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# Efficacy of Omalizumab in Treatment of Therapy-Resistant Atopic Dermatitis and Contact Dermatitis

## Omalizumabin Tedaviye Dirençli Atopik Dermatit ve Kontakt Dermatit Tedavisindeki Etkinliği

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### Abstract

Omalizumab selectively binds to immunoglobulin E antibodies and is approved for treatment of allergic asthma. However, its use in dermatologic diseases is increasing. Here, we report three treatment resistant cases, one with atopic dermatitis the other two with contact dermatitis successfully treated with omalizumab with no side effect.

**Key Words:** Atopic Dermatitis, Contact Dermatitis, Omalizumab

### Öz

Omalizumab selektif olarak immünoglobulin E antikorlarına bağlanır ve alerjik astım tedavisi için onaylanmıştır. Bununla birlikte dermatolojik hastalıklarda kullanımı giderek artmaktadır. Bu makalede, omalizumab ile başarılı bir şekilde ve yan etki görülmeden tedavi edilmiş biri atopik dermatitli, diğer ikisi kontakt dermatitli olmak üzere tedaviye direnç gösteren üç olgu sunduk.

**Anahtar Kelimeler:** Atopik Dermatit, Kontakt Dermatit, Omalizumab

### Introduction

Omalizumab is a recombinant immunoglobulin (Ig) IgG1 monoclonal antibody binding to serum free IgE, leading to down-regulation of IgE receptors and thus mediator release of basophils and mast cells (1).

Although mostly used for chronic idiopathic urticaria, uses in atopic dermatitis, bullous pemphigoid, hyper-IgE syndrome, and toxic epidermal necrolysis are recently reported (2).

### Case Reports

#### Case 1

A 28-year-old Caucasian male with atopic dermatitis since the age of two had been treated with systemic cyclosporine (5 g/kg/day for three years), azathioprine (100 mg/day for

six months), mycophenolate mofetil (2 g/day for one year); narrow-band ultraviolet B (NB-UVB) and psoralen plus UV a phototherapy (PUVA) without benefit. To assist these agents he also received systemic corticosteroid injections at least four times a year together with topical corticosteroids, tacrolimus, emollients and systemic antihistamines. However, none of these reached even near-complete healing. He also had allergic rhinitis, conjunctivitis and asthma. His mother, uncle and younger sister had atopic dermatitis too. He had widespread erythematous lesions on the chest, back, inguinal region, arms, popliteal fossae, face, neck and sacral area (Figure 1a, b). The patient's SCORAD index was 46. Total serum IgE level was 5335.6 IU/mL (normal range: 0-100), total serum eosinophil count was 230/mm<sup>3</sup> (normal range: 40-400). Omalizumab 300 mg/month subcutaneously is started. Patient had partial response after five months. However, he did not need any systemic corticosteroid injections. Therefore, dose of omalizumab is increased to 450

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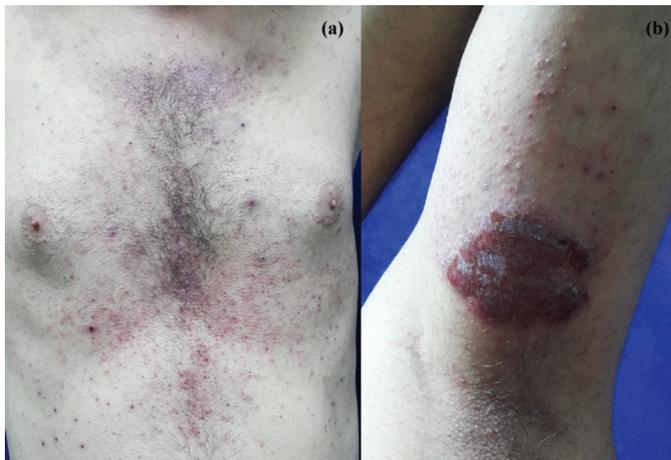
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mg/month. After three more months, a better clinical response was achieved (Figure 2a, b). Total IgE level was 677.4 IU/mL, eosinophil count was 99/mm<sup>3</sup> and SCORAD index was 18 at the end of the 24-month-therapy. Patient never received steroid injections and was clear of symptoms of allergic rhinitis and asthma.

## Case 2

A 64-year-old Caucasian male had pruritic rash on arms and legs with a diagnosis of contact dermatitis for seven years. He also had systemic hypertension and Familial Mediterranean Fever and was receiving oral colchicine 1 g/day for the last ten years. The patient was treated with topical and systemic steroids, tacrolimus, pimecrolimus, and NB-UVB. Nevertheless, no satisfactory clinical response was achieved. Patch test was positive to cobalt, nickel sulfate, potassium dichromate and formaldehyde. He had erythematous lesions on arms, legs, gluteal region and bilateral palmar regions (Figure 3a). Meanwhile, serum total IgE level was 25 IU/mL and total serum eosinophil count was 231/mm<sup>3</sup>. Omalizumab 300 mg was



**Figure 1:** a) Erythematous squamous papules and plaques on the trunk before therapy, b) Erythematous infiltrated annular plaque on the flexural surface of the left arm before therapy



**Figure 2:** Erythematous lesions on the trunk a) and left arm b) were regressed after therapy

started every four weeks. Lesions healed completely after first injection (Figure 3b). On eighth month total serum IgE level was 17 IU/mL and total serum eosinophil count was 243/mm<sup>3</sup>. No side effect was observed.

