



doi • 10.5578/tt.20229815

Tuberk Toraks 2022;70(2):215-219

Geliş Tarihi/Received: 15.03.2022 • Kabul Ediliş Tarihi/Accepted: 15.05.2022

Severe asthma concomitant with allergic bronchopulmonary aspergillosis (ABPA) and non-steroid exacerbated respiratory disease (N-ERD) successfully treated with mepolizumab: A case report

Mehmet Erdem
ÇAKMAK (ID)

Clinic of Allergy and Clinical Immunology, Başakşehir Çam and Sakura City Hospital, İstanbul, Turkey

Başakşehir Çam ve Sakura Şehir Hastanesi, İmmünoloji ve Alerji Hastalıkları Kliniği, İstanbul, Türkiye

ABSTRACT

Severe asthma concomitant with allergic bronchopulmonary aspergillosis (ABPA) and non-steroid exacerbated respiratory disease (N-ERD) successfully treated with mepolizumab: A case report

Allergic bronchopulmonary aspergillosis (ABPA) is a lung disease characterized by a hypersensitivity reaction to *Aspergillus fumigatus*. Allergic bronchopulmonary aspergillosis is characterized by increased serum IgE levels, peripheral blood eosinophilia and radiographic pulmonary infiltrates, central bronchiectasis, and mucus plugs. Mepolizumab, a monoclonal interleukin (IL)-5 antibody, reduces eosinophilic inflammation and improves symptom control in severe eosinophilic asthma. A 74-year-old male patient arrived at our allergy outpatient clinic complaining of shortness of breath and cough. He had a history of asthma, NSAIDs Exacerbated Respiratory Disease (N-ERD) and endoscopic sinus surgery (ESS) due to chronic sinusitis with nasal polyps (CRSwNPs). At the time of admission to our clinic, his asthma control test (ACT) score was 5. The laboratory test results= eosinophil count (cells/mcL)= 570, total IgE= 3976 IU/mL, *Aspergillus*-specific IgE= 1.87 kIU/L (>0.35 positive). In the pulmonary function tests, forced expiratory volume in 1s (FEV₁) was 28%. Thoracic computed tomography of the patient revealed central cystic bronchiectatic areas and mucus plugs. The patient was diagnosed with ABPA. The case reported here is of a patient diagnosed with severe asthma concomitant with ABPA and N-ERD, who was successfully treated with mepolizumab. Randomized double-blind placebo-controlled studies are needed to evaluate the efficacy of mepolizumab treatment in these patients.

Key words: Allergic bronchopulmonary aspergillosis; mepolizumab; drug allergy; asthma; eosinophil

Cite this article as: Çakmak ME. Severe asthma concomitant with allergic bronchopulmonary aspergillosis (ABPA) and non-steroid exacerbated respiratory disease (N-ERD) successfully treated with mepolizumab: A case report. *Tuberk Toraks* 2022;70(2):215-219.

Address for Correspondence (Yazışma Adresi)

Dr. Mehmet Erdem ÇAKMAK
Clinic of Allergy and Clinical Immunology,
Başakşehir Çam and Sakura City Hospital
İSTANBUL - TURKEY
e-mail: mehmeterdemcakmak@gmail.com

ÖZ

Alerjik bronkopulmoner aspergilloz (ABPA) ve non-steroidal anti-enflamatuvar ilaçlarla alevlenen hava yolu hastalığının (N-ERD) eşlik ettiği ağır astım mepolizumab ile başarılı bir şekilde tedavi edildi: Olgu sunumu

Alerjik bronkopulmoner aspergilloz (ABPA), Aspergillus fumigatus'a karşı aşırı duyarlılık reaksiyonu ile karakterize bir akciğer hastalığıdır. Alerjik bronkopulmoner aspergilloz artmış serum IgE seviyeleri, periferik kan eozinofili ve radyografik pulmoner infiltratlar, santral bronşektazi ve mukus tıkaçları ile karakterizedir. Bir monoklonal interleukin (IL)-5 antikorunu olan mepolizumab, eozinofilik inflamasyonu azaltır ve şiddetli eozinofilik astımda semptom kontrolünü iyileştirir. Yetmiş dört yaşında erkek hasta nefes darlığı ve öksürük şikayeti ile alerji polikliniğimize başvurdu. Özgeçmişinde astım, nazal polipin eşlik ettiği kronik sinüzit (CRSwNPs) nedeniyle endoskopik sinüs cerrahisi (ESS) ve non-steroidal anti-enflamatuvar ilaçlarla alevlenen hava yolu hastalığı (N-ERD) öyküsü vardı. Kliniğimize başvuru anında astım kontrol testi (ACT) skoru 5 idi. Laboratuvar tetkiklerinde eozinofil sayısı (hücre/mcL)= 570, total IgE= 3976 IU/mL, Aspergillus özgül IgE= 1,87 kIU/L (>0,35 pozitif) ölçüldü. Solunum fonksiyon testlerinde birinci saniyedeki zorlu ekspiratuar volüm (FEV₁) %28 idi. Hastanın toraks bilgisayarlı tomografisinde santral kistik bronşektatik alanlar ve mukus tıkaçları görüldü. Hastaya ABPA tanısı konuldu. Burada ABPA ve eşlik eden N-ERD tanısı olan ve mepolizumab ile başarılı bir şekilde tedavi edilen ağır astımlı bir hasta sunulmaktadır. Bu hastalarda mepolizumab tedavisinin etkinliğini değerlendirmek için randomize, çift kör, plasebo kontrollü çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Alerjik bronkopulmoner aspergillozis; mepolizumab; ilaç alerjisi; astım; eozinofil

