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Case Report

Phenotyping Bronchial Asthma and use of Biologics in Airway Disease.

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ABSTRACT

Bronchial asthma is a heterogeneous condition with varying degrees of severity and phenotypes. Despite standard treatments, some patients exhibit persistent symptoms and frequent exacerbations, categorized as severe asthma. This manuscript presents two cases of severe eosinophilic asthma managed with benralizumab, an anti-IL-5 receptor monoclonal antibody. The cases illustrate the clinical course, treatment, and outcomes, emphasizing the role of biologics in reducing exacerbations and oral corticosteroid (OCS) dependence. The manuscript also discusses the pathophysiology of severe asthma, the impact of chronic OCS use, and the necessity of personalized treatment approaches.

Introduction

Asthma is a chronic inflammatory disease of the airways, characterized by symptoms such as wheezing, shortness of breath, chest tightness, and coughing. Severe asthma, a subset of difficult-to-treat asthma, significantly affects patients' quality of life and poses a substantial healthcare burden. Despite high doses of inhaled corticosteroids (ICS) and long-acting beta-agonists (LABA), patients with severe asthma often require systemic corticosteroids to manage exacerbations, leading to significant long-term side effects such as osteoporosis, hypertension, diabetes, and adrenal insufficiency.

Advancements in asthma management have led to the identification of various phenotypes, allowing for more targeted therapies. Eosinophilic asthma, characterized by elevated levels of eosinophils in the blood and airway tissues, responds well to biologic therapies targeting specific inflammatory pathways. Benralizumab, an anti-IL-5 receptor monoclonal antibody, has shown promise in reducing exacerbations, lowering OCS use, and improving overall asthma control in patients with severe eosinophilic asthma. This manuscript presents two cases of severe asthma treated with benralizumab, highlighting its efficacy and the importance of personalized treatment approaches.

Case 1

Patient Profile

Age/Gender: 34-year-old female

Medical History: Bronchial asthma for 8 years with repeated exacerbations in the past 2 years, requiring one ICU admission 8 months ago.

Pulmonary Function Tests (PFT): Severe obstruction.

Current Treatment: Long-acting beta-agonists (LABA) and inhaled corticosteroids (ICS), oral corticosteroids (OCS) for exacerbations.

Symptoms: Unable to perform routine activities, frequent outpatient department (OPD) visits, and hospitalizations.

Blood Eosinophil Count: 1200 cells/µL.

Intervention

Biologic Therapy: Fasenra (Benralizumab) 30 mg subcutaneously (4 doses).

Outcome

-Eosinophil Count: Immediate decrease.

-Exacerbations: Significant reduction.

-OCS Use: Discontinued.

Case 2

Patient Profile

Age/Gender: 54-year-old female

Medical History: Chronic bronchial asthma with repeated exacerbations over the last 2 years, history of pulmonary tuberculosis treated 20 years ago, and hypertension.

Current Medications: Formoterol 12 mcg + Budesonide 800 mcg twice daily, Methylprednisolone 8 mg once daily, Montelukast, Levocetirizine, Levosalbutamol metered-dose inhaler (MDI) as needed.

Symptoms: Progressive shortness of breath (SOB), worsening from mMRC grade 2 to grade 4 within 2 days despite being on controller medications and increased doses of relievers along with OCS.

Physical Exam

SpO2: 78% on room air.

Respiratory Rate: 36/min.

Pulse Rate:122/min.

Blood Pressure:110/70 mmHg.

Respiratory System: Extensive bilateral rhonchi.

Systemic Examination: Unremarkable.

Hospital Course

Provisional Diagnosis: Acute exacerbation of bronchial asthma.

Initial Treatment: IV steroids, ICS, LABA, LAMA, and oxygen supplementation.

Persistent Symptoms: Despite treatment, the patient had persistent wheezing and type 1 respiratory failure, necessitating non-invasive ventilation (NIV).

Progression: On Day 2, the patient required IV Deriphylline and IV Magnesium Sulfate. By Day 4, the patient exhibited hypercapnia, worsening hypoxia, tachypnea, and accessory muscle usage, leading to elective intubation and mechanical ventilation.

Advanced Interventions: The patient was treated with inhalational anesthetic agent Sevoflurane, Tolubuterol patch, lignocaine nebulization, bronchoscopy to check for airway compression, intratracheal adrenaline, mycophenolate 500 mg BD, and azithromycin 250 mg OD.

