Brief report

Tezepelumab treatment in severe asthma with recurrent chronic rhinosinusitis with nasal polyps: Case series

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Background: Tezepelumab is a human IgG2 mAb that inhibits thymic stromal lymphopoietin (TSLP) and is approved for treatment of severe asthma. Bronchial asthma, usually a type 2 inflammatory disease, often co-occurs with chronic rhinosinusitis with nasal polyps (CRSwNP). However, tezepelumab has unknown effects on severe asthma with CRSwNP. Patients with CRSwNP are frequently candidates for endoscopic sinus surgery (ESS). CRSwNP is a crucial factor influencing asthma symptoms. However, some patients experience recurrent CRSwNP.

Objective: Tezepelumab was approved for use with CRSwNP, and TSLP is involved in the pathogenesis of CRSwNP. This study presents the cases of 2 patients with severe asthma complicated with recurrent CRSwNP after ESS in whom tezepelumab rapidly improved asthma and sinusitis symptoms.

Methods: We evaluated tezepelumab treatment in patients with severe asthma with recurrent CRSwNP based on symptoms, asthma exacerbation, level of type 2 cytokines, and lung function.

Results: After they had received a high-dose inhaled corticosteroid and long-acting β_2-agonist, the patients' asthma remained uncontrolled, as defined by a low Asthma Control Test score. However, tezepelumab reduced severe asthma exacerbation, improved lung function, and controlled asthma symptoms. It improved CRSwNP, asthma-related symptoms, and exercise tolerance, and it inhibited type 2 cytokines extensively, indicating its effectiveness in treating CRSwNP. Tezepelumab was efficacious in these patients and improved their symptoms in terms of comorbidities of the upper and lower airways.

Conclusion: Tezepelumab was effective in treating asthma complicated with CRSwNP recurrence after ESS. However, further studies are required to identify the general and specific roles of tezepelumab in treating severe asthma and recurrent CRSwNP. (J Allergy Clin Immunol Global 2025;4:100396.)

Key words: *Asthma, chronic rhinosinusitis with nasal polyps, thymic stromal lymphopoietin, tezepelumab*

INTRODUCTION

Severe asthma, usually a type 2 inflammatory disease, is characterized by eosinophilic airway mucosal infiltration. By definition, severe asthma remains uncontrolled despite high-dose inhaled corticosteroid (ICS) and long-acting β2-agonist (LABA) treatment. Type 2 asthma is characterized by eosinophilic inflammation, variable recurring symptoms, and airflow obstruction. More than 40% of patients with severe type 2 asthma have the comorbidity of chronic rhinosinusitis with nasal polyps (CRSwNP).[1] Eosinophilic chronic rhinosinusitis is a bilateral refractory form of CRSwNP associated with eosinophilic mucosal infiltration.[2] CRSwNP negatively influences asthma control and frequently requires sinonasal passage clearance and repeated endoscopic sinus surgery (ESS).[2]

Tezepelumab is a human IgG2 mAb that inhibits thymic stromal lymphopoietin (TSLP) and is approved for severe asthma treatment. Clinical trials have revealed that tezepelumab significantly reduces severe asthma exacerbations, improves lung function, and improves asthma symptoms.[3] Tezepelumab is not approved for CRSwNP; however, it is effective for severe uncontrolled asthma with and without nasal polyps, with unclear efficacy against nasal polyps. We describe 2 cases of severe asthma with recurrent CRSwNP after ESS whose asthma and sinusitis symptoms were rapidly improved by tezepelumab.

