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Severe Eosinophilic Asthma and Persistent Airflow Obstruction Treated with Biologic Therapy A Case Report

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ABSTRACT

Background: Severe eosinophilic asthma is a Type-2 inflammatory phenotype characterized by recurrent exacerbations, persistent airflow obstruction, and poor disease control despite optimized therapy.

Objectives: To describe the clinical characteristics and early response to benralizumab in a patient with severe eosinophilic asthma and persistent airflow obstruction.

Case presentation: A 43-year-old woman with recurrent asthma exacerbations and previous hospitalization had persistent symptoms despite optimized triple inhaled therapy. Pretreatment eosinophil counts ranged from 586 to 837 cells/µL, and spirometry showed severe airflow obstruction (FEV_1 49.3–53.2% predicted; FEV_1/FVC 52.5–54.5%). Clinical history, examination findings, laboratory results, spirometry, treatment, and response were retrospectively reviewed from medical records.

Benralizumab 30 mg was initiated. The reported absolute eosinophil count decreased from 837 to 111 cells/µL, and the Asthma Control Test score reached 25 at follow-up. The patient reported improvement in daily activities and sleep, with no exacerbations documented during the available follow-up. Post-treatment spirometry and long-term outcomes were unavailable.

Conclusion: This case illustrates an early hematologic and clinical response to benralizumab and the potential value of phenotype-guided biologic therapy in severe eosinophilic asthma. Longer follow-up is needed to assess sustained clinical and lung-function outcomes.

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INTRODUCTION

Asthma is a chronic heterogeneous inflammatory airway disease characterized by variable respiratory symptoms, bronchial hyperresponsiveness, mucus hypersecretion, and expiratory airflow limitation. Typical symptoms include wheezing, shortness of breath, chest tightness, and cough that vary over time and in intensity. Asthma affects more than 300 million individuals worldwide and remains a major public health concern. Although most patients achieve adequate control with standard therapy, approximately 5–10% remain uncontrolled despite optimized treatment and are classified as having severe asthma.[1]

According to The Global Initiative for Asthma (GINA), severe asthma is asthma that remains uncontrolled despite optimized high-dose inhaled corticosteroids (ICS) plus a second controller, usually a long-acting β2-agonist (LABA), or worsens when treatment is reduced. Despite its relatively low prevalence, severe asthma is associated with substantially greater morbidity, healthcare utilization, and mortality.[1]

Asthma is increasingly recognized as a group of inflammatory endotypes, among which Type-2 (T2) inflammatory is one of the most clinically relevant. T2-high asthma is characterized by eosinophilic airway inflammation, elevated blood eosinophil counts, increased fractional exhaled nitric oxide (FeNO), recurrent exacerbations, impaired lung function, and poor disease control. It is also frequently associated with allergic rhinitis and chronic rhinosinusitis with nasal polyps.[2]

The immunopathology of T2 inflammation involves airway epithelial cells, Th2 lymphocytes, group 2 innate lymphoid cells (ILC2), eosinophils, mast cells, basophils, and B lymphocytes. Epithelial-derived cytokines, including thymic stromal lymphopoietin (TSLP), IL-25, and IL-33, activate Th2 cells and ILC2, leading to the production of IL-4, IL-5, and IL-13. These cytokines drive eosinophilic inflammation, IgE production, mucus hypersecretion, airway remodeling, and bronchial hyperresponsiveness.[3,4]

Advances in understanding T2 inflammation have led to the development of biologic therapies targeting specific inflammatory pathways, including anti-IgE, anti-IL-5, anti-IL-5 receptor alpha (IL-5Rα), anti-IL-4 receptor alpha, and anti-TSLP agents.[5] Benralizumab is a humanized afucosylated monoclonal antibody targeting IL-5Rα on eosinophils and basophils. Through antibody-dependent cellular cytotoxicity (ADCC), benralizumab induces rapid and near-complete eosinophil depletion, resulting in profound suppression of eosinophilic inflammation.[6]

Clinical trials and real-world studies have demonstrated that benralizumab reduces exacerbation rates, improves asthma control and lung function, decreases oral corticosteroid requirements, and enhances quality of life in patients with severe eosinophilic asthma. Long-term studies further support its sustained efficacy and safety.[6,7,8]

Despite growing evidence supporting benralizumab for severe eosinophilic asthma, reports from Indonesia and other low and middle income countries remain limited. Differences in access to biologic therapy, diagnostic resources, and healthcare systems may influence patient selection and treatment outcomes. We report a patient with severe eosinophilic asthma and persistent airflow obstruction despite optimized inhaled therapy who demonstrated significant clinical improvement following benralizumab treatment. This case illustrates the feasibility of phenotype-guided biologic therapy in a resource-limited setting and adds to the limited evidence supporting endotype-driven management of severe eosinophilic asthma in Indonesia.