Biologic Therapy: Phenotyping revealed eosinophilic asthma. Benralizumab (Fasenra) was administered on 25/5/23.

Outcome: The patient was gradually weaned off mechanical ventilation, extubated on 30/5/23, and decannulated on 7/6/23. She was discharged after 36 days of hospitalization with home BiPAP therapy.

Discussion

Severe asthma is a significant health concern due to its chronic nature, frequent exacerbations, and substantial impact on patients' daily lives and the healthcare system. The disease often requires high doses of ICS and LABA, along with systemic corticosteroids during exacerbations, leading to substantial morbidity due to

long-term corticosteroid use. Eosinophilic asthma, a common phenotype of severe asthma, is characterized by elevated blood and airway eosinophils, contributing to airway inflammation and hyperresponsiveness.

Chronic use of systemic corticosteroids is associated with numerous side effects, including osteoporosis, hypertension, diabetes, and adrenal suppression, highlighting the need for alternative therapies. Biologic agents, such as benralizumab, target specific inflammatory pathways, offering a more effective and safer treatment option for severe eosinophilic asthma.

Benralizumab, an anti-IL-5 receptor monoclonal antibody, depletes eosinophils by inducing apoptosis, leading to significant reductions in blood and airway eosinophil counts. Clinical trials have demonstrated benralizumab's efficacy in reducing asthma exacerbations, improving lung function, and decreasing the need for OCS. In the cases presented, benralizumab was highly effective in managing severe eosinophilic asthma.

Case 1

In the first case, a 34-year-old female with longstanding bronchial asthma presented with severe exacerbations despite optimized treatment with high-dose LABA and ICS. Her condition had progressively worsened over two years, necessitating frequent hospitalizations. Pulmonary function tests revealed severe obstruction, indicative of poorly controlled asthma. With an elevated eosinophil count of 1200 cells/µL, she was classified as having eosinophilic asthma. Persistent symptoms and dependence on oral corticosteroids (OCS) prompted the initiation of benralizumab therapy.

Benralizumab, an anti-IL-5 receptor monoclonal antibody, swiftly reduced the eosinophil count, consistent with its mechanism of inducing eosinophil apoptosis. This intervention markedly decreased exacerbation frequency and allowed discontinuation of OCS, mitigating the risk of long-term corticosteroid-related side effects. The efficacy of benralizumab in this case underscores its role in managing severe eosinophilic asthma refractory to standard therapies. Improved asthma control post-benralizumab administration highlights the importance of personalized treatment approaches, enhancing quality of life and reducing healthcare utilization.

Case 2

The second case involved a 54-year-old female with chronic bronchial asthma and a history of severe exacerbations despite intensive therapy with high-dose controller medications and frequent OCS use. Her asthma rapidly progressed to mMRC grade 4, necessitating multiple hospitalizations and mechanical

ventilation. Complicating factors included a history of pulmonary tuberculosis and hypertension. On admission, she presented with severe hypoxia (SpO2 78%), tachypnea, and extensive bilateral rhonchi, indicative of a severe exacerbation.

Initial treatment with IV steroids, ICS, LABA, LAMA, and oxygen supplementation yielded inadequate results. Persistent respiratory failure led to advanced interventions, including NIV, and eventually, elective intubation and mechanical ventilation. Phenotyping identified eosinophilic asthma, prompting the initiation of benralizumab. This biologic therapy facilitated significant clinical improvements, resulting in successful weaning from mechanical ventilation, extubation, and discharge.

The patient's response underscores benralizumab's potential to rapidly reduce eosinophil counts and improve asthma control, even in life-threatening scenarios. This case highlights the importance of phenotype-driven management strategies in severe eosinophilic asthma, effectively reducing healthcare resource utilization and enhancing patient outcomes.

These cases underscore the critical role of asthma phenotyping in guiding personalized treatment approaches. By targeting specific inflammatory pathways, such as eosinophilic inflammation with benralizumab, clinicians can effectively manage severe asthma, reduce exacerbations, minimize OCS use, and ultimately improve patient quality of life while mitigating long-term treatment-related risks.

Conclusion

The phenotyping of bronchial asthma and the use of biologics, particularly benralizumab, are critical in managing severe eosinophilic asthma. These cases highlight the clinical benefits of benralizumab in reducing exacerbations, minimizing OCS use, and enhancing overall asthma control. Personalized treatment approaches, informed by asthma phenotyping, are essential for optimizing patient outcomes and preventing long-term complications associated with severe asthma.

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