A 60-year-old man was diagnosed with a CRSwNP 6 years ago; he underwent surgery 4 years ago. He is an ex-smoker (0.75 pack per day from age 20 years to age 57 years). Chest computed tomography (CT) revealed bronchial wall thickness without a low-attenuation area, which is a presentation of chronic obstructive pulmonary disease (Fig 1, *A*). He was diagnosed with asthma 3 years ago, and his CRSwNP relapsed 3 years ago. He experienced exertional dyspnea, continuous nasal congestion, and loss of smell. He experienced asthma exacerbations requiring systemic corticosteroid treatment twice per year. Aspirin-exacerbated respiratory disease and nonsteroidal anti-inflammatory drug–exacerbated respiratory disease were not observed. He was referred to our hospital for poorly controlled severe asthma and CRSwNP; he received a high-dose ICS and LABA (fluticasone propionate/formoterol, 1000/40 μg per day) and a leukotriene receptor antagonist (montelukast, 10 mg per day) for 2 years and 3 months. However, his symptoms remained and exacerbations occurred. Subcutaneous tezepelumab (210 mg

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Abbreviations used
ACT: Asthma Control Test
CRSwNP: Chronic rhinosinusitis with nasal polyps
CT: Computed tomography
ESS: Endoscopic sinus surgery
FENO: Fractional exhaled nitric oxide
ICS: Inhaled corticosteroid
LABA: Long-acting β2-agonist
SNOT-22: Sino-Nasal Outcome Test-22
TSLP: Thymic stromal lymphopoietin

every 4 weeks) was initiated in April 2023. Before tezepelumab administration, his Asthma Control Test (ACT) score was 18 and his Sino-Nasal Outcome Test-22 (SNOT-22) score was 53. His total serum IgE level was 483 IU/mL (0-148 IU/mL). His Multiple Allergen Simultaneous Test result, which is classified into 7 levels (0-6) based on specific IgE concentration, indicated *Dermatophagoides farina* as class 2 and house dust as class 1. Despite receiving a high-dose ICS and LABA, his inflammatory markers included high peripheral blood eosinophilia (318/μL) and elevated fractional exhaled nitric oxide (FENO) level (71 ppb). Testing of his pulmonary function (% predicted) revealed an FEV_1 value of 2590 mL (79.6%) and a ratio of FEV_1 to forced vital capacity of 0.753 (Table I). The normal values in Japanese adults are calculated using the Lambda-Mu-Sigma (LMT) method.[4] CT of the paranasal sinuses revealed soft-tissue density lesions in sinuses (Fig 1, *B*). Nasal endoscopy revealed nasal polyps (Fig 1, *C*). After 2 months of tezepelumab treatment, the patient's peripheral blood eosinophil count decreased to 36/μL, with improved airway and nasal symptoms, including dyspnea on exertion, nasal obstruction, and loss of smell. After 2 to 5 months of monoclonal therapy, his ACT and SNOT-22 scores improved from 18 to 25 and 53 to 18, respectively, marking a clinically significant improvement for both scores, and his FEV_1 (% FEV_1) value increased from 2590 (79.6%) to 2720 mL (85.5%) after 2 months and 2920 mL (92.1%) after 5 months (Table I). CT revealed reduced opacification in the paranasal sinus after 2 months of the treatment (Fig 1, *D*) and an absence of nasal polyps after 5 months (Fig 1, *E*), with no asthma exacerbation or adverse events. After 14 months of tezepelumab treatment, the patient required systemic corticosteroids and his exercise tolerance and sense of smell improved. After 12 months, the high-dose ICS and LABA were tapered to a moderate-dose ICS and LABA.