CASE PRESENTATION

A 43-year-old female non-smoker presented to the hospital with a chief complaint of shortness of breath that had persisted for seven days prior to admission and worsened one day before hospitalization. The dyspnea was triggered by cold weather, strenuous physical activity, exposure to smoke, and dust, but was not associated with food intake.

She was able to speak in full sentences but frequently awoke at night due to shortness of breath and reported limitations in daily activities.

Additional symptoms included a productive cough with thick yellowish-green sputum that was difficult to expectorate and rhinorrhea, both of which had been present for seven days before admission. Other symptoms, including fever, nausea, vomiting, loss of appetite, and weight loss, were denied. Bowel and urinary habits were reported to be normal.

The patient was a non-smoker and had a history of severe asthma with recurrent exacerbations. No personal or family history of atopic diseases, including allergic rhinitis, atopic dermatitis, food allergy, or drug allergy, was identified.

In February 2025, she was hospitalized with severe asthma accompanied by a moderate exacerbation. Laboratory examination revealed a total eosinophil count of 586 cells/μL. Spirometry demonstrated severe airflow obstruction with an FEV_1 of 49.3% predicted, FVC of 84.7% predicted, and an FEV_1/FVC ratio of 54.5%. During hospitalization, she received triple inhaled therapy.

Following discharge, she attended an outpatient follow-up visit in March 2025 and was diagnosed with controlled asthma. At that time, she reported no respiratory symptoms, including dyspnea, cough, or rhinorrhea, and maintenance therapy was continued.

In May 2025, she returned to the outpatient clinic with complaints of dyspnea and rhinorrhea. Assessment using the Asthma Control Test (ACT) yielded a score of 20, consistent with partly controlled asthma. She was diagnosed with partly controlled mild persistent asthma and continued on the same maintenance therapy.

In January 2026, she again attended the outpatient clinic because of a persistent cough. Her ACT score was 22, indicating partly controlled asthma, and maintenance treatment was continued.

On physical examination at the current admission, the patient appeared moderately ill and was fully conscious (compos mentis). Assessment using the Glasgow Coma Scale (GCS) yielded a score of 15 (E4V5M6). Vital signs showed a blood pressure of 120/70 mmHg, heart rate of 77 beats/minute, respiratory rate of 22 breaths/minute, and oxygen saturation of 92% on room air, which improved to 98% after administration of oxygen at 3 L/min via nasal cannula. Body weight was 63 kg and height was 158 cm.

Thoracic examination revealed no abnormalities of the neck and no evidence of cardiac enlargement. Cardiac auscultation demonstrated a regular rhythm without murmurs or gallops. Pulmonary examination revealed vesicular breath sounds with diffuse wheezing audible throughout all lung fields. Abdominal examination showed a mildly distended abdomen with normal bowel sounds and no hepatosplenomegaly. Examination of the extremities revealed no edema or cyanosis.

Laboratory evaluation, as presented in Table 1, demonstrated persistent eosinophilic inflammation. At the first hospitalization in February 2025, the absolute eosinophil count (AEC) was 586 cells/μL. Prior to benralizumab initiation during the second hospitalization in March 2026, eosinophilia became more pronounced, with an eosinophil percentage of 10.3% and an AEC of 837 cells/μL. Following benralizumab therapy, eosinophil levels markedly decreased to 0.1%, with an AEC of 111 cells/μL. The erythrocyte sedimentation rate (ESR) also decreased from 27 mm/hour to 19 mm/hour.

Table 1. Serial laboratory findings before and after benralizumab therapy

Parameter	19 Feb 2025	30 Mar 2026 Pre-treatment	02 Apr 2026 Post-treatment	Reference range
Hemoglobin (g/dl)	12.2	12.7	12.0	11.5–16.5
Hematocrit (%)	36.8	38.1	37.0	35–47
White blood cell count (10^3/μL)	8.88	8.13	11.63	4.0–11.0
White blood cell count (10^3/μL)	426	355	327	150–450
Neutrophils (%)	70.1	57.2	70.8	40–76
Lymphocytes (%)	17.0	25.6	21.9	20–45
Monocytes (%)	5.4	5.9	6.9	2–10
Eosinophils (%)	6.6	10.3	0.1	1–6
Basophils (%)	0.9	1.0	0.3	0–1

Parameter	19 Feb 2025	30 Mar 2026 Pre-treatment	02 Apr 2026 Post-treatment	Reference range
Absolute eosinophil count (cells/µL)	586	837	111	<300
Erythrocyte sedimentation rate (mm/hour)	93	27	19	<20

Spirometry performed before biologic therapy demonstrated severe airflow obstruction, with an FEV_1 of 53.2% predicted, FVC of 84.7% predicted, and an FEV_1/FVC ratio of 52.5%. A posteroanterior chest radiograph obtained on 30 April 2026 showed no significant cardiopulmonary abnormalities (Figure 1), helping to exclude pneumonia or other structural lung disease contributing to symptoms.



