was excluded.

Because the urticarial complaints started in addition to the angioedema complaints, our patient received 300 mg omalizumab (Xolair 150 mg; Novartis Pharmaceuticals, Basel, Switzerland) subcutaneously every 4 weeks according to conventional asthma treatment protocols. He was treated with omalizumab for 6 months. His angioedema attacks ceased completely within 2 weeks after the start of this treatment. Except for the very short period for the formal procedures required for the procurement of the drug, he had no other complaints during the 6 months follow-up.

In randomized, placebo-controlled trials, omalizumab was shown to have excellent efficacy in chronic spontaneous urticaria[1]. A growing number of case reports and series suggest that anti-IgE treatment may also be beneficial for patients with physical urticarias and chronic angioedema. Recently, omalizumab treatment for inducing and maintaining long-term remission in patients with severe chronic urticaria has been demonstrated[2]. Unfortunately, for such disorders with complex and unclear etiology, no randomized placebo-controlled trial has been performed yet[3]. The mechanism of omalizumab activity in angioedema is currently not well defined. However, several mechanism may be considered.

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Even if the pathogenesis of angioedema in the present case may not be directly mediated by IgE, omalizumab may be effective through an unidentified and indirect anti-inflammatory manner. Sayama et al.[4] reported that the stimulation of high-affinity IgE receptor (FceRI) in human umbilical cord mast cells causes substantial change in the expression of many genes, including *Interleukin-11* (*IL-11*), and at least 30 other cytokines and chemokines and several adhesion molecules involved in potential interactions with T cells, B cells, or dendritic cells. Another work, in which the anti-inflammatory activity of omalizumab was mediated, has provided evidence showing the efficacy of this drug in idiopathic angioedema through eosinophil apoptosis induction and downregulation of the inflammatory cytokines IL-2 and IL-13[5].

In conclusion, it seems that therapeutic efficacy spectrum of anti-IgE treatment comprises many allergic disorders with unknown etiology, including angioedema.

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