A 70-year-old male nonsmoker was diagnosed with CRSwNP 8 years ago; he underwent sinus surgery 6 years ago (Fig 2, *A* and *B*). He was diagnosed with asthma 6 years ago and CRSwNP relapse 3 years ago (Fig 2, *C-E*); his symptoms deteriorated, with increasing dyspnea, productive cough, nocturnal symptoms, continuous nasal congestion, and loss of smell. He experienced asthma exacerbations requiring systemic corticosteroid treatment twice per year. Aspirin-exacerbated respiratory disease and nonsteroidal anti-inflammatory drug–exacerbated respiratory disease were not observed. He received a high-dose ICS and LABA (fluticasone furoate/vilanterol, 200/25 μg per day) and a leukotriene receptor antagonist (montelukast, 10 mg per day) for 3 years. However, his symptoms remained and exacerbations occurred. Thus, subcutaneous tezepelumab (210 mg every 4 weeks) was initiated in July 2023. Before the treatment, his ACT result was 16 and his SNOT-22 score was 45. His total serum IgE level was 184 IU/mL (0-148 IU/mL). His Multiple Allergen Simultaneous Test results indicated all allergens as class 0. His peripheral blood eosinophil count (353/μL) and FENO levels (40 ppb) were high. Pulmonary function (% predicted) testing revealed an FEV_1 value of 3350 mL (121.8%) and a ratio of FEV_1 value to forced vital capacity of 0.749 (Table I). His peripheral blood eosinophil count decreased to 299/μL 2 months after tezepelumab treatment, with improved airway and nasal symptoms, including dyspnea on exertion, nasal obstruction, and loss of smell. His ACT score improved from 16 to 25 after 2 months of the treatment and remained at 25 after 5 months, and his SNOT-22 score improved from 45 to 12 after 2 months and to 10 after 5 months; however, his FEV_1 (%FEV_1) value was unchanged (Table I). CT of the patient's paranasal sinuses revealed negligible mucosal edema in the ethmoid sinus after 3 months of the treatment (Fig 2, *F*) and an absence of nasal polyps after 5 months of the treatment (Fig 2, *G*). Additionally, asthma exacerbations or adverse events were not observed. No systemic corticosteroids were necessary after 11 months of tezepelumab therapy. The patient's sense of smell and quality of life improved.

RESULTS AND DISCUSSION

We report 2 cases of severe asthma with recurrent CRSwNP after ESS who were successfully treated with tezepelumab. Asthma is a heterogeneous disease characterized by multiple phenotypes. Not all patients with asthma have type 2 inflammation.[5] Additionally, CRSwNP has a variable response to treatment according to phenotypes or endotypes.[6] Not all patients with CRSwNP have type 2 inflammation. The presence of neutrophils in nasal cytology is associated with uncontrolled disease.[6] Moreover, NP size may not improve despite the near elimination of polyp eosinophils.[7] Thus, effective treatment for patients with severe asthma with CRSwNP is required for type 2 and non–type 2 nasal inflammation.

Dupilumab, which is an anti–IL-4 receptor alpha biologic, is approved for use in patients wih CRSwNP in the European Union, United States, and Japan. Dupilumab is effective in patients with moderate-to-severe eosinophilic asthma, systemic corticosteroid–dependent asthma, atopic dermatitis, and CRSwNP. Dupilumab reduces polyp size and symptom severity in patients with CRSwNP.[8]

In contrast, TSLP is an alarmin that is produced by airway epithelial cells after tissue trauma, including mechanical stimuli, as well as in response to mucosal inflammation. TSLP plays a crucial role in activating mast cells, eosinophils, and group 2 innate lymphoid cells. Group 2 innate lymphoid cells produce type 2 cytokines, including IL-5 and IL-13, in response to TSLP. TSLP induces T_H17 cell activation associated with type 2 and non–type 2 inflammation. Tezepelumab, which is an anti-TSLP antibody, reduces asthma exacerbations and improves lung function and asthma control regardless of eosinophil count, FENO level, or allergic status.[3] TSLP activity is increased in the nasal polyps of patients with chronic rhinosinusitis.[9] Overall, tezepelumab is expected to have effects in CRSwNP. Furthermore, tezepelumab decreases the numbers of eosinophils in the blood and tissue; however, dupilumab frequently increases the number of eosinophils in the blood. Tezepelumab reduces levels of type 2 biomarkers, such as IL-5 and IL-13, and improves asthma control