## Case 3

A 57-year-old Caucasian male presented with a ten-month history of pruritic lesions on his arms. Patient stated exposure to garden chemicals for a few weeks after which the lesions started. Past medical history revealed gout, hypertension and coronary artery disease. He had erythema on the extensor surfaces of hands and forearms (Figure 4a). Prick test was positive for aspergillus mould, peach, walnut, orange, banana, tea, paprica, onion, cocoa, mosquito, secale cereale, composite and chicken meat. Patch test was positive for formaldehyde and mercaptobenzothiazole. Skin biopsy supported the diagnosis of allergic contact dermatitis. Serum total IgE level was 10.1



**Figure 3:** a) Erythematous papules on the palmar region before therapy, b) after therapy



**Figure 4:** a) Erythematous plaques on the dorsal surface of the hands, b) Lesions disappeared after therapy

IU/mL and total serum eosinophil count was 316/mm<sup>3</sup> Patient received topical and systemic steroid plus local PUVA three times a week (0.5-1.7 j/cm<sup>2</sup>) for seven weeks with no improvement. Omalizumab 300 mg is started every four weeks. Lesions healed completely following first injection (Figure 4b). After three injections, serum total IgE level and total serum eosinophil count were 43.8 IU/mL and 199/mm<sup>3</sup>, respectively.

## Discussion

Atopic dermatitis is a chronic condition affecting 1-3% of adults usually coexisting with allergic asthma, rhinitis and food allergy (3). Expression of high affinity IgE receptors on the surface of dendritic cells aggravates atopic dermatitis lesions (4,5). Increased number of eosinophils is shown in skin lesions which play role in inflammation and immune cell interactions (3). Conventional drugs such as systemic corticosteroids, antihistamines and cyclosporine usually don't achieve complete healing in severe cases (6). Omalizumab, being a recombinant anti-IgE antibody, is also used in atopic dermatitis with controversial results (7). In two randomized controlled studies and 13 case series a total of 103 patients were evaluated, 60.5% of these with severe disease; and 43.4% with serum IgE levels greater than 5000 IU/mL. Most patients (66.7%) needed 600 mg or higher doses every four weeks still, treatment failed in 30.1%. There was a better clinical response in patients with serum IgE levels lower than 700 IU/mL (8). Zink et al. (9) treated ten patients with severe and recalcitrant atopic dermatitis with a combination of immunoadsorption and omalizumab. They suggest that immunoadsorption decreasing highly elevated serum IgE concentration before omalizumab injection may increase clinical response (9). We experienced excellent clinical outcome with our atopic dermatitis patient. Serum IgE level was elevated and total eosinophil count was in normal limits at the start. However, patient showed a gradual but marked decrease in serum IgE level and total eosinophil counts. Omalizumab may be effective in atopic dermatitis, with both its anti-IgE, and eosinophil apoptosis effects.

Allergic contact dermatitis, on the other hand; is a common disease caused by chronic antigenic stimulation. It is a type 4 hypersensitivity reaction mediated mainly by T lymphocytes. It is important to determine the allergen(s) for effective treatment (10,11). However, it is not always easy to isolate and/or to avoid allergens. Therefore, allergic contact dermatitis is usually recurrent, chronic and treatment resistant. Systemic and topical corticosteroids, calcineurin inhibitors, NB-UVB, PUVA, cyclosporine, azathioprine, mycophenolate and acitretin are treatment options. Lately, efficacy of biologic agents like dupilumab [interleukin (IL)-4/IL-13 antagonist] or tocilizumab (IL-6 antagonist) is debated (11). Another off-label use of omalizumab is in contact dermatitis. Mur

Gimeno et al. (12) reported a 38-year-old male patient with widespread occupational wheat contact dermatitis lesions treated with 225 mg of omalizumab every two weeks. Clinical improvement was observed at the first month of therapy with complete clearance in 4 months (12). Clinical experience with omalizumab in treatment of allergic contact dermatitis is still insufficient. Mechanism of action is also not well understood. However, it is suggested that omalizumab can induce eosinophil apoptosis, reduce granulocyte-macrophage colony-stimulating factor production from lymphocytes, inhibit the release of pro-inflammatory mediators from mast cells or basophils and inhibit allergen-induced lymphocyte differentiation (13). It also inhibits differentiation of T lymphocytes to T-helper 2 (T<sub>H</sub>2) by reducing IgE receptors on these cells. It results in reduced T<sub>H</sub>2 cell differentiation to inhibit the allergic immune response. Downregulation of IgE receptor expression on dendritic cells also inhibits antigen presentation to T lymphocytes (13,14,15). Our patients with chronic systemic contact dermatitis had normal IgE levels and eosinophil counts allthrough their treatments which does not seem to be associated with clinical improvement. Therefore, we may suggest that omalizumab shows its effect through reduced dendritic cell and lymphocyte activation and reduced T helper action in patients with chronic systemic contact dermatitis.

## Ethics

**Informed Consent:** Written consent was obtained from all patients.

## Authorship Contributions

Surgical and Medical Practices: F.G.E., D.D.R., F.T., D.Y., Concept: F.G.E., Design: F.G.E., F.T., Data Collection or Processing: F.T., D.Y., Analysis or Interpretation: F.G.E., D.D.R., Literature Search: F.G.E., F.T., Writing: F.G.E., F.T.

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