

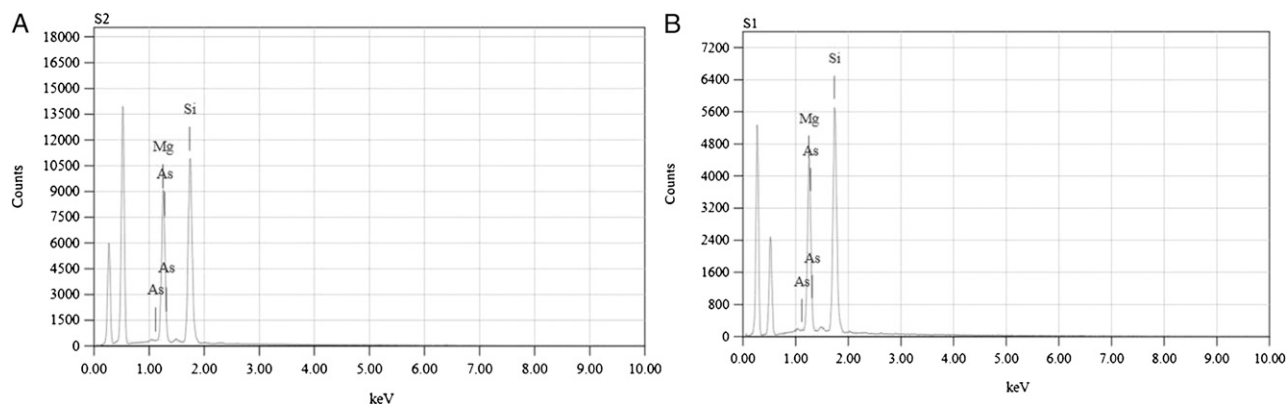


FIGURE 4. A, B, Spectral analysis of talc crystals (S1; B) and crystalline material in the biopsy specimen (S2; A) showing identical spectra, chiefly Mg and Si. Trace amounts of As were seen in both, confirming that the origin is the same; quantitative analysis of the pure talc showed the concentration of As to be <0.1 ppm, well within accepted safety limits. As = arsenic; Mg = magnesium; Si = silicon.

one or a few settings, which overwhelmed the patient's usual mucociliary clearance mechanisms and triggered an intense granulomatous endobronchial reaction. To our knowledge, this is the first time severe endobronchitis and airway stenosis caused by talc have been reported.

Both systemic² and inhaled glucocorticoids⁵ have been used for treatment of pulmonary talcosis. Little information exists regarding the optimal duration or dose of therapy. The patient's condition was treated with 20 mg/d po prednisolone for 2 weeks, followed by a slow taper over 2 months. She had marked improvement in symptoms. Her lung function also showed marked improvement, with the FEV₁ improving from 0.70 L (56% predicted) before treatment to 0.95 L (75% predicted) after completing steroid treatment. Follow-up chest radiography showed partial re-expansion of the right upper lobe. The patient has remained well in the 2 years since; she has stopped using talc.

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Omalizumab as a Steroid-Sparing Agent in Chronic Eosinophilic Pneumonia

Hatice Kaya, MD; Seyfettin Gümmüş, MD; Ergun Uçar, MD; Mehmet Aydoğan, MD; Uğur Muşabak, MD; Ergun Tozkoparan, MD; and Hayati Bilgiç, MD

Chronic eosinophilic pneumonia (CEP) is an idiopathic eosinophilic pulmonary disease characterized by an abnormal and marked accumulation of eosinophils in the lung. Common presenting complaints include cough, fever, dyspnea, wheezing, and night sweats. Common laboratory abnormalities are peripheral blood and BAL eosinophilia. The pathognomonic radiographic finding is bilateral peripheral infiltrates. Corticosteroids are the mainstay of therapy, and dramatic improvement follows treatment. Relapses are common, and most patients require prolonged therapy. Side effects associated with chronic corticosteroid therapy must be monitored. Our case was that of a 36-year-old woman who had characteristic clinical and radiologic features. She was treated with corticosteroids but she needed prolonged therapy, and side effects occurred. Because the patient had high IgE levels and a positive skin prick test result, we used omalizumab for the treatment. The patient

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Affiliations: From the Turkish Armed Forces Rehabilitation Center (Dr Kaya); the Department of Pulmonary Medicine (Drs Gümmüş, Uçar, Aydoğan, Tozkoparan, and Bilgiç); and the Department of Allergy and Clinical Immunology (Dr Muşabak), Gülhane Military Medical Academy, Ankara, Turkey.

