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CASE REPORT

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A case of allergic bronchopulmonary mycosis: 3D-CT Findings led to successful multidisciplinary treatment with dupilumab and cryoprobe

Masamitsu Hamakawa[1] | **Takafumi Yamano**[1] | **Machiko Arita**[1] | **Takashi Niwa**[2] | **Tadashi Ishida**[1]

[1]Department of Respiratory Medicine, Kurashiki Central Hospital, Okayama, Japan

[2]Department of Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, Kanagawa, Japan

Correspondence
Masamitsu Hamakawa, Department of Respiratory Medicine, Kurashiki Central Hospital, 1-1-1 Miwa, Kurashiki, Okayama 710-8602, Japan.
Email: mh16976@kchnet.or.jp

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Abstract

The present case involved a 78-year-old woman with repeated recurrences of allergic bronchopulmonary mycosis (ABPM) who presented to our outpatient clinic with a chief complaint of dyspnoea with respiratory failure. Computed tomography (CT) of the chest showed atelectasis of the lower lobes due to mucus plugs. Blood and biochemical tests showed a high peripheral blood eosinophil count (1330/μL) and elevated immunoglobulin E (15,041 IU/mL; normal, < 361 IU/mL). Recurrent ABPM was diagnosed. The patient also showed chronic lower respiratory tract infection associated with *Mycobacterium avium* complex and *Pseudomonas aeruginosa*. First, we removed the mucus plug with a cryoprobe to avoid administering corticosteroids. However, subsequent 3-dimensional CT showed residual mucus plugs, so we administered dupilumab as an additional treatment. After initiating dupilumab, mucus plugs disappeared and respiratory failure resolved. We were able to implement multidisciplinary treatment that did not rely on corticosteroids.

KEYWORDS
3D-CT, ABPM, cryoprobe, dupilumab, mucus plug

INTRODUCTION

Several case reports in recent years have described successful treatment of allergic bronchopulmonary mycosis (ABPM) with dupilumab,[1,2] but none have reported multidisciplinary treatment with dupilumab and a cryoprobe after visualizing mucus plugs obstructing the entire bronchus using 3-dimensional (3D) computed tomography (CT).

CASE REPORT

A 78-year-old woman visited the outpatient clinic complaining of dyspnoea with respiratory failure. ABPM caused by *Aspergillus fumigatus* had been diagnosed 10 years earlier. That diagnosis of ABPM had been made based on the diagnostic criteria proposed by the ISHAM Working Group, and all items in those diagnostic criteria had been met.[3] In addition, she also had a chronic lower respiratory tract infection associated with *Mycobacterium avium* complex and *Pseudomonas aeruginosa*. She had been treated with prednisolone (PSL), itraconazole and erythromycin. Although she had experienced repeated relapses after dose reductions and discontinuations of PSL, she had been treated with PSL at 5 mg/day, itraconazole at 100 mg/day and erythromycin at 400 mg/day with no relapse in the last 4 years. We had therefore been tapering the PSL dose by 1 mg/day every 6 months. At the time of this ABPM recurrence, the PSL dose had been reduced to 3 mg/day. As itraconazole could increase blood levels due to the inhibitory effects of erythromycin on cytochrome P450 3A4, the patient was administered itraconazole at 100 mg/day. Chest CT showed atelectasis of the lower lobe of the left lung due to mucus plugs, bronchiectasis, bronchial wall thickening, and central

