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Biologics for Severe Asthma in Elderly Patients with Chronic Kidney Disease and Cirrhosis: A Case Report

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Abstract

Background: In recent years, several new biologics, such as benralizumab has been developed to treat patients suffering from asthma poorly controlled by high-dose Inhaled Corticosteroids (ICS) and long-acting bronchodilators. Benralizumab is a humanized, interleukin (IL)-5Rα-specific monoclonal antibody that effectively ameliorates asthmatic episodes by inducing rapid and nearly complete depletion of eosinophils.

Case presentation: The patient was a man in his 70s who had a history of bronchial asthma since his 30s and of heavy smoking for 70 pack years. Benralizumab (30 mg/body) was started in 2018 because of the risk of systemic steroids to control asthma attacks. He had Chronic Kidney Disease (CKD) and cirrhosis due to the hepatitis C virus. The asthma exacerbations have disappeared. During the three years, he has had an exacerbation only once because of pneumonia. No significant change in renal function or liver function occurred during this period.

Conclusions: It is extremely important for physicians to be aware that in elderly patients, various organ functions are generally impaired, including both hepatobiliary and renal functions; as in this case, biologics can definitely be administered safely.

Background

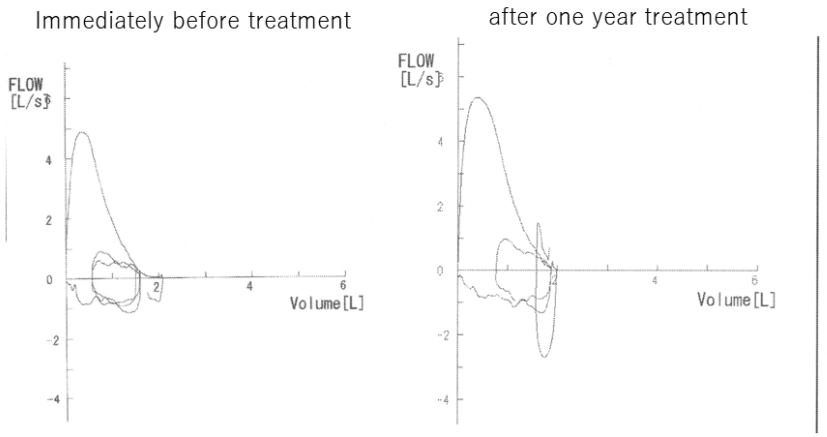
In recent years, several new biologics, such as benralizumab, have been developed to treat patients suffering from asthma poorly controlled by high-dose inhaled corticosteroids (ICS) and long-acting bronchodilators. Benralizumab is a humanized, interleukin (IL)-5Rα-specific monoclonal antibody that effectively ameliorates asthmatic episodes by inducing rapid and nearly complete depletion of eosinophils [1,2]. Dupilumab is an IL-4 receptor alpha antibody and a biologic that blocks both IL-4 and IL-13. Recently, evidence of anti-IL-5 efficacy in Chronic Obstructive Pulmonary Disease (COPD) has also been shown [3], and benralizumab is shown to be effective in patients with adult-onset asthma with peripheral blood eosinophilia rather than the phenotype of childhood-onset, allergic asthma. The administration of biologics to a wide range of phenotypes and rigid phenotypes is becoming increasingly recommended, and the administration of biologics in the real world is becoming increasingly important. In fact, we have recently identified a distinct phenotype of severe eosinophilic asthma with greater Forced Expiratory Volume in one second (FEV1) responsiveness to benralizumab in a real-world setting [4], which included aged smokers, as the case reported here. This report presents a patient with COPD complicated by severe eosinophilic asthma who was unsuitable for systemic steroid

administration because of repeated pneumonia. In addition, he had Chronic Kidney Disease (CKD) and cirrhosis due to the hepatitis C virus. A hepatic physician treated him with pibrentasvir, which can also be used for impaired renal function associated with cirrhosis.

Case Presentation

The patient was a man in his 70s who had a history of bronchial asthma since his 30s and of heavy smoking for 70 pack years. He was treated with high-dose inhaled corticosteroids and long-acting β2-agonists and also took anti-leukotriene antagonists. Systemic steroids were introduced several times a year when he had an asthma attack. However, he was not taking them regularly because of frequent infections. Benralizumab (30 mg/body) was started in 2018 because of the risk of systemic steroids to control asthma attacks. At the time of the drug's commencement, the eosinophils were 200-300/μL, FeNO was 30-60 ppb, and IgE was within the normal range. There was no liver damage at that time, and the renal function was 1.5 mg/dL–2.5 mg/dL for serum creatinine, 20 mg/dL–30 mg/dL for blood urea nitrogen, and 20–30 for the estimated Glomerular Filtration Rate (eGFR). In the year before starting benralizumab treatment, he had had four exacerbations due to pure asthma attacks and infections such as pneumonia.

Benralizumab was administered monthly for the first three months and once every two months thereafter. (Figure) shows the disease status immediately before treatment and one year after treatment. To date, he has been taking biologics for about three years, including the time when he temporarily switched to dupilumab at his request. The asthma exacerbations have disappeared. During the three years, he has had an exacerbation only once because of pneumonia. No significant change in renal function or liver function has occurred during this period. The asthma control test has increased from 15 points to 22 points. The asthma symptoms are very stable, and only symptoms of general malaise and edema associated with cirrhosis and renal dysfunction remain.



Number of exacerbations per year	4	0
Inhaled steroid amount Fluticasone equivalent	1000 μg/day	500 μg/day
FEV_1(L)	1.58	1.72
%FEV_1	64.2	71.7
FEV_1%(G)	75.60	86.43

Figure: Comparison of one year before and after treatment. A prominent effect was obtained in the one year before and after the treatment, including exacerbation.

Discussion

Here, we have shown that asthma exacerbations were successfully controlled by using benralizumabin in the elderly person with the eosinophilic phenotype of chronic airway diseases and a number of chronic malady. Small-molecule biologics such as benralizumab are administered subcutaneously and then carried systemically by diffusion, so basically, the dose does not need to be adjusted even in patients who are older or have renal or liver disorders [5]. Patients who are not suitable for systemic steroids, such as the patient, in this case, may be overlooked as being trapped in the typical asthma phenotype, even though biologics should be very effective. In this case, reducing inhaled steroids by controlling allergic inflammation of the respiratory tract with biologics that do not make it vulnerable to infectious diseases may also be a factor in reducing the exacerbations caused by infectious diseases.

It is extremely important for physicians to be aware that in elderly patients whose various organ functions are generally impaired, including both hepatobiliary and renal functions, as in this case, biologics can definitely be administered safely. Therefore, it is hoped that a large study will prove that biologics for severe asthma are sufficiently valuable even in high-risk cases, such as the case presented here, rather than just in adjusted cases, such as being enrolled in a clinical trial.

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Disclosure Statement

Hideyasu Yamada, has received lecture fees from AstraZeneca and Sanofi. N. Hizawa has received research support from AstraZeneca. The other authors have no relevant conflicts of interest to declare.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Informed consent was obtained for this publication.

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