Case report

Tezepelumab for asthma with current or previous smoking habit: Case series

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Tezepelumab effectively treated severe asthma in a current smoker and a former smoker, suggesting that thymic stromal lymphopoietin is involved in the pathogenesis of severe asthma in these patients. Tezepelumab may additionally be used for severe asthma in current and former smokers. (J Allergy Clin Immunol Global 2025;4:100420.)

Key words: *Asthma, smoker, TSLP, tezepelumab*

Tezepelumab, a human IgG2 mAb, blocks thymic stromal lymphopoietin (TSLP).[1] In the NAVIGATOR study, tezepelumab treatment improved exacerbation rates, lung function, and asthma symptoms in patients with severe asthma.[2] TSLP, an alarmin released by airway epithelial cells in response to viruses and smoking, plays a critical role in the activation of inflammatory cells, including mast cells, eosinophils, and group 2 innate lymphoid cells.[3] The clinical efficacy of tezepelumab in patients with severe asthma who are current or former smokers remains unclear. We present the cases of 2 patients with severe asthma, one a current smoker and the other a former smoker, whose symptoms were improved following treatment with tezepelumab, suggesting that TSLP is involved in the pathogenesis of severe asthma in these patients.

Abbreviations used
ACO: Asthma–chronic obstructive pulmonary disease overlap
ACT: Asthma Control Test
CAT: COPD Assessment Test
COPD: Chronic obstructive pulmonary disease
CT: Computed tomography
FENO: Fractional exhaled nitric oxide
FVC: Forced vital capacity
LAMA: Long-acting muscarinic antagonist
TSLP: Thymic stromal lymphopoietin

CASE 1

A 59-year-old male with a history of type 2 diabetes and hypertension was an ex-smoker (4.5 packs per day from age 20 years to age 42 years). He experienced nocturnal cough and dyspnea on exertion and was diagnosed with asthma 7 years before admission. The patient was administered desloratadine, an antihistamine; however, he was not receiving any regular medical treatment. He was referred to our hospital because of poorly controlled severe asthma. Chest radiography and computed tomography (CT) revealed mild bronchial wall thickening without low-attenuation areas and was thus not indicative of chronic obstructive pulmonary disease (COPD) (Fig 1, *A-D*). Eosinophilic chronic rhinosinusitis was not detected. Wheezing was confirmed in both lung fields. The patient received a high-dose inhaled corticosteroid/long-acting β_2-agonist/long-acting β_2-agonist (LAMA) (fluticasone 200 μg/umeclidinium 62.5 μg/vilanterol 25 μg) but was at risk of asthma exacerbation, requiring systemic corticosteroids 3 times per year. His Asthma Control Test (ACT) score was 5, his total serum IgE level was 518 IU/mL (range 0-148 IU/mL), and his peripheral blood eosinophil count was 236/μL. His fractional exhaled nitric oxide (FENO) level was elevated at 28 ppb. Testing of his pulmonary function (% predicted) showed an FEV_1 value of 3010 mL (87.7%) and a ratio of FEV_1 to forced vital capacity (FVC) of .838 (Table I). Subsequently, the patient was administered tezepelumab (210 mg every 4 weeks) subcutaneously in March 2023. Four weeks later, his peripheral eosinophil count and IgE level decreased to 86/μL and 284 IU/mL, respectively, and his FENO level decreased to 12 ppb. His airway symptoms, including dyspnea on exertion, improved substantially. The patient's ACT score improved to 18, and his FEV_1 ($\%FEV_1$) value increased to 3270 mL (95.3%) (Table I). After 8 weeks of tezepelumab treatment, his ACT score rose to 25. He did not experience any asthma exacerbations. After being administered tezepelumab 4 times administrations, patient opted to discontinue treatment because of stabilization of his symptoms. However, 4 months later, in October 2023, he was hospitalized for asthma exacerbation. After discharge, tezepelumab was resumed, and his asthma control improved.

CASE 2

A 73-year-old female patient with a history of hypertension was a smoker (0.75 pack per day from age 20 years to age 73 years). She was diagnosed with COPD and treated with a LAMA (5 μg of tiotropium). Her condition deteriorated with increasing dyspnea, productive cough, and nocturnal symptoms. In April 2023, she was referred to our hospital because of dyspnea and quit smoking during hospitalization. Chest radiography and CT revealed bronchial wall thickening without low-attenuation areas

