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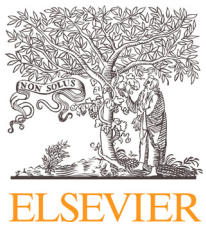

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Case Report

Autoimmune pulmonary alveolar proteinosis presenting as localized multifocal GGOs: A case report ☆

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ABSTRACT

Pulmonary alveolar proteinosis (PAP) is a rare disease, which is characterized by the alveolar accumulation of surfactant. A crazy-paving appearance on chest thin-section computed tomography (TSCT) is a characteristic feature of this disease. We report an unusual case of PAP, which presented as multiple localized ground glass opacites (GGOs) on TSCT in an 80-year-old female. As one of these lesions at the apex of the right lung increased in size, it was suspected to be a pulmonary adenocarcinoma. However, the others became smaller during the follow-up period. Right upper lobectomy was performed, and PAP was histologically diagnosed. In cases exhibiting multiple localized GGOs, PAP should be considered, even if GGOs with a crazy-paving-like appearance are distributed in a lobular rather than diffuse manner.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Introduction

Pulmonary alveolar proteinosis (PAP) is a rare respiratory condition, in which surfactant-derived eosinophilic granular protein-like substances abnormally accumulate in the alveolar space due to alveolar macrophage dysfunction, leading to impaired gas exchange. There are 3 types of PAP, each with different causes: autoimmune, secondary, and congenital [1]. The typical thin-section computed tomography (TSCT) findings of PAP include ground glass opacities (GGOs) with a patchy geographic pattern, the diffuse spread of unclearly demarcated GGOs, and inter- and intralobular septal thickening with patchy GGOs [2].

We have experienced an unusual case of autoimmune PAP, which showed multiple localized GGOs on TSCT.

Case report

An 80-year-old female presented with occasional coughing. She had no history of smoking or pulmonary disease. Her cough became progressively worse, and she visited a local hospital, where chest CT was performed. TSCT showed multiple focal GGOs with clear and straight boundaries in the peripheral area of the right upper lobe (Figs. 1A, 2A, and 3A). Seven months after the first TSCT scan, she presented with a worse cough. The second TSCT scan showed an enlarged GGO in the apex of the right lung (Fig. 1B), and she was referred to our hospital so that the disease could be investigated. A third TSCT scan performed 1 month after the second CT scan showed that the GGO in the apex of the right lung had become denser (Fig. 1C). Therefore, it was suspected to be a pulmonary adenocarcinoma. However, the other GGOs had generally decreased in size and become fainter (Figs. 3B and C).

The patient's preoperative blood tests were normal, including her tumor marker levels, such as those of carcinoembryonic antigen and cytokeratin 19 fragment.

An upper right lobectomy was performed under video-assisted thoracoscopy. A histological examination showed the accumulation of eosinophilic granular material in the alveolar space, which was positive for periodic acid-Schiff (PAS) and surfactant protein A (Fig. 4). No atypia was observed in the alveolar epithelium, and no fibrosis or atypical cell proliferation was observed. The patient's serum anti-granulocyte-macrophage colony-stimulating factor (GM-CSF) level was 10.6 μg/mL (normal range: <1.0 μg/mL), and autoimmune PAP was diagnosed.

Since she had no respiratory symptoms after the surgery, she received no further treatment. Follow-up chest CT showed no recurrence of the PAP.

Discussion

PAP was first described as a disorder involving the filling of the alveoli by a PAS-positive proteinaceous material in 1958 [3]. PAP is currently considered to be a disease that is characterized by the accumulation of alveolar surfactant and results in hypoxemic respiratory insufficiency [1]. PAP is classified in accordance with its underlying pathogenetic mechanism into primary (autoimmune or heredity), secondary, or congenital [1]. Autoimmune PAP is the most common type. Patients with autoimmune PAP have high levels of anti-GM-CSF immunoglobulin G antibodies, which bind to GM-CSF with high affinity, blocking its activity. As a result, alveolar macrophages are unable to clear pulmonary surfactant [4].

The symptoms of autoimmune PAP are mainly characterized by exertional dyspnea, eventually accompanied by nonspecific respiratory symptoms, like a cough and/ or the production of white foamy sputum, or systemic symptoms, such as fatigue and/or weight loss. On the other hand, one third of patients are asymptomatic [5].

