CASE REPORT

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A Rare Geriatric Case: Omalizumab As a Rescue Therapy For Asthma-Chronic Obstructive Pulmonary Disease Overlap

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Abstract

The most common obstructive lung diseases observed during clinical practice include chronic obstructive pulmonary disease (COPD) and asthma. They share similarities in terms of clinical presentation. Asthma-COPD overlap is defined as an obstructive lung condition with clinical and inflammatory characteristics of asthma and COPD or predominantly COPD combined with bronchodilator responsiveness and elevated peripheral eosinophil count.

Keywords: ACO, clinical geriatrics, frailty, omalizumab, rescue therapy

Introduction

The present case highlights the efficacy of omalizumab as a rescue therapy for Asthma and chronic obstructive pulmonary disease (COPD) Overlap (ACO) in a frail older patient. Omalizumab should be considered in patients who are unresponsive to standard treatment.

Case Report

A 74-year-old male patient presented to the emergency department with dyspnea. He resided with his wife, and he did not use any assistive devices before hospitalization. He was assessed as semi-dependent in activities of daily living (ADL) and dependent in instrumental activities of daily living (IADL). Frailty and nutritional status were assessed using the FRAIL score and the mini nutritional assessment (MNA) score, respectively. A FRAIL score of 3/5 indicated frailty, whereas an MNA score of 10/14 was considered as malnutrion risk. The patient with no known comorbidities other than COPD reported a pattern of staying up late and experiencing excessive daytime sleepiness but did not report any forgetfulness, malaise, or anhedonia. In the past year, he did not report any falls or urinary incontinence. There was no reported pain. His vaccination history included 2 doses of inactivated Sars-Cov-2 vaccine, 4 doses of mRNA vaccine, and 1 dose of pneumococcal conjugate 13 vaccine. He had pollen,dust, and perfume allergies and was an ex-smoker with a smoking history of 25 pack years.

The patient had a history of COPD with long-term use of inhaled glucocorticoids combined with short-acting β2 receptor agonists (SABAs) and a need for long-term oxygen therapy. He presented with shortness of breath and increased need for oxygen. Emphysematous changes were observed in the bilateral lung parenchyma on chest computed tomography (CT) scan performed over 4 years ago. Upon admission, the patient complained of dry cough for several days and breathlessness for several hours. Clinical examination revealed tachypnea with prolonged expiration, a silent chest on auscultation, and hypoxemia with an SpO_2 of 90% on 15 L of oxygen. Chest CT showed air trapping, peribronchial wall thickening, interlobular septal thickening, and ground glass appearance in both lungs, along with pleural effusion measuring 1 cm in the thickest part in both hemithorax (Figure 1). Arterial blood gas analysis showed hypercapnia with a partial pressure of carbon dioxide

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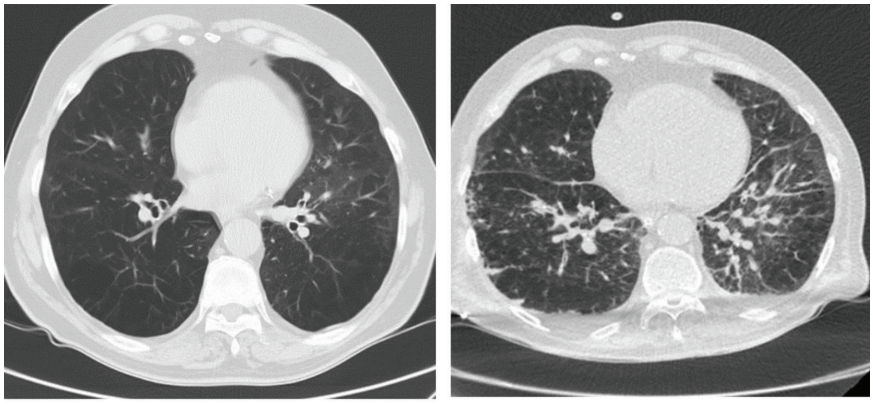

Figure 1. Chest CT showed air trapping, peribronchial wall thickening, interlobular septal thickening, and ground glass appearance in both lungs, along with pleural effusion measuring 1 cm in the thickest part in both hemithoraxes

CT: Computed tomography

($PaCO_2$) of 80 mm Hg (pH=7.08 and PaO_2=56). The patient was diagnosed with COPD exacerbation, and noninvasive mechanical ventilation (NIMV) was initiated to the patient. Due to worsening hypercapnia and respiratory failure, the patient was intubated and referred to the intensive care unit (ICU).

