

Case Report

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**Benralizumab Treatment in a Patient with
Severe Eosinophilic Exacerbation of Chronic
Obstructive Pulmonary Disease: a Case
Report**

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Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is characterized by sudden worsening of dyspnea, often accompanied by increased cough and sputum production in patients with chronic obstructive pulmonary disease (COPD). Current standard treatment involves systemic corticosteroids; however, there are no clear guidelines for patients who are unresponsive to this therapy. This case report describes a 64-year-old female with COPD on triple inhaler therapy who presented with acute eosinophilic exacerbation. Despite prompt administration of systemic corticosteroid therapy and empirical antibiotics, her condition continued to deteriorate. Given her markedly elevated blood eosinophil count, a single 30 mg subcutaneous dose of benralizumab, a monoclonal antibody targeting interleukin-5 receptor-alpha, was administered. Following treatment, her blood eosinophil count decreased rapidly, oxygen demand decreased, and symptoms improved significantly. This case highlights the potential role of benralizumab as a therapeutic option for AECOPD in patients with high eosinophil counts.

Keywords: Disease exacerbation, Chronic obstructive pulmonary disease, Corticosteroid, Eosinophils, Benralizumab

Introduction

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) refers to the sudden worsening of dyspnea in patients with chronic obstructive pulmonary disease (COPD). This exacerbation is often accompanied by increased coughing and sputum production [1]. This condition may present with tachypnea and tachycardia, which are typically triggered by increased local or systemic inflammation due to infection, air pollution, or other airway irritants [2]. Physical examination commonly reveals wheezing, and respiratory acidosis is often observed [1].

Systemic steroids are the most commonly used treatment for managing AECOPD [3-5]. However, clear guidance is lacking for cases in which the disease remains uncontrolled despite systemic steroid therapy, as there are no other proven pharmacological treatment options. Here, we report the case of a patient with severe AECOPD who was successfully treated with benralizumab after the failure of systemic steroid therapy.

Case report

A 64-year-old female patient presented with worsening shortness of breath over the previous three days. She reported a prior episode of fainting accompanied by severe shortness of breath and coughing three days prior.

The patient was diagnosed with COPD after a long period of secondhand smoke exposure at a young age and was classified as having Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage II airflow limitation. Her pulmonary function test results showed a forced vital capacity (FVC) of 2.84 L (90% of predicted value), forced expiratory volume in 1 second (FEV1) of 1.36 L (53% of predicted value), FEV1/FVC of 0.48, and mild diffusion impairment (68% of predicted value). A recent chest computed tomography scan showed diffuse bronchial thickening and emphysema in both lungs, consistent with her diagnosis (Fig. 1). She had a history of acute exacerbations that required emergency department visit (4 years ago) or admission (1 year ago requiring 17 days of hospitalization) and was on maintenance therapy with olodaterol/tiotropium (5 µg/5 µg) two puffs daily and ciclesonide (160 µg) two puffs daily. The patient denied any history of tuberculosis exposure, recent travel, or symptoms suggestive of in-

fection, such as fever or chills; her medical history included impaired fasting glucose and panic disorder.

The patient initially presented to the outpatient clinic with dyspnea, which was severe enough to warrant referral to the emergency department for further evaluation. Upon arrival at the emergency department, the patient had a heart rate of 117 bpm and an initial room air oxygen saturation (SpO₂) of 81%, which improved to 93% following the application of nasal oxygen at 3 L/min. On physical examination, diffuse wheezing in both lungs was detected during pulmonary auscultation. Chest radiography revealed hyperinflated lungs with flattened hemidiaphragms and mild emphysema in both lung fields (Fig. 2). Laboratory tests showed a white blood cell count of 10,720/µL, suggesting mild leukocytosis and a blood eosinophil count of 2,337/µL. The hemoglobin level was 16.1 g/dL, indicating no anemia, and the coagulation profile—including prothrombin time and partial thromboplastin time—and the D-dimer level was within the normal range. The Troponin-T level was slightly elevated at 0.171 ng/mL, whereas the creatine kinase-MB (CK-MB) level was within normal limits. An electrocardiogram demonstrated sinus tachycardia without any specific abnormalities. The C-reactive protein was 0.20 mg/dL, indicating a low likelihood of infection. Arterial blood

