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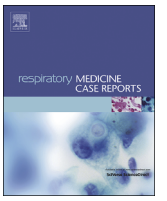

Case Report

Primary lung cancer with pulmonary alveolar proteinosis treated with immune checkpoint inhibitor: A case report

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ABSTRACT

Primary lung cancer with pulmonary alveolar proteinosis (PAP) is a rare condition. We present a case of a patient with primary lung cancer with PAP treated with an immune checkpoint inhibitor (ICI). A 62-year-old man was diagnosed with autoimmune PAP 8 years prior to current admission. Lung adenocarcinoma was found in his right lung, and platinum-based chemotherapy was administered, followed by atezolizumab. He experienced disease progression after atezolizumab treatment, whereas ICI-induced pneumonia or exacerbation of PAP did not occur. This indicates that ICI may be safely used in patients with primary lung cancer with PAP.

1. Introduction

Pulmonary alveolar proteinosis (PAP) is characterized by abnormal accumulation of surfactant in the alveoli and peripheral airways. Autoimmune PAP (APAP) is caused by an abnormally produced anti-granulocyte-macrophage colony-stimulating factor (anti-GM-CSF) antibody. APAP is a rare disease with a prevalence of 1 in 6 million [1]. The prevalence of primary lung cancer with PAP as comorbidity is even lower. The incidence of primary lung cancer with PAP in Japan has been 0.4 % of 212 cases [1]. Currently, information about a safe usage of immune checkpoint inhibitor (ICI), the primary drug used to treat lung cancer, remains unknown for patients with primary lung cancer with PAP. Here, we present a case of a patient with primary lung cancer with PAP treated with atezolizumab.

2. Case presentation

The patient was a 62-year-old man experiencing mild respiratory symptoms. He was diagnosed with APAP in 2010 (Fig. 1A). Bronchoalveolar lavage fluid was characterized as milky-opaque in appearance, and the presence of an anti-GM-CSF antibody confirmed the diagnosis. In July 2018, he presented with dyspnea on exertion and an elevated serum Krebs von den Lungen 6, whereas carcinoembryonic antigen remained unchanged at 15 ng/mL. Computed tomography revealed a new 30 mm nodule in the lower lobe of the right lung and extended ground-glass opacification (Figs. 2A and 1B). We considered this to be indicative of primary lung cancer complicated by PAP progression. To address respiratory symptoms, we conducted a left lung lavage under general anesthesia. After lavage, respiratory symptoms improved, and imaging showed that the shadows indicative of PAP had partially disappeared (Fig. 1C). We then performed a transbronchial lung biopsy on the nodule and diagnosed it as an invasive adenocarcinoma. Metastasis to the pleura, multiple bones, and right adrenal gland was noted consistent with a clinical stage T2aN0M1c, stage IVB (Union for Interna-

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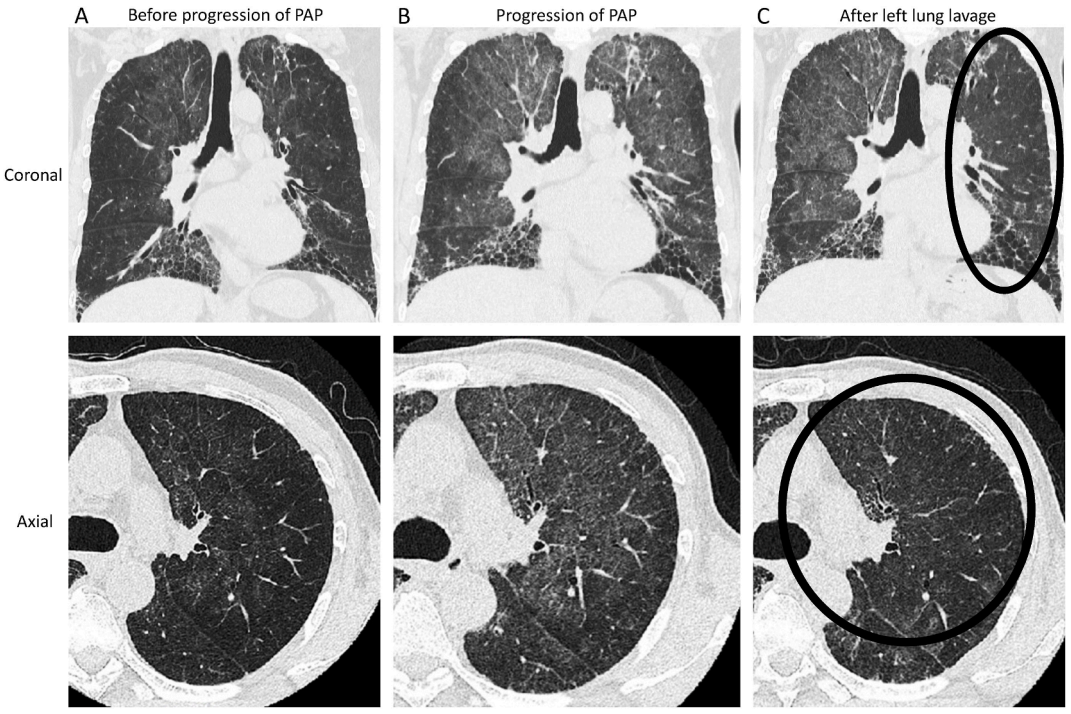

Fig. 1. The computed tomography image showing progress of PAP (A) The image before progression of PAP. (B) PAP progressed in 2018, and (C) left lung lavage performed. The shadow of left lung improved (circle). PAP, pulmonary alveolar proteinosis.