Figure 1. Posteroanterior chest radiograph showing no acute cardiopulmonary abnormalities

Triple inhaled therapy was continued during hospitalization. Before initiation of biologic therapy, potentially modifiable factors contributing to uncontrolled asthma were evaluated. The patient had received optimized high-dose ICS/LABA/LAMA therapy with good adherence to maintenance treatment, appropriate inhaler technique following repeated education, and no major treatable comorbidities, including gastroesophageal reflux disease (GERD), obesity, obstructive sleep apnea (OSA), or significant environmental or occupational exposures.

Based on recurrent exacerbations, persistently elevated blood eosinophil counts (586–837 cells/µL), severe airflow obstruction despite optimized therapy, and exclusion of modifiable factors, the patient fulfilled the GINA criteria for severe eosinophilic asthma and was considered eligible for biologic treatment with benralizumab. Following treatment, the absolute eosinophil count decreased from 837 cells/µL to 111 cells/µL, indicating a favorable hematologic response. This biological response was accompanied by marked clinical improvement.

In April 2026, during a scheduled outpatient follow-up visit, the patient received the second dose of benralizumab. Her asthma was fully controlled, and she reported no respiratory symptoms. The ACT score improved to 25, indicating complete symptom control. The patient also reported marked improvement in daily activities and sleep quality compared with before benralizumab treatment. Maintenance therapy was continued, and no exacerbations were documented during the available follow-up period.

DISCUSSION

The choice of benralizumab in this patient was supported by the predominance of eosinophilic inflammation. The patient had no history of allergic disease, while serum total IgE levels were within the normal range, and evaluation for atopy was negative. These findings made an allergic asthma phenotype less likely. In contrast, persistently elevated blood eosinophil counts (586–837 cells/μL), recurrent exacerbations, and severe airflow limitation despite optimized triple inhaled therapy strongly supported the diagnosis of severe eosinophilic asthma. Elevated blood eosinophil counts are well-established biomarkers of Type-2 eosinophilic inflammation and are among the strongest predictors of response to therapies targeting the IL-5 pathway.[9] Current evidence suggests that patients with higher baseline eosinophil counts, frequent exacerbations, and impaired lung function derive the greatest clinical benefit from anti-IL-5 receptor therapy. Taken together, these clinical and biomarker characteristics supported the selection of benralizumab for the present patient.[10]

Although blood eosinophil count is widely used to guide biologic selection, it should not be interpreted as a standalone biomarker. Blood eosinophil levels may fluctuate over time and do not always correlate with eosinophilic airway inflammation. Discordance between peripheral blood eosinophils and sputum eosinophils has been reported, therefore integrating blood eosinophil counts with clinical characteristics and additional biomarkers, such as fractional exhaled nitric oxide (FeNO) when available, may improve patient selection for biologic therapy. In the present case, the persistently elevated blood eosinophil count was interpreted together with recurrent exacerbations and severe airflow obstruction, supporting the diagnosis of severe eosinophilic asthma and the decision to initiate benralizumab.

Severe eosinophilic asthma is driven by Type-2 inflammation, in which IL-5 plays a central role in eosinophil maturation, activation, and survival. Persistent eosinophilic inflammation contributes to airway hyperresponsiveness, mucus production, and airway remodeling, providing the biological rationale for targeting the IL-5 pathway.[12] Unlike mepolizumab and reslizumab, which neutralize circulating IL-5, benralizumab binds directly to IL-5Rα on eosinophils and basophils, inducing antibody-dependent cellular cytotoxicity and near-complete eosinophil depletion. Given this patient's marked eosinophilia, recurrent exacerbations, and persistent airflow obstruction despite optimized inhaled therapy, benralizumab was considered the most appropriate biologic therapy.[13]

The marked reduction in blood eosinophil count from 837 cells/μL to 111 cells/μL following benralizumab administration provides biological evidence of treatment effectiveness. Similar eosinophil depletion has been consistently demonstrated in randomized clinical trials and real-world studies evaluating benralizumab in severe eosinophilic asthma. Nevertheless, eosinophil depletion alone should not be considered synonymous with clinical success. The ultimate goals of biologic therapy include reducing exacerbation frequency, improving symptom control and quality of life, preserving lung function, minimizing corticosteroid exposure, and achieving clinical remission.[14]

In the present case, the biological response was accompanied by clinically meaningful improvement in asthma control. Before initiation of benralizumab, the patient experienced recurrent symptoms despite optimized triple inhaled therapy, with ACT scores of 20 in May 2025 and 22 in January 2026. Following treatment, the ACT score improved to 25, indicating complete symptom control. Improvement in ACT and marked eosinophil depletion preceded objective assessment of lung function because repeat spirometry had not yet been performed. Consequently, changes in FEV_1 could not yet be evaluated. In addition, validated quality-of-life assessment and long-term evaluation of systemic corticosteroid requirements were unavailable. Therefore, the long-term effectiveness of benralizumab in this patient could not yet be fully assessed.