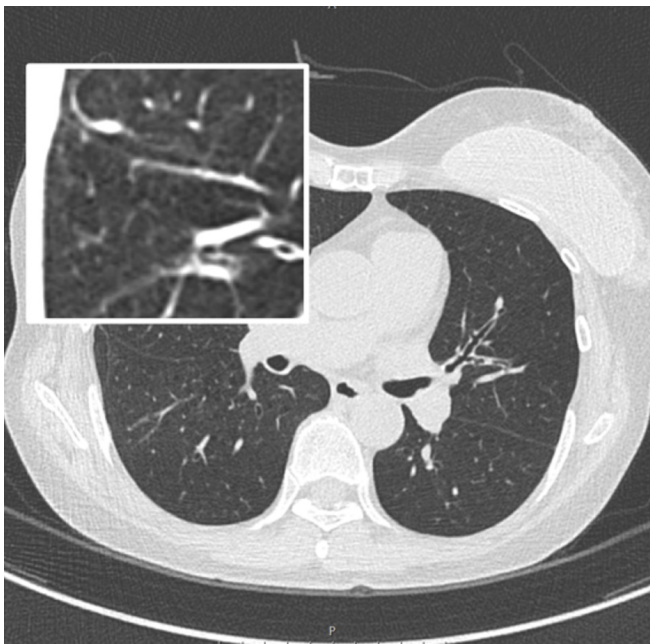


Fig. 1. The chest computed tomography scan shows diffuse bronchial wall thickening, air-trapping, and mild emphysema in both lungs. A magnified view of the region demonstrating prominent centrilobular emphysema is inserted in the upper left portion and outlined in white.

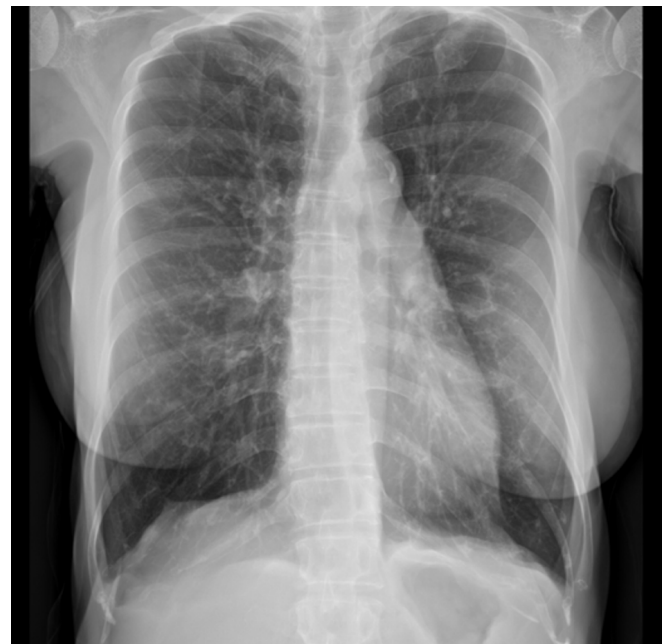


Fig. 2. Chest radiography taken at the emergency department visit shows hyperinflated lungs with flattened hemidiaphragms and mild emphysema in the lung fields.

gas (ABG) analysis revealed a pH of 7.318, a partial pressure of carbon dioxide (pCO₂) of 57.7 mmHg, a partial pressure of oxygen (pO₂) of 62.6 mmHg, and a bicarbonate (HCO₃⁻) level of 28.7 mmol/L, consistent with respiratory acidosis and hypoxemia. Given the clinical suspicion of acute exacerbation of COPD, the patient was hospitalized for treatment with intravenous hydrocortisone 100 mg three times per day, along with nebulized salbutamol 2.5 mg four times per day, ipratropium 500 µg 4 times per day, acetylcysteine 800 mg four times per day, and budesonide 500 µg twice per day.

Two days after admission, the patient's respiratory distress worsened, with more pronounced wheezing and increased use of the accessory respiratory muscles. Venous blood gas analysis revealed a pH of 7.250 and pCO₂ of 74.5 mmHg, confirming progressive respiratory acidosis. In response, the patient was administered a single dose of benralizumab (humanized monoclonal antibody targeting interleukin-5 receptor- α [IL-5 α]) 30 mg, and high-flow nasal cannula (HFNC) therapy was initiated. In hospital day 3, one day after the administration of benralizumab, the blood eosinophil count rapidly decreased to 0/µL (Fig. 3), with a pH of 7.416 and a pCO₂ of 47.7 mmHg, indicating resolution of respiratory acidosis. The patient's oxygen therapy was transitioned

from HFNC to nasal prongs as the desaturation resolved. The patient was stabilized without needing supplemental oxygen and was deemed ready for discharge.

Discussion

To the best of our knowledge, this is the first case report describing the use of benralizumab in a patient with AECOPD and high eosinophil count who was unresponsive to systemic corticosteroid therapy.

Previous studies have established that an elevated blood eosinophil count is associated with an increased risk of exacerbation [6,7] and is a predictive marker for future exacerbation [8,9]. In this context, inhaled corticosteroids to long-acting bronchodilators are recommended for patients at high risk of exacerbation [6,10]. Additionally, oral corticosteroids are commonly prescribed to patients with recent exacerbations to prevent subsequent episodes [11].