Correspondence to: Hatice Kaya, MD, TSK Rehabilitasyon Merkezi, 06540, Bilkent, Ankara, Turkey; e-mail: drhaticekaya@yahoo.com

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responded well. To our knowledge, this is the first CEP case in the literature successfully treated with omalizumab. *CHEST* 2012; 142(2):513–516

Abbreviations: CEP = chronic eosinophilic pneumonia; CSS = Churg-Strauss syndrome

Chronic eosinophilic pneumonia (CEP) is an idiopathic pulmonary disease characterized by an abnormal and marked accumulation of eosinophils in the lung.¹ Corticosteroids are the mainstay of therapy for CEP. A case of corticosteroid-dependant CEP who was treated successfully with omalizumab is presented.

CASE REPORT

A 36-year-old woman with asthma was admitted with wheezing, cough, night sweats, and weight loss. Chest radiograph revealed bilateral peripheral infiltrates in the upper zones. A CT scan showed bilateral subpleural nonsegmental infiltrates in the upper lobes (Fig 1). Her peripheral blood eosinophil count was 2,790 cell/mm³ with a leukocyte differential of 45%. Sputum examination revealed no microorganisms, including fungi such as *Aspergillus*, and no parasitic agent was detected by examination of stool and sputum. She had no documented vasculitis or extrapulmonary organ involvement including neuropathy, renal disease, and paranasal sinus abnormality. Skin prick tests for *Aspergillus* antigen and antineutrophil cytoplasmic antibodies were negative. Total IgE level was 335 IU/mL, and skin prick test was positive for mite, grass mix, and tree mix. Flow cytometry analysis of lymphocyte subpopulations revealed lowered CD19⁺CD23⁺ cells, indicating defective expression of CD23 on CD19⁺B cells.

The diagnosis of CEP was made by clinical, laboratory, and radiologic findings. The patient began prednisone treatment with a starting dose of 40 mg/d, which was gradually tapered off and stopped at the sixth month. The patient responded well to prednisone. However, the disease relapsed 4 weeks after cessation of treatment as revealed by peripheral eosinophilia and radiologic findings, and prednisone treatment was restarted for 2 years with the fixed dose of 10 mg/d. During prolonged treatment, amenorrhea and major depression developed as side effects. Only 3 weeks after cessation of the second treatment, the disease relapsed again and a third prednisone regimen was given. At this point, an anti-IgE agent, omalizumab, 300 mg every 4 weeks, was started. Prednisone was discontinued at the fourth week of the omalizumab treatment. The patient responded well and all clinical, laboratory, and radiologic findings disappeared (Fig 2). At the 15th month of omalizumab treatment, CEP is in complete remission, with all clinical and laboratory findings normal.

DISCUSSION

Patients with CEP are generally responsive to corticosteroid therapy and the prognosis is usually favorable. Initial treatment consists of oral prednisone at a dose of 0.5 mg/kg/d. Then the dose can be tapered by one-half after the clinical and radiologic resolution. The optimal duration of therapy is not known. Symptomatic and radiographic relapse is common either after cessation of therapy or with tapering of the dose. Some patients can be weaned off therapy within 6 months, but most patients require prolonged or lifelong therapy.¹ Although this patient had recurrences, she was also responsive to corticosteroid

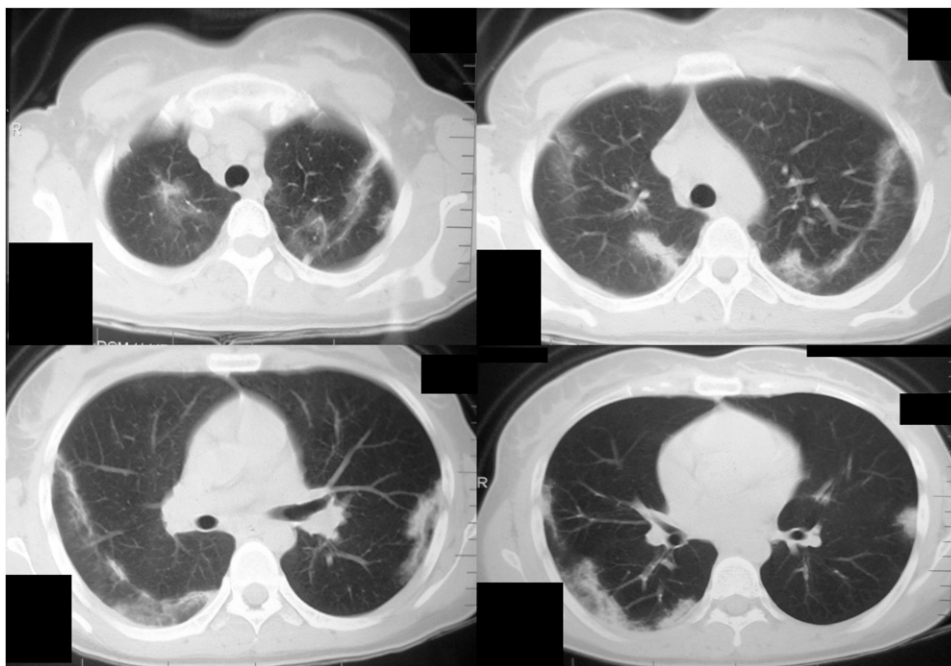


FIGURE 1. High-resolution CT scans of the patient before the omalizumab treatment (at the time of second recurrence) shows peripheral upper-lobe predominance infiltrates appearing as ground glass, dense consolidation, and nodular opacities.

