
Failure of omalizumab for treatment of severe adult atopic dermatitis

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Atopic dermatitis has been associated with elevated levels of IgE. Omalizumab is a monoclonal anti-IgE antibody currently approved for the treatment of asthma. We report the failure of omalizumab to improve atopic dermatitis in 3 patients when administered for 4 months. (J Am Acad Dermatol 2005;53:338-40.)

Atopic dermatitis (AD), most frequently seen in children, may persist into adulthood as a chronic inflammatory skin disease. Therapeutic options for chronic AD abound, with the mainstay of therapy being topical corticosteroids. At times, patients require short courses of systemic corticosteroid therapy with the potential for serious potential side effects. Elevated serum IgE levels are commonly found in AD. Laske and Niggeman¹ found a positive correlation between the severity of AD and serum IgE levels in children.

Omalizumab (Xolair; Genentech, South San Francisco, Calif) is a humanized monoclonal anti-IgE antibody that binds to the IgE molecule at the high-affinity FcεRI receptor binding site, significantly reducing the amount of free IgE circulating in serum.² Omalizumab has been approved by the Food and Drug Administration for use in asthma in adults and adolescents (≥ age 12 years) based on its performance in pivotal clinical trials demonstrating efficacy for this disease.³⁻⁵ Dosing of this monoclonal antibody is administered in a subcutaneous injection every 2 to 4 weeks and is based on both serum IgE level and body weight. Omalizumab has also been found to be useful for treatment of allergic rhinitis and occupational latex allergy in health care workers.⁶⁻⁸ AD is one third of the classic allergic triad, completed by asthma and allergic rhinitis. Johansson

et al⁹ previously postulated the use of omalizumab in AD, although we were not able to find any reports of its efficacy for this use in the literature.

Severe AD would most conveniently be treated with a safe systemic medication with minimal adverse effects. Topical application of medications over a significant proportion of body surface area is cumbersome, time consuming, and often not practical. Other systemic alternatives that have previously been tried, including psoralen plus ultraviolet A therapy, azathioprine, mycophenolate mofetil, and intravenous immunoglobulin vary in efficacy and have many potential side effects, including the development of malignancies.¹⁰⁻¹³

Omalizumab was chosen as a potential new systemic therapy for AD based on its efficacy in asthma and allergic rhinitis, the association of AD with elevated IgE levels, and its side effect profile. Here we describe a case series of omalizumab for the treatment of severe adult AD in 3 patients.

PATIENT DATA AND OUTCOME

All patients were informed that this was an off-label use of this medication before beginning therapy. The side effect profile and all related concerns were addressed. A baseline IgE level was checked before medication administration. All patients had a history of chronic severe lichenified AD with periodic flares of acute disease approximately every 4 weeks. All patients also had either current symptoms of asthma or history of asthma, allergic rhinitis, or both. No patient found any benefit from omalizumab at 450 mg injected subcutaneously every other week for 4 months. There was no improvement in their chronic lichenified eczema or reduction in symptomatic flares of their disease. Patient 3 experienced a significant improvement of her asthma after starting omalizumab and chose to continue the medication

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Table I. Patient data summary

Patient age (y)/sex	Comorbid conditions	Starting IgE level, IU/mL	Prior therapy	Dose of omalizumab, mg SC qowk	Duration of therapy with omalizumab	Change in atopic dermatitis
34/Male	History of asthma	23,000	Topical steroids, systemic steroids, PUVA, azathioprine, mycophenolate mofetil, thalidomide, methotrexate	450	4 mo	No objective or subjective change
48/Male	Allergic rhinitis, hypertension	5440	Topical steroids, systemic steroids, mycophenolate mofetil	450	4 mo	No objective or subjective change
36/Female	Severe asthma, allergic rhinitis	24,400	Topical steroids, systemic steroids	450	4 mo	No objective or subjective change

PUVA, Psoralen plus ultraviolet A therapy; qowk, every other week; SC, subcutaneously.

for that reason. A summary of relevant patient data can be found in Table I.

DISCUSSION

Omalizumab, previously referred to in the literature as rhuMab-E25, is a humanized monoclonal anti-IgE antibody that binds IgE at the same site as the high-affinity receptor, FcεRI, thereby blocking the interaction of IgE with its receptor and preventing propagation of the allergic cascade.² It binds only to free IgE and not to IgG or IgA or to IgE bound to basophils or mast cells.² Treatment with omalizumab down-regulates expression of the FcεRI receptor on basophils and dendritic antigen-presenting cells and may decrease T-cell activation, as well.^{2,14} This may translate into even further suppression of allergic reactions and further benefit to patients.

The use of this medication in asthma has decreased exacerbations of disease, improved peak expiratory flow rates (an objective measure of restrictive airway disease), decreased steroid dependence, and improved the overall quality of life in those with asthma.^{3-5,15-18} AD, like asthma, is at least in part allergic in nature and is associated with increased levels of IgE.¹ Unfortunately, that link did not translate into clinical benefit in our patients.

Omalizumab appears to be a very safe medication, with injection site reaction often cited as the most common adverse event.^{3,4} The other most common adverse reactions found included urticaria, headache, upper respiratory tract infection, viral infection, and pharyngitis.^{3-5,19,20} In one study, however, the incidence of urticaria was greater in the placebo group than in the treatment group.³ Busse et al³ reported an identical overall incidence of

adverse reactions in the placebo and treatment arms of their double-blinded placebo-controlled trial. There were no antibodies found formed against omalizumab.^{4,19,20} None of our patients reported any adverse effects from the medication.

None of our patients experienced any improvement in their AD after 4 months of therapy with high doses of omalizumab. All 3 of our patients had IgE levels much higher than any of those included in the initial asthma studies done previously. The dosing recommendation for omalizumab is scaled, in part, according to pretreatment IgE levels, where upper limit is 700 IU/mL. A pretreatment IgE level higher than 700 IU/mL is not a contraindication for therapy. There simply is not a recommended dose from the pharmaceutical company and, thus, all patients were started at the highest recommended dose of omalizumab. All patients were fully informed and consented for off-label use of this medication. A possible reason for treatment failure was insufficient dosing of omalizumab because of the very high levels of IgE in these patients. However, a higher dose of omalizumab would likely lead to increased side effects (William Busse, MD, written communication) and would also be prohibitively expensive. Another reason for treatment failure is that there is more to the pathophysiology of AD than elevated IgE levels. Simply administering an anti-IgE medication may not be sufficient to reverse the changes of AD.

This medication certainly has a place in treating asthma, allergic rhinitis, and possibly latex allergy, and may yet be useful in other diseases, such as hyper-IgE syndrome or hypereosinophilic syndrome. There may be some benefit of omalizumab in treating AD that would be uncovered with a controlled clinical trial.

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