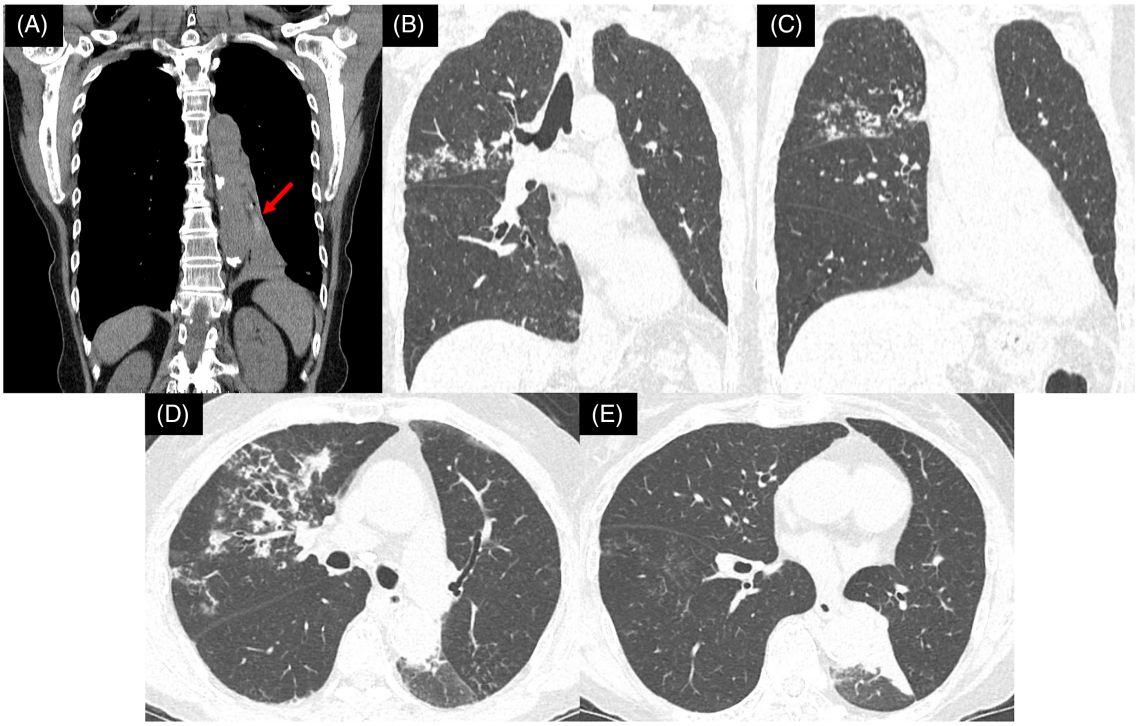

FIGURE 1 Chest computed tomography (CT) findings during allergic bronchopulmonary mycosis exacerbation. (A) Chest CT shows atelectasis in the lower lobe of the left lung and high-attenuation mucus (arrow). (B–E) CT of the chest shows bronchiectasis, bronchial wall thickening, and central lobar shadow, mainly in the upper lobe of the right lung.