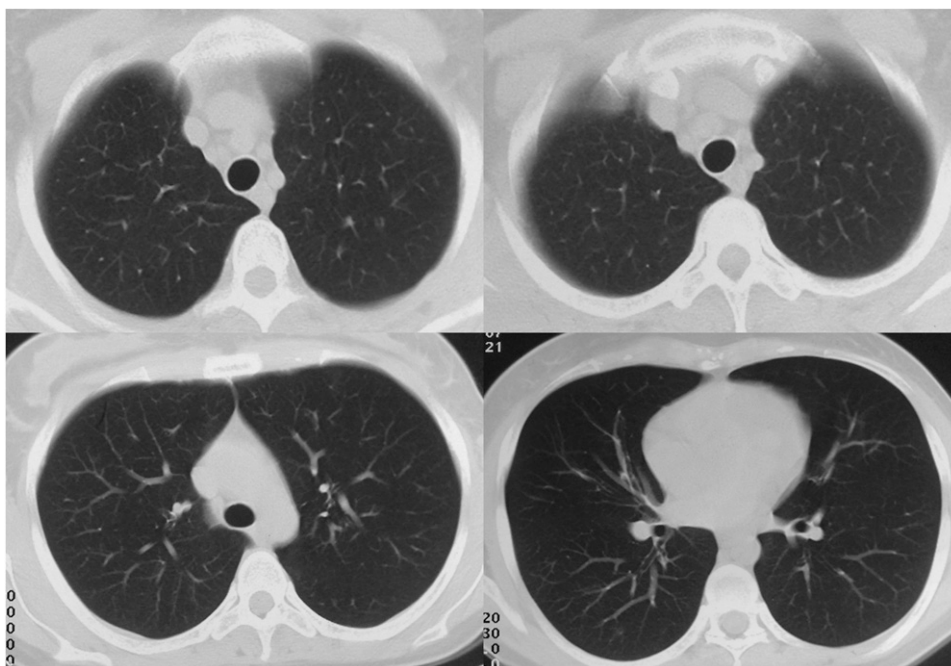


FIGURE 2. High-resolution CT scans of the patient after the omalizumab treatment shows complete resolution.

therapy. However, we had to stop the therapy because of side effects. At this point, we decided to use omalizumab, a recombinant humanized monoclonal antibody against IgE, because the patient had severe persistent asthma, high IgE levels, and a positive skin prick test for mite, grass mix, and tree mix.

The medical literature reports increased use of omalizumab for various allergic disorders as well as allergic asthma, including allergic rhinitis, food allergy, and atopic dermatitis.² However, the association between omalizumab use and Churg-Strauss syndrome (CSS) development is unclear. In several case reports, CSS and eosinophilic pneumonia have been noted in patients with asthma receiving omalizumab.^{3,4} This association is most likely an unmasking of underlying CSS due to cessation or tapering of oral corticosteroids, rather than a causal relationship. Furthermore, omalizumab has been administered as an investigational therapy in three cases with CSS that were resistant to corticosteroids.⁵ It has been suggested that omalizumab may have a proapoptotic effect on eosinophils.⁶ According to these data, we concluded that there was no scientific evidence to contraindicate the use of omalizumab in CEP. However, in any case treated with omalizumab, systemic corticosteroids should be tapered with caution and the patients must be monitored for signs of CSS.

We found defective expression of CD23 on B cells on flow cytometry analysis in our case. CD23, also known as the low-affinity receptor for IgE, is expressed on the B cells, monocytes, eosinophils, and Langerhans cells and plays an important role in the regulation of IgE production by B cells. CD23 mediates the activation of IgE-dependent cellular cytotoxicity by macrophages, eosinophils, and

platelets.^{7,8} We suggest that because B cells are involved in IgE production and IgE-mediated eosinophilic inflammation, the alterations on B cell-surface antigen expressions and those of soluble fragments in serum might have a role in the pathogenesis of CEP.

In conclusion, to our knowledge, this is the first CEP case successfully treated with omalizumab. Although CEP and CSS have been reported in omalizumab treatment probably because of tapering or cessation of corticosteroids in patients with severe persistent asthma, omalizumab might be borne in mind as an alternative treatment choice when confronted with prolonged need for corticosteroids and/or corticosteroid intolerance in selected patients with CEP. At this point, mepolizumab, a humanized anti-IL-5 antibody, might be another treatment choice because its efficacy has been shown in hyper-eosinophilic syndromes.^{9,10} Further studies focused on the effect of B cells and their receptors on IgE production and eosinophilic cytotoxicity may provide new therapeutic approaches in the future.

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