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CASE REPORT

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Combination effect of Mepolizumab and Endobronchial Watanabe Spigot (EWS) in drug-induced eosinophilic pneumonia complicated by refractory pneumothorax

Nana Ayame[1,2] | Yuki Tanabe[1,2] | Mai Motojima[1,2] | Ryosuke Tachi[3,4] | Fumihiko Makino[1,2] | Shiaki Oh[3,4] | Shinichi Sasaki[1,2] | Kazuhisa Takahashi[1]

[1]Department of Respiratory Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan

[2]Department of Respiratory Medicine, Juntendo University Urayasu Hospital, Chiba, Japan

[3]Department of General Thoracic Surgery, Juntendo University Graduate School of Medicine, Tokyo, Japan

[4]Department of General Thoracic Surgery, Juntendo University Urayasu Hospital, Chiba, Japan

Correspondence
Yuki Tanabe, Department of Respiratory Medicine, Juntendo University Graduate School of Medicine, 3-1-3 Hongo, Bunkyo-ku, Tokyo, 113-8431, Japan.
Email: yutanabe@juntendo.ac.jp

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Abstract

Few reports have described the treatment of eosinophilic pneumonia (EP) complicated by refractory pneumothorax. A 62-year-old man with a medical history of ulcerative colitis who was undergoing maintenance treatment presented with fever, cough, and diffuse bilateral consolidation on chest radiography. Laboratory findings showed peripheral eosinophilia, and he was hospitalized with a diagnosis of drug-induced EP and started on corticosteroid therapy. During the course, he developed refractory pneumothorax, and it was difficult to control the air leakage. As it was necessary to control the eosinophilic inflammation and air leakage, mepolizumab, a humanized anti-interleukin-5 monoclonal antibody, and an endobronchial Watanabe spigot (EWS), were introduced. After EWS insertion, the leakage of the refractory pneumothorax disappeared. The patient continued to have no recurrence of EP or pneumothorax after the removal of the EWS. The combination of mepolizumab and an EWS may be effective in cases of EP complicated by refractory pneumothorax.

KEYWORDS
endobronchial Watanabe spigot, eosinophilic pneumonia, EWS, mepolizumab, refractory pneumothorax

INTRODUCTION

Chronic eosinophilic pneumonia (CEP) is an idiopathic inflammatory lung disease characterized by eosinophilic stromal and alveolar infiltrates. It responds well to corticosteroids. Most patients require long-term corticosteroid treatment, which has side effects. Mepolizumab is a humanized anti-interleukin (IL)-5 monoclonal antibody that has been approved for the treatment of severe eosinophilic asthma and other eosinophilic diseases. It has been used off-label for CEP, and its efficacy has been reported in some cases. It induces disease remission and avoids relapse upon steroid discontinuation, thus saving systemic corticosteroids.[1]

An endobronchial Watanabe spigot (EWS) is a silicone device used to manage refractory pneumothorax that is difficult to treat with a chest tube alone. It is inserted into the bronchus at the site of a bronchopulmonary fistula to stop or reduce air leakage.[2]

Herein, we present a case of refractory pneumothorax complicated by eosinophilic pneumonia that was successfully treated with mepolizumab in combination with an EWS.

CASE REPORT

A 62-year-old man with a smoking history of approximately 40 pack-years was diagnosed with ulcerative colitis 8 months prior to admission to the hospital. He also had a history of rhinitis and mild bronchial asthma with grass pollen allergy. The patient was administered mesalazine and prednisolone sodium succinate (PSL). One month prior to admission, he was started on golimumab (GLM), and after his gastrointestinal symptoms stabilized, PSL was tapered to 2.5 mg just