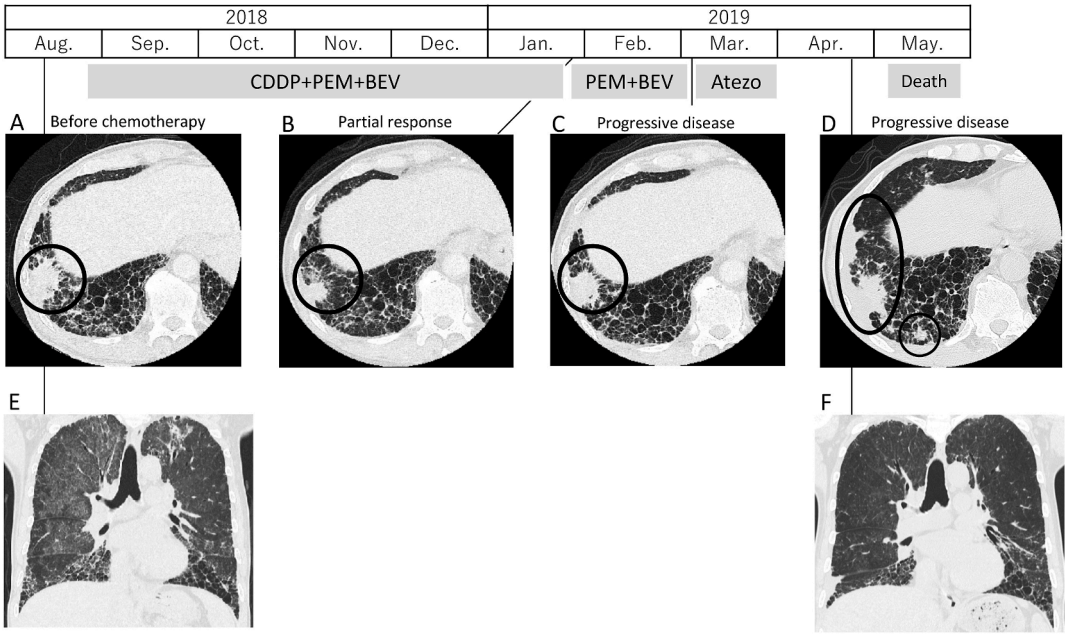

Fig. 2. Patient's clinical course with computed tomography images after chemotherapy (A, B) The tumor (circle) decreased in size after CDDP, PEM, and BEV. (C) The tumor had increased in size since the PEM and BEV. (D) New pulmonary metastasis appeared after atezolizumab treatment, whereas (E, F) pneumonia or PAP progression did not occur. CDDP, cisplatin; PEM, pemetrexed; BEV, bevacizumab; PAP, Pulmonary alveolar proteinosis; Atezo, atezolizumab.

tional Cancer Control. The 8th TNM). The programmed cell death 1 ligand tumor proportion score was 0 %, and no driver mutations, including epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase, and c-ros oncogene 1 genes were noted. We selected cisplatin, pemetrexed, and bevacizumab as first-line chemotherapy in August 2018, to which the patient had a partial positive response (Fig. 2B). Following maintenance with pemetrexed and bevacizumab in January 2019, he experienced only grade 1 constipation. Owing to disease progression (Fig. 2C), atezolizumab was administered in March 2019. After two cycles of atezolizumab, can-

cer progression was noted (Fig. 2D). However, the patient did not experience any adverse events, including pneumonia or PAP exacerbation (Fig. 2E and F). The patient was unable to continue treatment and died of cancer progression.

3. Discussion

To the best of our knowledge, this is the first case to use ICI as a treatment for patients with primary lung cancer with PAP. ICI clinical trials have indicated that careful attention should be given to ICI-induced pneumonia [2–4]. Pre-existing interstitial lung disease (ILD), especially idiopathic pulmonary fibrosis (IPF), is a risk factor for drug-induced pneumonia or Acute exacerbation of ILD [5,6]. Therefore, ICI is usually not used for patients with primary lung cancer with ILD. In this case, we administered ICI, even though PAP is a type of ILD. PAP differs from IPF in both cause and pathology, and the PAP condition was stable after lavage. Consequently, neither ICI-induced pneumonia nor exacerbation of PAP occurred.

There are several reports of other anticancer agents employed to treat primary lung cancer with PAP, such as EGFR-tyrosine kinase inhibitor, cisplatin, pemetrexed, and vinorelbine [7–9]. Among those, only one detailed a patient with kidney cancer with PAP that used ICI as treatment [10]. In this case and the previous studies, PAP was stable before and after treatment, and no drug-induced pneumonia occurred.

This patient with lung cancer with PAP safely used ICI. However, it should be noted that only 2 cycles of atezolizumab were administered, and the period of observation after atezolizumab was short (2 months).

4. Conclusion

This case and the previous reports suggest that ICIs can be safely used as a treatment agent for patients with primary lung cancer with PAP.

Consent for publication

Informed consent was obtained from the patient's family.

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Author contributions

Mika Horie, Kazuhisa Nakashima: Conceptualization, Visualization, Writing - original draft.
Yoshihiro Amano, Yohei Shiratsuki, Kotaro Murakami, Takeshi Isobe: Writing -reviewing & editing.
Yukari Tsubata: Supervision.

Declaration of competing interest

Yukari Tsubata reports receiving an honorarium from AstraZeneca, Daiichi-Sankyo, Chugai Pharma, and Kyowa Kirin and grants from Ono Pharma, and Pfizer outside of submitted work. Takeshi Isobe reports receiving an honorarium from AstraZeneca, Daiichi-Sankyo, and Boehringer lngelheim and grants from Konica Minolta; IQVIA Services Japan, and Insmed. The remaining authors declare no conflict of interest.

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