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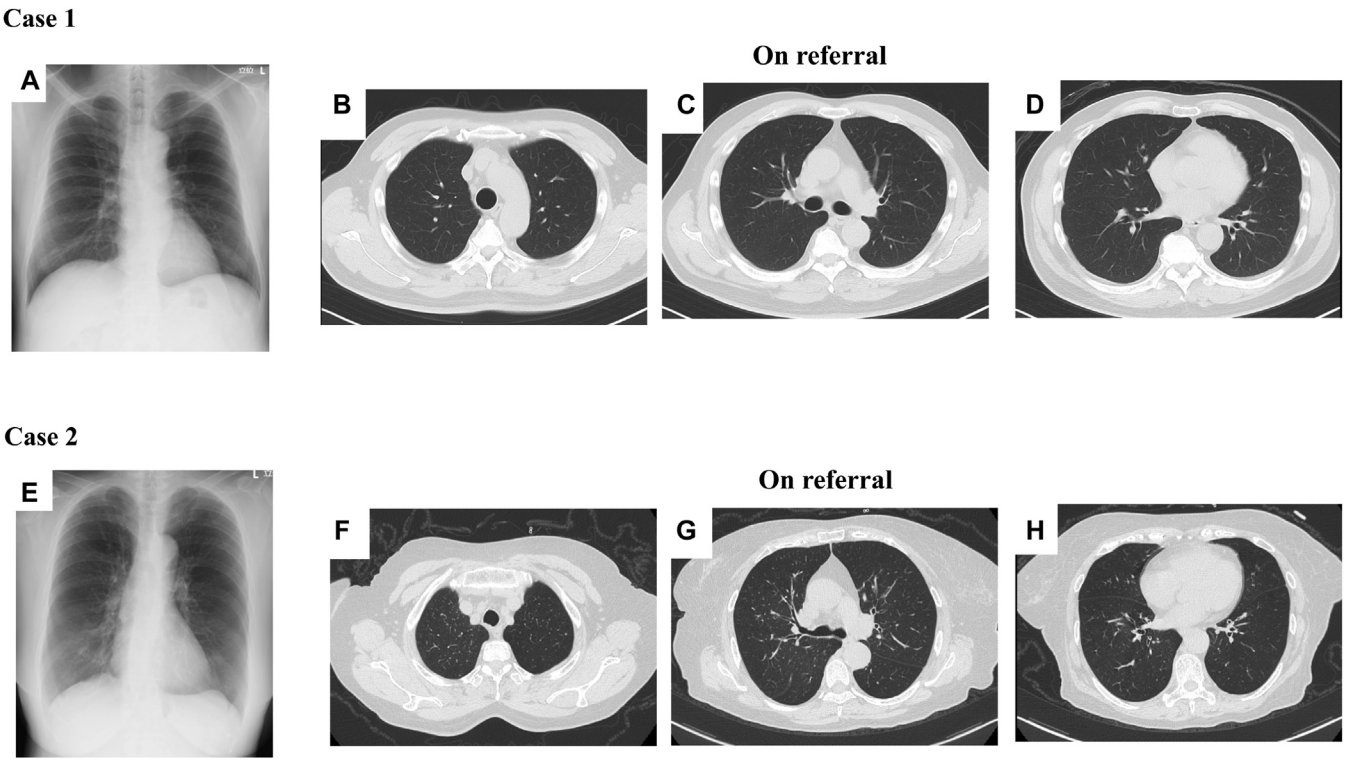

FIG 1. Patient 1 underwent chest radiography (**A**) and chest computed tomography (**B-D**) before tezepelumab administration. Mild bronchial wall thickening was observed. No low-attenuation area characteristic of COPD was observed. Patient 2 underwent chest radiography (**E**) and chest computed tomography (**F-H**) before tezepelumab administration. Bronchial wall thickening was observed. No low-attenuation area was observed.

TABLE I. Efects of tezepelumab treatment in case patient 1 at 4 weeks after tezepleumab administration

Indicator	Before tezepelumab administration	4 wk after tezepelumab initiation
VC (mL)	3720	4120
%VC (%)	88.3	97.8
FEV_1 (mL)	3010	3270
%FEV_1 (%)	87.7	95.3
FEV_1/FVC ratio (%)	.838	.834
FENO level (ppb)	28	12
Peripheral eosinophil level (count/μL)	236	86
IgE level (U/L)	518	284
ACT score	5	18

VC, Vital capacity.