INTRODUCTION

Allergic bronchopulmonary aspergillosis (ABPA) is a lung disease characterized by a hypersensitivity reaction to *Aspergillus fumigatus*. Allergic bronchopulmonary aspergillosis is characterized by increased serum IgE levels, peripheral blood eosinophilia and radiographic pulmonary infiltrates, central bronchiectasis, and mucus plugs. In chronic cases, recurrent episodes of bronchial obstruction, inflammation, and mucoid impaction can lead to bronchiectasis, fibrosis, and respiratory failure. Systemic corticosteroids and antifungal agents are important in treating the disease and controlling its progression (1).

In a group of patients with asthma/rhinitis/nasal polyps as an underlying disease, it has been shown that exposure to aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) causes respiratory complaints such as runny nose, sneezing, nasal congestion, cough, shortness of breath, and severe bronchospasm. This disease, which used to be called Samter's syndrome, is now called "Non-steroidal Anti-Inflammatory Drug (NSAID) Exacerbated Respiratory Disease" (NSAID-Exacerbated Respiratory Disease: N-ERD). Most of these patients have severe eosinophilic asthma, and patients with N-ERD have a higher rate of severe asthma than other asthmatic patients (2).

Mepolizumab, a monoclonal interleukin (IL)-5 antibody, reduces eosinophilic inflammation and improves symptom control in severe eosinophilic asthma (3). The case reported here is of a patient diagnosed with severe asthma concomitant with

ABPA and N-ERD, who was successfully treated with mepolizumab.

CASE REPORT

A 74-year-old male patient was admitted to our allergy outpatient clinic with complaints of shortness of breath and cough. He had a history of asthma for 40 years, diabetes and hypertension for 15 years, N-ERD (culprit drugs: aspirin, diclofenac, and ibuprofen) for 20 years, and endoscopic sinus surgery (ESS) 20 years ago due to chronic sinusitis with nasal polyps (CRSwNPs). The physical examination of the respiratory system revealed rhonchi in both lung fields. Saturation was 94% without supplemental nasal oxygen. Other physical examination findings were normal. The patient had been using salmeterol fluticasone 50/500 mcg 2 x 1/day, montelukast 10 mg/day, levocetirizine 5 mg/day, and intranasal mometasone 2 x 2 puffs/day. The patient's inhaler technique and treatment compliance were good. At the time of admission to our clinic, his asthma control test (ACT) (4) score was 5. The laboratory tests showed eosinophil count (cells/mcL)= 570, total IgE= 3976 IU/mL, *Aspergillus*-specific IgE= 1.87 kIU/L (>0.35 positive), *Dermatophagoides pteronyssinus*-specific IgE= 2.08 kIU/L (>0.35 positive), other aeroallergen-specific IgE's <0.35 kIU/L (negative), sedimentation= 2 mm/h, and negativity of serum proteinase-3 anti-neutrophil cytoplasmic antibody (ANCA) and myeloperoxidase-ANCA. In the pulmonary function tests, forced expiratory volume in 1s (FEV₁) was 28%. Thoracic computed tomography of the patient revealed central cystic bronchiectatic areas and mucus plugs (Figure

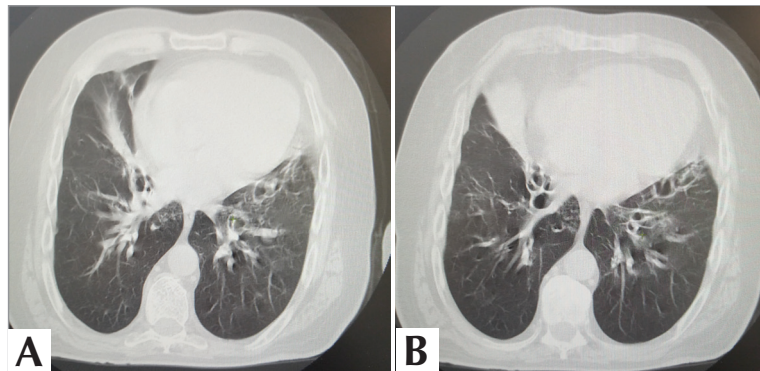


Figure 1. (A). Thoracic computed tomography of the patient revealed central cystic bronchiectatic areas and mucus plugs before mepolizumab treatment. **(B).** Thoracic computed tomography of the patient after mepolizumab treatment in 6th month.