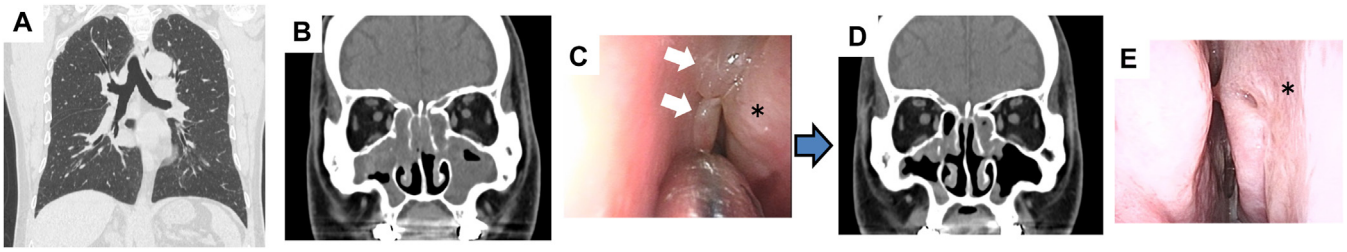

FIG 1. CT imaging and flexible rhinoscopy photographs of case patient 1. **A,** Coronal chest CT image (April 2023). **B,** Paranasal sinus CT image before tezepelumab treatment (April 2023). **C,** Nasal findings (*left*) obtained via flexible rhinoscopy before tezepelumab treatment (April 2023). **D,** Paranasal sinus CT image after 2 months of tezepelumab treatment (June 2023). **E,** Nasal findings (*left*) obtained via flexible rhinoscopy after 5 months of tezepelumab treatment (September 2023).

TABLE I. Time course of tezepelumab treatment

Indicator	Before tezepelumab	After tezepelumab for 2 mo	After tezepelumab for 5 mo
Case 1			
VC (mL)	3710	3730	3880
PP VC (%)	92.7	95.3	99.4
FEV_1 value (mL)	2590	2720	2920
PP FEV_1 value (%)	79.6	85.5	92.1
FEV_1/FVC	.753	.749	.783
FENO level (ppb)	71	46	28
Peripheral eos count (/μL)	318	36	43
IgE level (U/L)	483	513	571
ACT score	18	25	25
SNOT-22 score	53	18	15
Case 2			
VC (mL)	4560	4700	4620
PP VC (%)	130.2	134.2	132.3
FEV_1 value (mL)	3350	3190	3250
PP FEV_1 value (%)	121.8	116.0	118.6
FEV_1/FVC	.749	.738	.711
FENO level (ppb)	40	34	37
Peripheral eos count (/μL)	353	299	92
IgE level (U/L)	184	186	147
ACT score	16	25	25
SNOT-22 score	45	12	10

eos, Eosinophil; *VC*, Vital capacity.

and CRSwNP symptoms. Consequently, tezepelumab may be effective for patients with CRSwNP.

Peripheral eosinophil count, FENO level, and IgE level were elevated in our 2 reported case patients (Table I), indicating multiple pathway activation. Tezepelumab improved CRSwNP- and asthma-related symptoms, as well as exercise tolerance, in our 2 case patients and in the NAVIGATOR study.[3,10] Moreover, CT revealed a reduced CRSwNP severity 2 or 3 months after the treatment.

The rationale for utilizing tezepelumab in the 2 patients described here was based on the apparently greater efficacy of tezepelumab in treating type 2 asthma and the possibility that type 2 inflammatory disease is associated with CRSwNP. Tezepelumab suppresses the upstream factors that cause type 2 inflammation. It extensively inhibits type 2 cytokines, suggesting the effectiveness of tezepelumab in treating CRSwNP. Furthermore, the CASCADE study reported that tezepelumab reduced type 2 airway inflammation.[11] A subanalysis of the phase 3 NAVIGATOR study revealed that tezepelumab reduced SNOT-22 scores in patients with NPs.[10]

To the best of our knowledge, there are 2 other reports of CRSwNP treated with tezepelumab, with both cases occurring in patients who also had severe asthma.[12,13] The first case is that of a 74-year-old woman with a peripheral eosinophil count of 1220/μL, FENO level of 33 ppb, and IgE level of 179 U/L.[12] The second case is that of a 74-year-old woman with a peripheral eosinophil count of 1500/μL, FENO level of 42 ppb, and IgE level of 2595 U/L.[13] Tezepelumab improved upper and lower airway type 2 inflammation. Tezepelumab affects upper and lower airway mucosa. The CASCADE study revealed that tezepelumab reduced airway eosinophil counts in bronchoscopic biopsy samples.[11] Further support for the improvement of upper airway type 2 inflammation with tezepelumab is provided by a report that this biologic reduced middle ear mucosal eosinophil count in a patient treated for secretory otitis media in association with eosinophilic chronic rhinosinusitis and asthma.[12] Further studies are warranted to investigate the general and specific roles of tezepelumab in treating CRSwNP first as a treatment for asthma irrespective of whether CRSwNP is proved.