(Fig 1, *E-H*). Eosinophilic chronic rhinosinusitis was not detected. Wheezing was confirmed in both lung fields. Therefore, the patient was diagnosed with asthma-COPD overlap (ACO). She received systemic corticosteroids intravenously and a high-dose inhaled corticosteroid/long-acting β_2-agonist/LAMA (fluticasone 200 μg/umeclidinium 62.5 μg/vilanterol 25 μg) and was discharged after 8 days. Despite discharge, her ACT score remained at 18, and her COPD Assessment Test score was 35. Her total serum IgE level was 204 IU/mL (range 0-148 IU/mL). Testing for inflammatory markers indicated peripheral blood eosinophilia (213/μL). Her FENO level was 12. Pulmonary function (% predicted) testing showed an FEV_1 value of 1140 mL (67.8%) and FEV_1/FVC ratio of .467 (Table II). In August 2023, the patient was subcutaneously administered tezepelumab (210 mg every 4 weeks). Eight weeks later, her peripheral eosinophil count decreased to 130 /μL and her IgE level decreased to 169 IU/mL. Her FENO level decreased to 11 ppb. Her airway symptoms improved greatly, and her ACT and COPD Assessment Test scores improved to 25 and 8, respectively. Her FEV_1 value increased to 1250 mL (74.8%) (Table II). The patient has not experienced any asthma exacerbations for 20 months and enjoys family vacations with her grandchild.

DISCUSSION

We report 2 cases of severe asthma—one in a current smoker and another in a former smoker—who were successfully treated with tezepelumab. TSLP induces type 2 cytokines, including IL-5, IL-4, and IL-13.[1] TSLP activity is higher in current and former smokers than in never smokers.[4] In the NAVIGATOR study, tezepelumab reduced exacerbations and improved lung function and asthma control.[2] However, the efficacy of tezepelumab in current or former smokers with severe asthma remains unclear.

In case 1, the patient, a former smoker, was at risk of asthma exacerbation and required treatment with systemic corticosteroids 2 times a year. Chest CT showed no low-attenuation areas and an FEV_1/FVC ratio of .838, which was not indicative of COPD. Therefore, the patient had severe asthma that was not accompanied by COPD. In case 2, the patient was a current

TABLE II. Efects of tezepelumab treatment in case patient 2 at 8 weeks after tezepleumab administration

Indicator	Before tezepelumab administration	8 wk after tezepelumab initiation
VC (mL)	2480	2630
%VC (%)	107.8	114.8
FEV_1 (mL)	1140	1250
%FEV_1 (%)	67.8	74.8
FEV_1/FVC ratio (%)	.467	.512
FENO level (ppb)	12	11
Peripheral eosinophil level (count/μL)	213	130
IgE level (U/L)	204	169
ACT score	18	25
CAT score	35	8

CAT, COPD assessment test; *VC*, vital capacity.

smoker diagnosed with COPD at a clinic. She was hospitalized because of an asthma attack and quit smoking during hospitalization. Wheezing was observed on admission, and nocturnal cough was also found. Although chest CT did not reveal any low-attenuation areas, the patient's FEV_1/FVC ratio was .467, thus indicating obstructive dysfunction. Therefore, the patient was diagnosed with ACO.

Both patients had elevated peripheral eosinophil and IgE levels, and the patient in case 1 also had an elevated FENO level, indicating type 2 inflammation. After tezepelumab treatment, his peripheral eosinophil, IgE, and FENO levels (case 1 only) decreased, suggesting a blockade of type 2 upstream biomarkers. Tezepelumab also improved lung function and ACT scores, reflecting better asthma control. Chronic airway diseases, including asthma and COPD, are prevalent and complex conditions that frequently coexist in the same patient, which is known as ACO.[5] Smoking-induced TSLP is linked with type 2 inflammation, and blocking TSLP with tezepelumab may offer a novel therapeutic approach for smokers and ex-smokers. In the NAVIGATOR study, a randomized, placebo-controlled study, subgroup analysis data revealed that tezepelumab reduced asthma exacerbations compared with placebo: by 48% and 58% in former smokers and never-smokers, respectively.[6] Current and former smokers with a smoking history of 10 pack years history or less are excluded from registrational trials of all asthma biologics, as regulators aim to exclude any patient who may have COPD. The PASSAGE study is an ongoing postmarketing study that aims to evaluate the efficacy of tezepelumab in patients with severe asthma who have a substantial smoking history, including current smokers. Through this study, we can further emphasize the relevance of tezepelumab for diverse patient populations and demonstrate progress in understanding its impact on patients who were excluded from earlier trials.[7] Limited data exist on the effectiveness of biologics (mepolizumab, benralizumab, dupilumab, omalizumab, or tezepelumab) in patients with severe asthma who have a substantial smoking history, including current smokers. In a systematic review and bayesian network meta-analyses, tezepelumab and dupilumab were associated with greater improvements in exacerbation rates and lung function than benralizumab or mepolizumab.[8]

The cases presened here suggest that tezepelumab is effective in treating severe asthma in this population; however, further studies are needed to assess its efficacy and safety for uncontrolled severe asthma in current and former smokers.

Data sharing statement: Data sharing is not applicable to this article, as no data sets were generated or analyzed during the current study.

Consent statement: Appropriate written informed consent was obtained for publication of this case report and the accompanying images.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

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