On radiographs, PAP typically shows bilateral central and symmetric lung opacities, with relative sparing of the apices and costophrenic angles. CT provides a much clearer picture

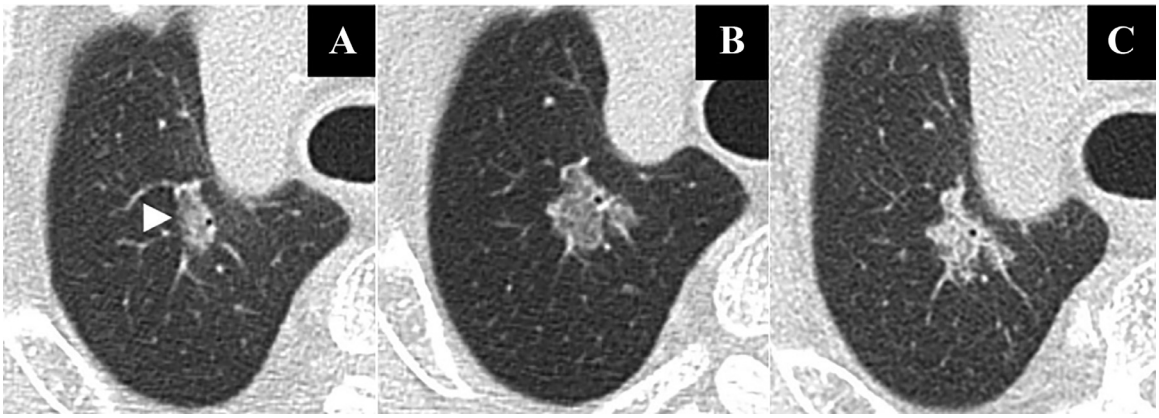

Fig. 1 – Chest TSCT (thickness: 1 mm) showed 3 GGOs in the right upper lobe (Segment 1). (A) The first TSCT scan showed a pure GGO (diameter: 15 mm) at the apex of the upper lobe of the right lung (white arrowhead). (B) The second TSCT scan (performed 7 months after the first CT scan) showed that the GGO, which had a crazy-paving-like appearance, had increased in size. (C) The third TSCT scan (performed 8 months after the first CT scan) showed that the GGO had clear margins. It had increased in size and become denser than it was on the second CT scan.

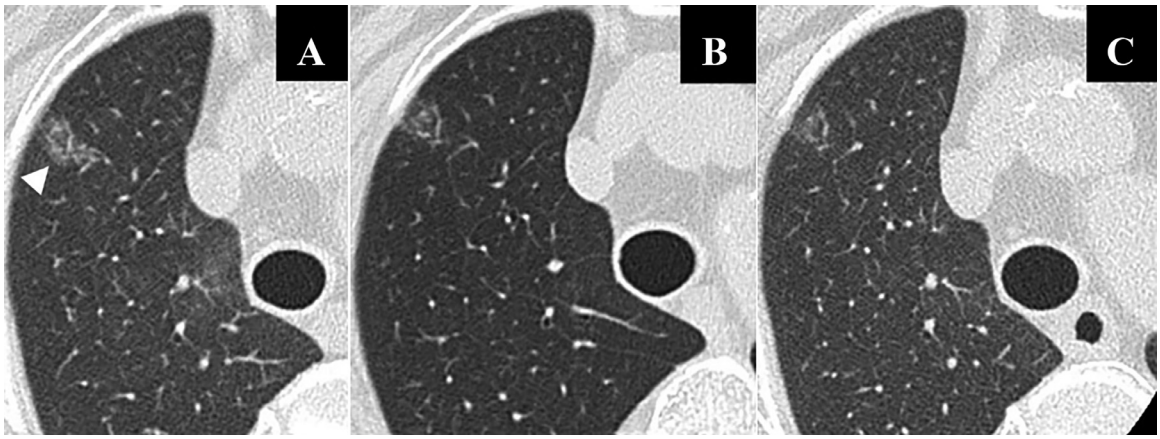

Fig. 2 – Chest TSCT (thickness: 1 mm) showed 3 GGOs in the right upper lobe (Segment 1). (Slightly caudal from Fig. 1). (A) The first TSCT scan showed a nonhomogeneous, rectilinear GGO (diameter: 12 mm) (white arrowhead). (B) The second TSCT scan (performed 7 months after the first CT scan) showed that the GGO had slightly decreased in size and become fainter than it was on the first CT scan. (C) The third TSCT scan (performed 8 months after the first CT scan) showed that the GGO had slightly decreased in size and become fainter than it was on the second CT.