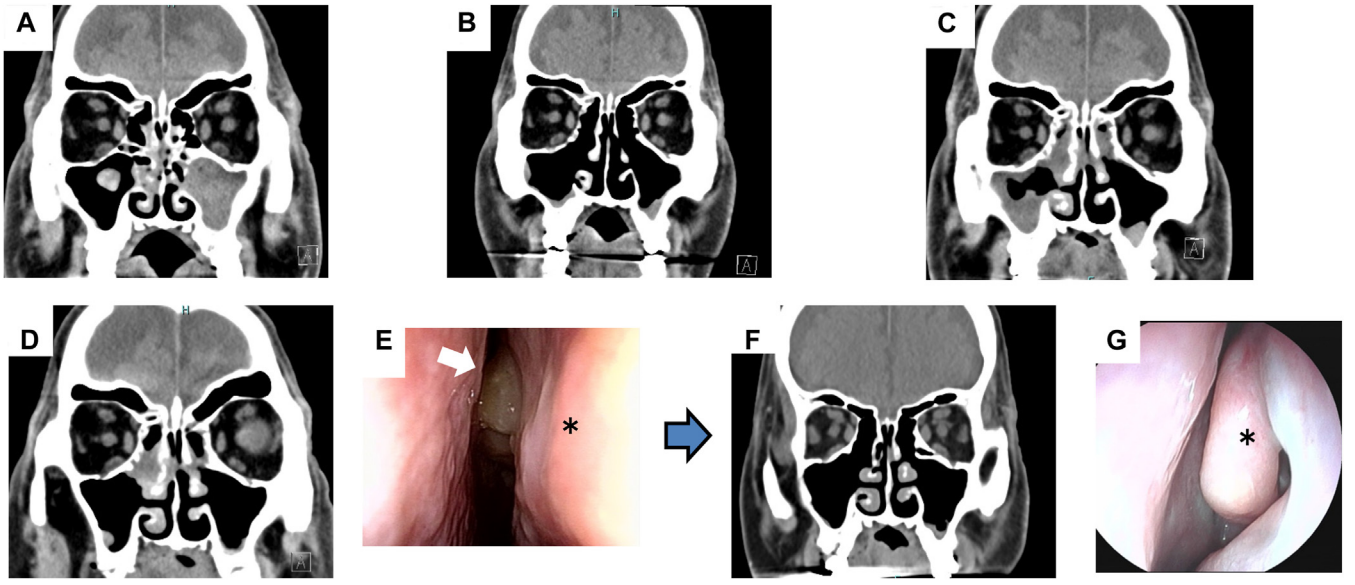

FIG 2. CT imaging and flexible rhinoscopy photographs of case patient 2. **A,** Paranasal sinus CT image before ESS (March 2017). **B,** Paranasal sinus CT image after 5 months of ESS (September 2017). **C,** Paranasal sinus CT image during recurrence (May 2020). **D,** Paranasal sinus CT image before tezepelumab treatment (July 2023). **E,** Nasal findings (*left*) obtained via flexible rhinoscopy before tezepelumab treatment (July 2023). **F,** Paranasal sinus CT image after 3 months of tezepelumab treatment (October 2023). **G,** Nasal findings (*left*) obtained via flexible rhinoscopy after 5 months of tezepelumab treatment (December 2023). White arrow indicates nasal polyp, and asterisk indicates middle nasal turbinate.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The author declares no relevant conflicts of interest.

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Clinical implications: Tezepelumab was effective in treating asthma complicated with CRSwNP recurrence after ESS and reduced the need for corticosteroids.

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