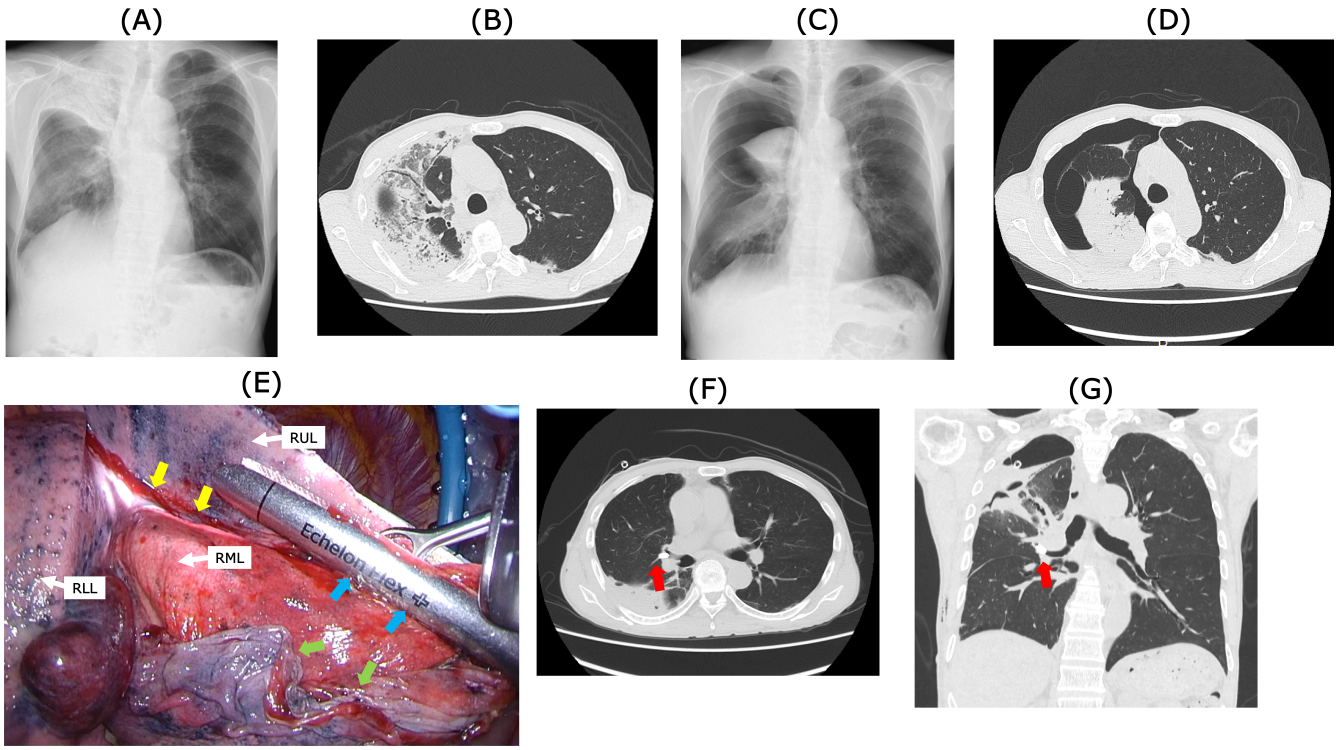

FIGURE 1 (A, B) Chest x-ray and chest computed tomography on the day of admission showed consolidations in in the right upper field on the day of admission. (C, D) Chest x-ray and chest computed tomography on day 11 showed right pneumothorax and consolidations. (E) Intraoperative view: A bulla in the middle lobe pulling and peeling the visceral pleura (green arrows) with inflammatory adhesions (yellow arrows), which were considered the causes of the refractory pneumothorax, leading to a right middle lobe wedge resection. Blue arrows indicate major air leakage sites. RUL, right upper lobe; RML, right middle lobe; RLL, right middle lobe. (F, G) Chest computed tomography on day 39 obtained after endobronchial Watanabe spigot (EWS) implantation in the right B4 (arrows).

prior to admission. About a month after tapering the PSL dose, on the day of his regular outpatient visit to the gastroenterologist, he had fever, high eosinophilia (7000/mm^3, 47%), and infiltrates in both lungs, and was diagnosed with eosinophilic pneumonia (Figure 1A,B). Bronchoalveolar lavage fluid from the right upper lobe (B3) revealed a remarkable increase in the eosinophil count, to 91%. Considering drug-induced eosinophilic pneumonia caused by mesalazine or GLM, they were discontinued, and the PSL dose was increased to 50 mg (1 mg/kg/day). The patient developed a right pneumothorax on day 11 of admission (Figure 1C,D). Because there was very high air leakage with chest tube drainage alone, the patient was diagnosed with refractory pneumothorax and surgery was performed on day 18. A bulla in the middle lobe was found to be pulling and peeling the visceral pleura, with inflammatory adhesions present between the upper and middle lobes. Multiple air leakages were observed in the lung parenchyma in the area surrounded by the bulla, and in the inflammatory adhesions between the upper and middle lobes. These were considered the causes of the refractory pneumothorax, leading to a right middle lobe wedge resection (Figure 1E). Immediately after surgery, a significant reduction in air leakage was observed. However, presumably due to the effects of corticosteroid therapy and pleural thickening, the integrity of the staple line was compromised, leading to a recurrence of air leakage, albeit less severe than the initial massive air leakage.