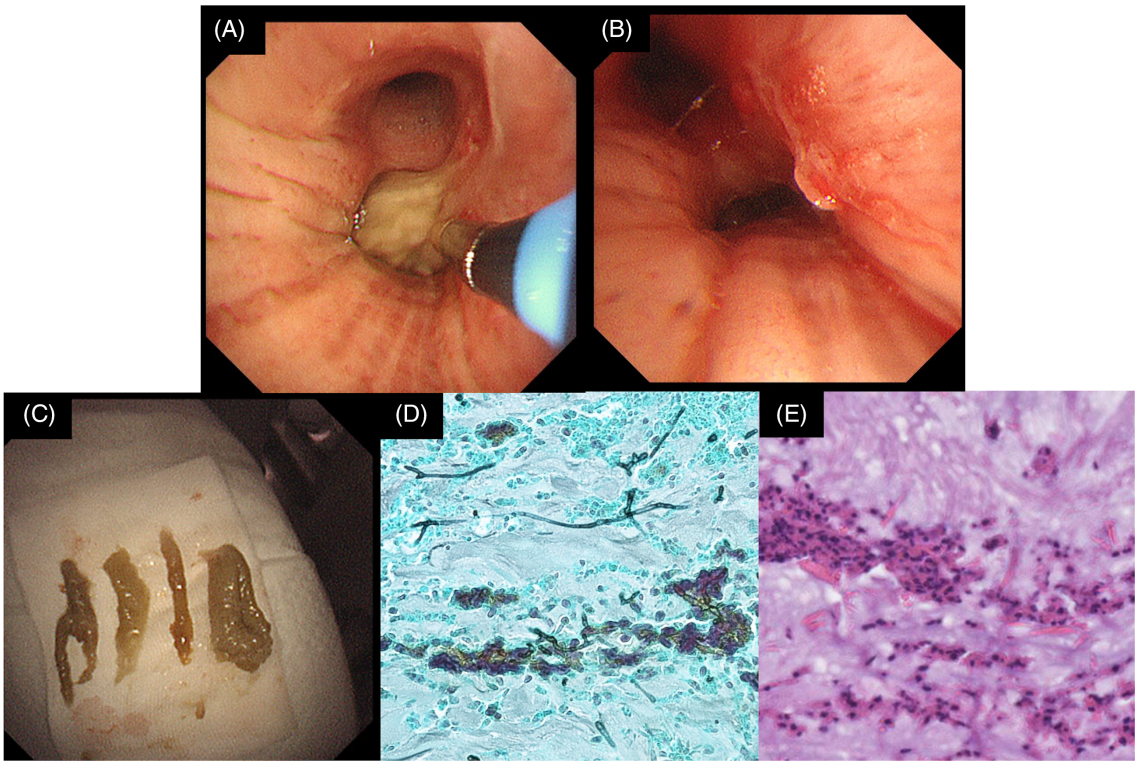

FIGURE 2 Process of mucus plug removal by cryoprobe and histopathological findings. (A) Bronchoscopy reveals a mucus plug in the left basilar trunk. The plug was very viscous and difficult to remove by bronchoscopic aspiration. The mucus plug was frozen using a cryoprobe and removed. (B) Bronchoscopic findings after removal of the mucus plug. All mucus plugs had been removed from the visible area. (C) Mucus plug removed by cryoprobe. (D) Histopathological findings of the mucus plug using Grocott's stain. The specimen shows mycelia. (E) Histopathological findings for mucus plug using haematoxylin and eosin staining. The specimen shows a cluster of eosinophils and Charcot–Leyden crystals.

lobar shadows mainly in the upper lobe of the right lung (Figure 1). Bronchoscopy revealed a mucus plug in the left basilar trunk (Figure 2A). Blood and biochemical tests showed a high peripheral blood eosinophil count (1330/μL) and an elevated immunoglobulin (Ig)E level (15,041 IU/mL; normal, < 361 IU/mL). We diagnosed recurrent ABPM, but refrained from increasing the PSL dose due to concerns about the risk of exacerbating the chronic lower respiratory tract infection. We initially froze the mucus plug using a cryoprobe connected to ERBECRYO® 2 (Erbe, Tübingen, Germany), allowing successful removal (Figure 2A–C). Histopathological examination of mucus plugs using Grocott's stain showed mycelia (Figure 2D), and culture testing detected *Aspergillus terreus*. Numerous eosinophils and Charcot–Leyden crystals were evident in the mucus plug (Figure 2E). Although atelectasis improved after this procedure, chronic respiratory failure remained and the patient required supplemental oxygen (2 L/min) on exertion. After removal of the mucus plug, 3D-CT using a Ziostation2 medical workstation (Ziosoft Inc., Tokyo, Japan) showed inadequate delineation of the peripheral bronchi from the left basilar trunk branch (Figure 3A-1,A-2,B-1,B-2). This suggested the possibility of small, residual mucus plugs. We then administered dupilumab to the patient subcutaneously at 300 mg every 2 weeks. After dupilumab administration, subjective symptoms gradually improved. After 7 months of treatment with dupilumab, the maintenance dose of PSL was able to be reduced to 1 mg/day. Findings from blood and biochemical tests showed that the peripheral blood eosinophil count had decreased to 335/μL and IgE level had decreased to 6125 IU/mL. Further, 3D-CT showed disappearance of the mucus plug, and peripheral bronchi were visible, unlike before treatment (Figure 3C-1,C-2).

DISCUSSION

Compared to images from horizontal-section chest CT, 3D-CT findings provide a simplified view of the entire bronchus. McIntosh et al. reported that improvements evident on 3D-CT were associated with improvements in mucus plug score and subjective symptoms in a study of benralizumab in poorly controlled asthma, although that was only a small case study.[4] In the present case, 3D-CT was also very useful for evaluating small mucus plugs and determining the effectiveness of treatment.

In the present case, the cryoprobe was used to freeze and remove the mucus plug, followed by administration of dupilumab to avoid the adverse effects of corticosteroids. There are two reasons for combining these two new treatment modalities. The first is the immediate effect of the cryoprobe in removing the mucus plugs. In previously