1a,1b). The patient was diagnosed with ABPA and severe asthma, and treatment was started with oral methylprednisolone at 32 mg/day (0.5 mg/kg). The oral methylprednisolone dose was reduced to 16 mg on the 7th day of treatment and to 8 mg on the 14th day. On the 20th day of oral methylprednisolone treatment, mepolizumab was started at a dose of 100 mg/sc every four weeks due to an increase in respiratory complaints. The oral methylprednisolone dose was gradually reduced and stopped on the 60th day of treatment. After the mepolizumab treatment, improvements were observed in asthma control and pulmonary function tests at the 3rd, 6th, and 12th-month follow-up examinations. The number of asthma attacks requiring emergency department admission, eosinophil count, and total IgE values were decreased. (Table 1). Because the patient had limited respiratory functions and severe asthma, drug provocation tests with NSAIDs or aspirin desensitization could not be performed. The patient has been receiving mepolizumab treatment in our allergy clinic for one year and his asthmatic symptoms are under control.

DISCUSSION

The case presented here is of a patient with severe asthma concomitant with ABPA and N-ERD, who was successfully treated with mepolizumab. After the mepolizumab treatment, a decrease was observed in the patient's respiratory symptoms (cough, dyspnea) and improvements in pulmonary function tests and asthma control. To the best of our knowledge, this report is the first case of severe asthma concomitant with ABPA and N-ERD to be treated with mepolizumab.

In the literature, there is a limited number of studies and case reports of treating an ABPA diagnosis with mepolizumab. In a study of 20 cases by Schleich et al. (5), it was observed that mepolizumab treatment led to a decreased oral corticosteroid dose and rate of exacerbation, and improved asthma control and quality of life in patients with ABPA. The authors stated that mepolizumab is an effective treatment for ABPA. In a case report by Altman MC et al. (6), the use of mepolizumab was reported to be an additional and effective treatment option for severe allergic

Table 1. ACT, FEV₁, blood eosinophil, and total IgE values of the patient at baseline and at 3, 6, and 12 months post-mepolizumab treatment and the number of asthma attacks

	Baseline	3 rd month	6 th month	12 th month
ACT	5	20	24	20
FEV ₁ (%)	28	41	50	54
Blood eosinophil count (cells/mcL)	570	120	40	70
Total IgE (kU/L)	3976	3168	2040	1444
Before mepolizumab treatment in one year		After mepolizumab treatment in one year		
Number of asthma attacks*	4		1	

* Requiring emergency department admission and systemic steroid use for more than three days.

bronchopulmonary aspergillosis resistant to corticosteroids, antifungal therapy, and omalizumab. There are also case reports in the literature showing that mepolizumab is effective in the treatment of ABPA (1,7-11).

Mepolizumab is a monoclonal antibody developed against IL-5, and this cytokine releases eosinophils from the bone marrow and activates eosinophil functions (3). It has been shown that mepolizumab reduces the frequency of asthma exacerbations and the need for systemic corticosteroids in patients with severe eosinophilic asthma. The pre-treatment total IgE level does not affect the efficacy or side effects of mepolizumab treatment. Mepolizumab has been recommended as an effective treatment option in severe eosinophilic asthma with total IgE > 1500 IU/mL (12,13). In the current case, the patient had severe eosinophilic asthma and concomitant N-ERD. In patients with N-ERD, respiratory symptoms are caused by increased cysteinyl leukotriene levels as a result of dysregulation in arachidonic acid metabolism and increased eosinophilic inflammation of the airways. After the use of aspirin and other NSAIDs, there is an increase in leukotrienes in the airway as a result of the inhibition of the cyclooxygenase (COX) one enzyme, which causes respiratory symptoms. Patients with N-ERD have lower FEV₁ and a higher prevalence of CRSwNP (14).

The underlying pathogenetic mechanisms in patients with ABPA are complex. In patients with ABPA, the secretion of IL-4 and IL-5 from peripheral blood cells is increased, which contributes to the pathogenesis of ABPA by increasing TH2 (T Helper 2) inflammation (15). As patients with ABPA have high total IgE levels and specific antibodies to *Aspergillus fumigatus*, these patients may benefit from omalizumab therapy, and there are studies in the literature showing the efficacy of omalizumab treatment in patients with ABPA (16). In the current case, we administered mepolizumab because he had high levels of blood eosinophils but omalizumab was also a treatment option.

In conclusion, this case of severe asthma concomitant with ABPA and N-ERD was successfully treated with mepolizumab. Randomized double-blind placebo-controlled studies are needed to evaluate the efficacy of mepolizumab treatment in these patients.

CONFLICT of INTEREST

The authors have no conflict of interest to declare.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: MEÇ

Analysis/Interpretation: MEÇ

Data Acquisition: MEÇ

Writing: MEÇ

Critical Revision: MEÇ

Final Approval: MEÇ

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