Two hypotheses were made for this phenomenon. First, the increased dosage of corticosteroids administered for eosinophilic pneumonia may have contributed to tissue fragility, resulting in delayed wound healing and compromised integrity of the staple line. This necessitated a reduction in steroid use, leading to the consideration of introducing mepolizumab, a humanized anti-IL-5 monoclonal antibody, to control eosinophilic inflammation while allowing for steroid reduction. Second, the persistent air leak and recurrent pneumothorax, despite initial surgical intervention, indicated significant lung tissue fragility. Given this fragility, there was concern that further surgical intervention could lead to a recurrence of leakage from the suture site. Consequently, alternative treatment with an endobronchial Watanabe spigot (EWS) was considered as a less invasive approach to manage the persistent air leak, avoiding the risks associated with subjecting the fragile lung tissue to additional surgical trauma. Hence, mepolizumab was introduced on day 29 to control eosinophilic inflammation and an EWS was inserted on day 39 to embolize the bronchial segments that caused air leakage in this refractory pneumothorax (Figure 1F,G). To determine the optimal site for EWS insertion, air leakage was quantitatively assessed using a motorized low-pressure suction device (Thopaz+™). The identification process involved selective occlusion of suspected bronchial segments using a Fogarty catheter. This systematic evaluation led to the insertion of a single EWS into the right B4 bronchus, which resulted in a significant reduction in air leakage. Thus, the

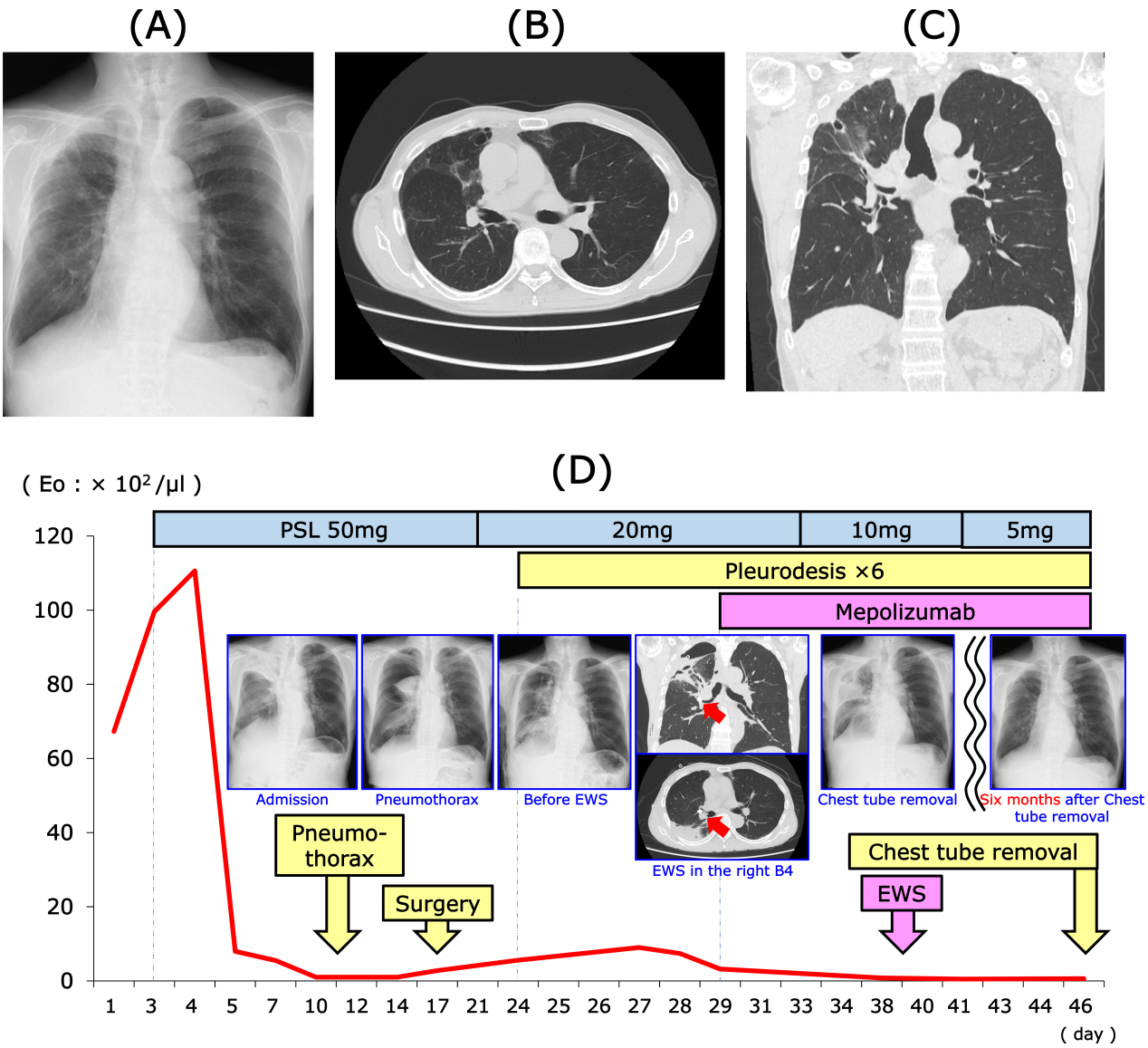

FIGURE 2 (A–C) Chest x-ray and Chest computed tomography 6 months after chest tube removal showed that the right upper lobe was almost fully re-expanded. (D) The summary of the patient's course.