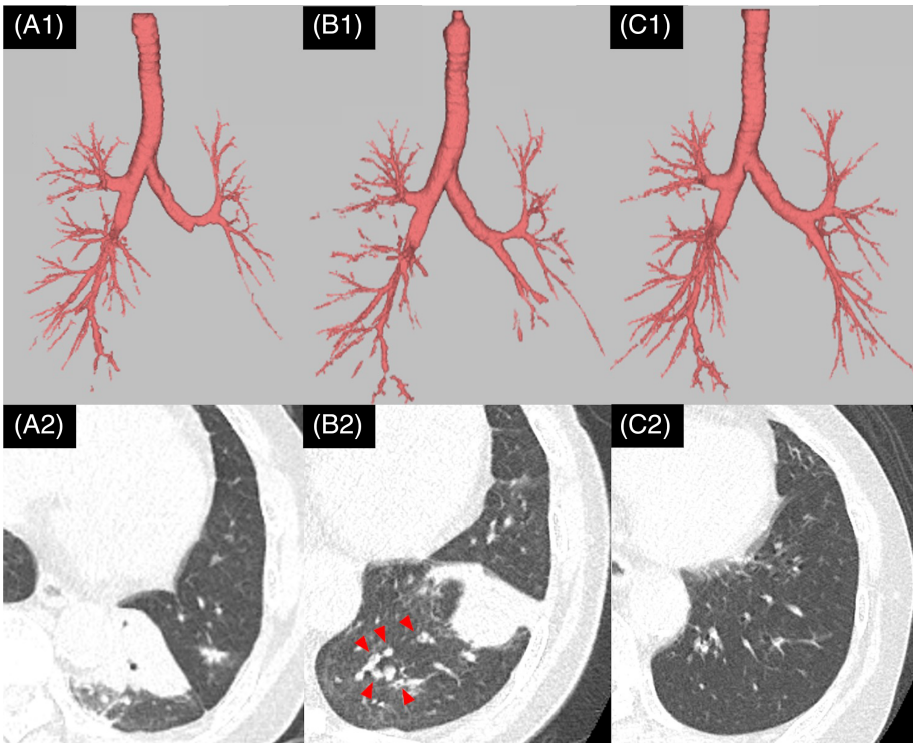

FIGURE 3 Pre- and post-treatment evaluation of the mucus plug on 3D-computed tomography (CT) and horizontal chest CT. (A-1,2) Chest images taken before treatment. The bottom trunk branch cannot be seen in 3D-CT images due to obstruction by the mucus plug. (B-1,2) Chest imaging after removal of the mucus plug using the cryoprobe. Compared to before treatment, 3D-CT shows the left basal trunk branch, but the peripheral bronchus is not fully visible. Horizontal-section chest CT shows a small mucus plug (triangle). (C-1,2) Chest imaging after 7 months of treatment with dupilumab. On 3D-CT, peripheral bronchi can be seen with disappearance of the mucus plug compared to before the start of treatment. Horizontal-section CT of the chest also shows no small mucus plugs.

reported cases of ABPM that responded to dupilumab, the mucus plugs were relatively small or located peripherally.[1,2] When a relatively large mucus plug located centrally results in atelectasis, as in the present case, treatment with dupilumab alone may take longer to improve clinical symptoms. The second reason was the need to focus on the mechanisms of mucus plug formation in ABPM and the fact that ABPM is caused by type I and type III hypersensitivity reactions to filamentous fungi. In the present case, numerous eosinophils and Charcot–Leyden crystals were evident in the mucus plug, strongly suggesting the involvement of eosinophilic extracellular trap cell death (Figure 2E).[5] The mechanisms underlying the success of dupilumab in this case likely involved the drug suppressing eosinophil migration into the lungs by inhibiting interleukin 4 and interleukin 13, suppressing the mucus plug formation in which eosinophils are strongly involved. Administration of dupilumab also suppressed the activity of helper T cells, which may have inhibited differentiation of B cells into plasma cells, thereby preventing the production of IgE and suppressing type I allergic mechanisms. In this case, the blood IgE level was markedly high at 15,041 IU/mL before treatment, but decreased to 6125 IU/mL after treatment. This was consistent with the good response to dupilumab. Svenningsen et al. reported that dupilumab tended to eliminate mucus plugs and improved the percentage ventilation defect evident on ^{129}Xe magnetic resonance imaging in cases of moderate to severe asthma.[6] On the other hand, few reports have shown the utility of dupilumab for mucus plugs associated with ABPM. However, in the present case, this new treatment combined with cryoprobe with reference to 3D-CT evaluation appeared useful with few adverse events.

AUTHOR CONTRIBUTIONS

MH wrote the manuscript. TY, TN, MA and TI contributed to data collection. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ETHICS STATEMENT

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

ORCID

Masamitsu Hamakawa https://orcid.org/0009-0002-4635-4034

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