During the patient's ICU follow-up, blood and sputum cultures were obtained. Subsequently, antibiotic therapy with piperacillin-tazobactam 4.5 grams every 6 hours and clarithromycin 500 mg twice daily was initiated. Additionally, a respiratory viral pathogen panel, nasal swab COVID-19 PCR test, Legionella urine antigen test, sputum culture, Mycoplasma pneumoniae, and Chlamydia pneumoniae immunoglobulin M antibodies were requested, and all results were negative. Bronchoscopy and chest radiography excluded pneumothorax and obstruction from a foreign body or mucus.

The patient received methylprednisolone (320 mg for 2 days, 240 mg for 1 day, and 160 mg from day 4 and gradually tapered and discontinued in 40 days), theophylline 480 mg/day, inhaled corticosteroids (ICS), and SABAs every 2 hours, montelukast 10 mg/day and cetirizine 10 mg/day along with intravenous magnesium sulfate. Ketamine (150 mg/h) was used for sedation because of its bronchodilatory effect. Despite these treatments, the patient's extubation attempts failed. Clinical examination revealed prolonged expiration and a silent chest on auscultation. Asthma-COPD ACO was suspected based on the patient's history and clinical presentation.

The patient had a previous total immunoglobulin E (IgE) level of 369.00 IU/mL, so the current total IgE blood level was 281.00 IU/mL (normal, <100 IU/mL). His eosinophil level was 0.00x10^3 /µl (normal 0.0-0.7 x10^3 /µl) in the complete blood count.

Omalizumab 450 mg subcutaneously was administered on the 7th day of hospitalization. Extubation was attempted again on the following day, and the patient tolerated it NIMV was applied for 12 h/day. High flow nasal oxygen therapy was administered during intervals. On the 11th day of ICU admission, the patient no longer required NIMV. Normal lung sounds became audible during auscultation.

During follow-up, the maximum CO_2 level in arterial blood gas was measured at 60 mmHg. The patient was transferred to the pulmonary medicine department on the 14th day of hospitalization which was the 7th day of omalizumab therapy. In the pulmonary medicine department, the second dose of omalizumab was administered 4 weeks after the first dose, followed by subsequent doses every 4 weeks. He was discharged on day 71.

Throughout this process, the patient did not experience any relapses, and his or her clinical condition returned to baseline levels. In the current geriatric examination, the patient was evaluated as having FRAIL: 2/5 (prefrail), MNA: 13/14 (normal), good appetite, ADL: semi-dependent, and IADL: independent.

Discussion

The most common obstructive lung diseases observed in medical practice are COPD and asthma. Both diseases are significantly heterogeneous, but they share significant similarities and clinical features. Differentiating asthma from COPD can be difficult, particularly in smokers and older patients (1). Therefore, the term Asthma-COPD ACO was proposed to represent the intersection of these two disease groups in clinical use. ACO is a spectrum of overlapping features of asthma and COPD. Although defined as an obstructive lung disorder with the clinical and inflammatory features of asthma and COPD or predominantly COPD, with bronchodilator sensitivity and high peripheral eosinophil count, there is no consensus on a clear definition for ACO (2). Estimating the prevalence of ACO is challenging because of differences in definitions between studies. Despite heterogeneity among studies, the estimated global prevalence of asthma +COPD was

2.0%, compared with 6.2% and 4.9% for asthma and COPD alone in a meta-analysis by Hosseini et al. (3). In an Italian study, ACOs were 1.6 %, 2.1 %, and 4.5 % prevalent among 20-44, 45-64 and 65-84 year olds respectively (4). Identification of patients diagnosed with ACO is important because they represent a distinct clinical phenotype with increased disease exacerbations and hospitalizations, decreased health-related quality of life, and higher healthcare costs. Therefore, there is a need to better define the management and treatment of this syndrome (5).