Systemic corticosteroids are considered a standard treatment for preventing and managing patients with AECOPD, often in combination with antibiotics. However, clinical trial evidence supporting its efficacy remains limited [4]. Previous studies have demonstrated that systemic corticosteroids re-

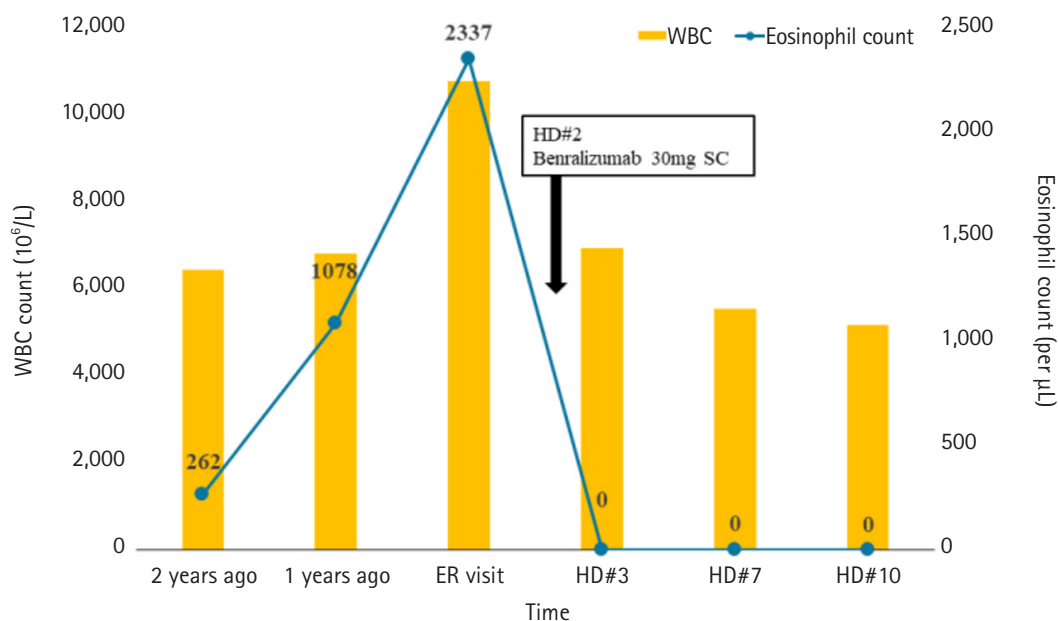


Fig. 3. The bar graph illustrates the change in WBC count (10⁶/L), while the line graph shows the change in blood eosinophil count (per µL) from two years before the AECOPD event to HD 10 (HD#10). A 30 mg dose of benralizumab was administered subcutaneously on HD 2, resulting in a rapid depletion of eosinophils and normalizing WBC count. WBC, white blood cell; HD, hospital day; SC, subcutaneous; ER, emergency room; AECOPD, acute exacerbation of chronic obstructive pulmonary disease.

duce the risk of treatment failure in AECOPD by approximately 10%, decreasing the risk from 40% to 30% [3]. Similarly, a systematic review by Walter et al. reported a treatment failure rate of 13% with systemic corticosteroids compared to 23% with placebo [4]. These findings suggest that despite their benefits, 13%–30% of patients with AECOPD treated with systemic corticosteroids still experience treatment failure, which represents a substantial proportion.

Benralizumab, a monoclonal antibody against IL-5 α , achieves rapid and sustained depletion of eosinophils [12]. It is currently approved for the prevention of exacerbations in patients with severe eosinophilic asthma [13]. Given the critical role of blood eosinophil levels in the pathogenesis of eosinophilic COPD exacerbation [14], benralizumab has emerged as a potential therapeutic option in such cases.

Recent findings from the Acute exacerbations treated with BenRALizumab (ABRA) trial, a randomized controlled study evaluating the efficacy of benralizumab in eosinophilic exacerbations of asthma and COPD, demonstrated favorable outcomes [15]. The trial reported that in AECOPD patients with a blood eosinophil count of more than 300/ μ L, a single subcutaneous dose of benralizumab reduced the 90-day treatment failure rate, improved symptoms, and resulted in fewer adverse events compared to standard systemic corticosteroid therapy.

In our case, the patient had been on triple inhaled combination therapy—long-acting β 2-agonists, long-acting muscarinic antagonists, and inhaled glucocorticoids—due to a history of multiple exacerbations. Upon presentation to the emergency department, her blood eosinophil count was 2,337/ μ L, indicating an eosinophilic exacerbation and the ABG revealed hypercapnia with respiratory acidosis, consistent with a severe episode. The clinical features supported using benralizumab, and the response was dramatic. The patient's oxygen requirements gradually decreased, and her symptoms, including chest discomfort, cough, and sputum production, improved significantly.

This case highlights the potential role of benralizumab, a medication currently used for the management of asthma, in treating patients with COPD. A clinical trial has evaluated the efficacy of benralizumab in preventing AECOPD in patients with high eosinophil counts [16]. Although the study showed that benralizumab effectively reduced blood eosinophil levels, its impact on lowering the annual AECOPD rate was insignificant compared with that of the placebo. Further research is needed to identify factors beyond blood eosinophil counts that influence the risk of exacerbation and define subgroups

of patients who may benefit most from benralizumab in preventing and managing exacerbations.

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Ethics approval

The Institutional Review Board (IRB) of the Catholic University of Korea (IRB No. KC25ZISI0087) exempted this study from review. The requirement for written informed consent was waived by the IRB of Seoul St. Mary's Hospital.

Conflict of interest

The authors have nothing to disclose.

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