Long-term evidence further supports the effectiveness of benralizumab in achieving these outcomes. In the ANANKE study, treatment for up to 96 weeks resulted in a 94.9% reduction in annual exacerbations and a 96.9% reduction in severe exacerbations. Median Asthma Control Test (ACT) scores improved from 14 to 23, while median FEV_1 increased by approximately 400 mL, indicating substantial improvements in symptom control and lung function.[15] Treatment persistence remained high, with nearly 90% of patients continuing therapy throughout follow-up, suggesting durable clinical benefit.

A post-hoc analysis of the same study further demonstrated profound and sustained eosinophil depletion accompanied by increasing rates of clinical remission over 24 months.[16] Similar long-term benefits have also been reported in other real-world studies, including sustained improvements in lung function and high rates of clinical remission after four years of benralizumab therapy.[17]

Current guideline recommend reassessment of biologic response after approximately 4–6 months of therapy.[18] Clinical response is typically evaluated through exacerbation frequency, symptom control, lung function, corticosteroid requirements, and patient-reported outcomes. Treatment targets include achieving good asthma control, commonly reflected by an ACT score of at least 20, reducing or eliminating severe exacerbations, improving FEV_1, minimizing oral corticosteroid exposure, and, when possible, attaining clinical remission.[19]

In patients who demonstrate meaningful clinical benefit, benralizumab is generally continued as long-term maintenance therapy. At present, no universally accepted duration for treatment discontinuation has been established, as withdrawal may lead to recurrence of eosinophilic inflammation and loss of disease control in some patients.[17]

Although long-term clinical outcomes were not yet available in the present case, the substantial reduction in blood eosinophil count observed shortly after treatment initiation suggests an early biological response consistent with previous studies. These findings should be interpreted with caution because post-treatment spirometry was not yet available due to the short follow-up period, precluding assessment of changes in lung function. In addition, FeNO measurement, serial serum IgE assessment, and sputum eosinophil evaluation were unavailable. The relatively short follow-up also precluded evaluation of longer-term clinical outcomes, including exacerbation frequency, systemic corticosteroid requirements, and treatment persistence.

As this report describes a single patient, the findings cannot be generalized to the broader population with severe eosinophilic asthma. Nevertheless, this case highlights the importance of comprehensive phenotypic assessment for biologic selection. Despite the absence of allergic history, normal serum IgE levels, and negative atopy testing, persistent blood eosinophilia, recurrent exacerbations, and severe airflow obstruction identified a patient likely to benefit from anti–IL-5 receptor therapy. The marked reduction in blood eosinophil count following benralizumab administration further supports the value of blood eosinophils as an accessible biomarker for phenotype-guided biologic therapy, particularly in resource-limited settings.[20]

CONCLUSION

This case highlights the critical role of phenotypic assessment in identifying patients with severe eosinophilic asthma who remain uncontrolled despite optimized inhaled therapy. Benralizumab produced a marked reduction in peripheral blood eosinophil counts and meaningful improvement in asthma control, indicating its effectiveness as a targeted biologic for appropriately selected patients. This report further expands the limited evidence supporting phenotype-guided biologic therapy for severe eosinophilic asthma in Indonesia and underscores the need for broader access to and investigation of such targeted treatments in comparable settings.

LIST OF ABBREVIATIONS

ACT: Asthma Control Test; ADCC: Antibody-dependent cellular cytotoxicity; AEC: Absolute eosinophil count; ESR: Erythrocyte sedimentation rate; FeNO: Fractional exhaled nitric oxide; FEV_1: Forced expiratory volume in one second; FVC: Forced vital capacity; GCS: Glasgow Coma Scale; GERD: Gastroesophageal reflux disease; GINA: Global Initiative for Asthma; ICS: Inhaled corticosteroid; IgE: Immunoglobulin E; IL: Interleukin; ILC2: Group 2 innate lymphoid cells; LABA: Long-acting β_2-agonist; LAMA: Long-acting muscarinic antagonist; OSA: Obstructive sleep apnea; T2: Type 2; Th2: T-helper 2; TSLP: Thymic stromal lymphopoietin.

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