bronchial segment was identified as the primary source of air leakage. Air leakage decreased rapidly after the insertion of the EWS and disappeared on day 41. The chest tube was removed on day 43 and the patient was discharged on day 45. The EWS was removed 1 month after discharge, as the patient was stable with no recurrence of pneumothorax. Finally, the right upper lobe, which had collapsed due to prolonged air leakage from the refractory pneumothorax, also re-expanded almost fully 6 months after discharge (Figure 2A–C). His clinical course is illustrated in Figure 2D.

DISCUSSION

Herein, we report a case of refractory pneumothorax complicated by drug-induced eosinophilic pneumonia that was treated with mepolizumab and an EWS.

Mepolizumab, a humanized anti-IL-5 monoclonal antibody, has been approved for the treatment of eosinophilic diseases, such as severe eosinophilic asthma and eosinophilic granulomatosis with polyangiitis.[3,4] CEP responds well to corticosteroids; however, most patients require long-term treatment due to corticosteroid-derived side effects. Mepolizumab may be used off-label for CEP to avoid recurrent eosinophilic pneumonia and steroid side effects. Its efficacy has been reported, inducing disease remission and avoiding relapse after steroid discontinuation.1 This case was most likely drug-induced eosinophilic pneumonia related to the treatment of ulcerative colitis, which is generally relieved by discontinuation of the suspected drug and corticosteroid administration.[5]

The limited efficacy of surgery alone in resolving pneumothorax is likely due to several factors. We hypothesized two reasons for the refractory pneumothorax:

1. Corticosteroid-induced delayed wound healing: The increased dosage of corticosteroids administered for eosinophilic pneumonia may have contributed to delayed wound healing and compromised integrity of the staple line. This necessitated a reduction in steroid use, leading to the consideration of introducing mepolizumab to control eosinophilic inflammation while allowing for steroid reduction.
2. Significant lung tissue fragility: The persistent air leak and recurrent pneumothorax, despite initial surgical intervention, indicated significant lung tissue fragility. Given this fragility, there was concern that further surgical intervention could lead to a recurrence of leakage from the suture site. Consequently, alternative treatment with an endobronchial Watanabe spigot (EWS) was considered to manage the persistent air leak.

These hypotheses guided our treatment approach, combining mepolizumab for eosinophilic inflammation control and EWS for managing the persistent air leak, thus addressing both the underlying inflammation and the mechanical aspects of the refractory pneumothorax.

EWS is used for the treatment of refractory pneumothorax that is difficult to treat with a chest tube alone. It is placed in the bronchus with a bronchopulmonary fistula to stop or reduce air leakage.[2]

In this case, air leakage decreased to a certain extent postoperatively and completely disappeared after EWS insertion. To the best of our knowledge, there have been no reports of eosinophilic pneumonia complicated by refractory pneumothorax cured with mepolizumab and EWS insertion. When eosinophilic pneumonia is complicated by refractory pneumothorax, the combination of mepolizumab and EWS may be an effective treatment to suppress eosinophilic inflammation in the background lung, while avoiding steroid complications and controlling prolonged air leakage.

AUTHOR CONTRIBUTIONS

Conceptualization: Nana Ayame; Yuki Tanabe. *data curation*: Nana Ayame; Yuki Tanabe; Mai Motojima. *Investigation*: Nana Ayame; Yuki Tanabe; Mai Motojima; Ryosuke Tachi; Fumihiko Makino; Shiaki Oh. *Supervision*: Shinichi Sasaki; Kazuhisa Takahashi. *Visualization*: Nana Ayame; Yuki Tanabe. *Writing – original draft*: Nana Ayame; Yuki Tanabe. *Writing – review and editing*: Yuki Tanabe; Shinichi Sasaki; Kazuhisa Takahashi.

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CONFLICT OF INTEREST STATEMENT

Kazuhisa Takahashi is an Editorial Board member of Respirology Case Reports and a co-author of this article. He was excluded from all editorial decision-making related to the acceptance of this article for publication. The other authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

ORCID

Yuki Tanabe https://orcid.org/0000-0003-1463-2749

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