In the management of patients with ACO, priority should be given to nonpharmacological methods. Identifying and limiting the patient's exposures and quitting smoking are especially valuable for patients with ACO. To prevent disease exacerbations, recommendations such as annual influenza vaccination and pneumococcal vaccination, avoidance of allergens in patients suspected of having an allergic contribution to ACO, and participation in pulmonary rehabilitation programs should be made for patients diagnosed with ACO (2).

In patients with ACO, treatment should follow a step-by-step approach based on the control of symptoms and exacerbation history. Inhaler therapies are essential for managing mild-to-moderate disease. Although there is no clear evidence on the initial treatment approach, it is recommended to avoid the use of single long-acting beta agonist (LABA) therapy and start therapy with ICS to target airway inflammation, and then add LABA or long-acting muscarinic antagonists (LAMA) to ICS for concomitant airway obstruction (2). Gershon et al. (6) reported that among older adults with COPD, specifically if they had asthma and were not using long-acting anticholinergics, the risk of COPD-related death and hospital admission was significantly lower with the addition of LABA+ICS compared with LABAs alone (6). Patients treated with ICS/LABA who continue to have symptoms may benefit from long-acting bronchodilator therapy, such as those receiving LAMA. The use of a combination of three inhalers (ICS/LABA/LAMA) has been shown to be efficacious in the treatment of individuals with either asthma or COPD, particularly in patients with a history of frequent exacerbations and increased symptoms (7). If these patients do not respond to inhalation therapy, more advanced treatments can be considered, including the use of phosphodiesterase inhibitors, macrolides, and biologics (8).

Omalizumab is a human monoclonal antibody that recognizes and binds to IgE, leading to a rapid decrease in free IgE levels in the serum (9). Omalizumab has been safely used for many years for the treatment of allergic asthma and chronic urticaria. For many allergic and non-allergic diseases, such as non-atopic asthma, nasal polyps, and allergic bronchopulmonary aspergillosis, some case reports suggest that omalizumab may also be an effective treatment option (10). A diagnosis of COPD is usually an exclusion criterion for clinical trials on asthma, so there is limited clinical data on the effectiveness of these treatments in a population where asthma and COPD ACO, although case reports have been published regarding the use of omalizumab in patients with refractory status asthmaticus (11-13). Consequently, data on the efficacy of omalizumab in this patient group are also limited. In a study by Maltby et al. (14) using data from the Australian xolair registry, omalizumab was shown to improve asthma control and health-related quality of life in people with asthma-COPD ACO over a 6-month follow-up period, compared with responses seen in patients with severe allergic asthma alone (14). Similarly, in a retrospective study of 70 patients with a mean age of 56 years, Crowley et al. (15) reported that omalizumab treatment was effective and safe in patients diagnosed with asthma, COPD, and ACO, even in those with multiple comorbidities and a history of smoking during a 12-month follow-up period (15). Although evidence for the use of omalizumab in the over 65s is limited, several studies have shown that omalizumab is well tolerated and effective in the treatment of uncontrolled asthma and chronic spontaneous urticaria in patients over 65 years of age (16,17).

Conclusion

In our case, despite standard treatments, the patient did not show improvement in clinical status, and extubation attempts were unsuccessful. Therefore, omalizumab therapy was initiated. Following treatment, the patient's clinical condition began to improve, and he was successfully extubated on the first day of treatment. Although there may be insufficient data in the literature regarding the use of omalizumab in frail older patients, our case demonstrated benefits the following omalizumab therapy. Omalizumab treatment in frail older patients diagnosed with ACO can be a potential rescue treatment option.

Ethics

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Y.Y., E.Y., B.C., H.A., D.K., Ş.Y.O., S.K., Concept: Y.Y., E.Y., B.C., H.A., D.K., Ş.Y.O., S.K., Design: Y.Y., E.Y., B.C., H.A., D.K., Ş.Y.O., S.K., Data Collection or Processing: Y.Y., E.Y., B.C., H.A., D.K., Ş.Y.O., S.K., Analysis or Interpretation: Y.Y., E.Y., B.C., H.A., D.K., Ş.Y.O., S.K., Literature Search: Y.Y., E.Y., B.C., H.A., Writing: Y.Y., E.Y., B.C., H.A.

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