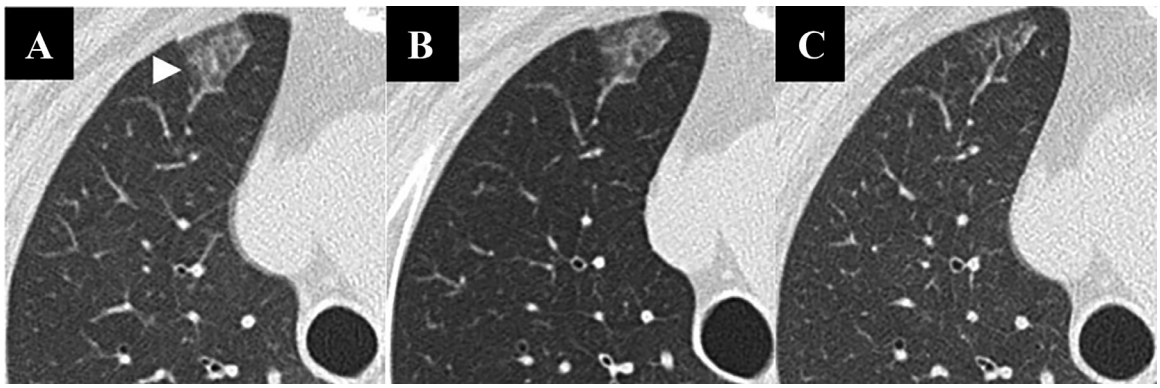

Fig. 3 – Chest TSCT (thickness: 1 mm) showed 3 GGOs in the right upper lobe (Segment 1). (Slightly caudal from Fig. 2). (A) The first TSCT scan showed a rectilinear GGO (diameter: 15 mm) with a crazy-paving-like appearance (white arrowhead). (B) The second TSCT scan (performed 7 months after the first CT scan) showed that the GGO had slightly decreased in size and become fainter than it was on the first CT scan. (C) The third TSCT scan (performed 8 months after the first CT scan) showed that the GGO had decreased in size and become fainter than it was on the second CT scan.

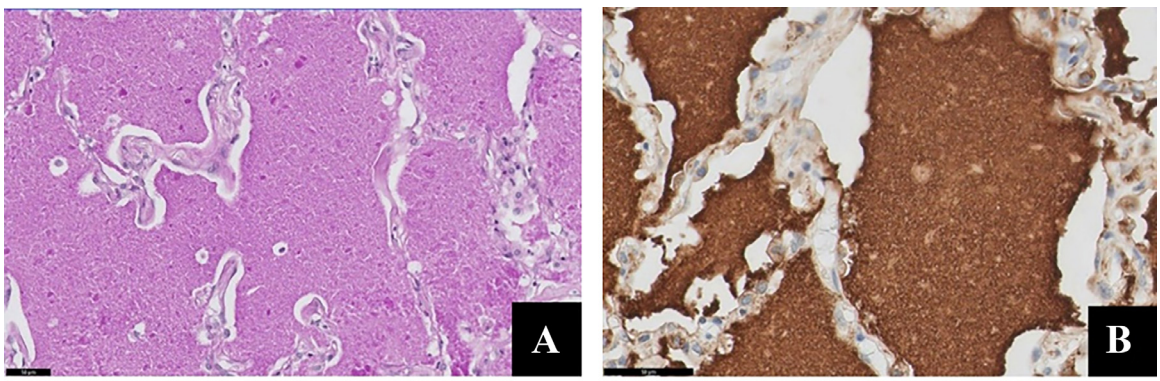

Fig. 4 – Histologically, a surgical specimen stained with hematoxylin and eosin showed eosinophilic granular material in the alveoli, which was positive for periodic acid-Schiff stain (A) and surfactant protein A (B).

of the progression and extent of PAP. The most characteristic TSCT feature of PAP is thickened septal lines on a background of widespread GGO, which is referred to as a crazy-paving-like appearance [2]. The GGOs are caused by the intraalveolar accumulation of proteinaceous material. The septal lines seen in PAP correlate with marked interlobular septal expansion due to edema and dilation of the pulmonary lymphatic system [2].

There have been some Japanese case reports of PAP with focal GGOs. Kojima et al. [6] reported the case of an 82-year-old female with PAP, who presented with a localized GGO with ill-defined margins at the bottom of the upper lobe of the right lung. Since the GGO had slightly increased in size after 5 months, it was suspected to be a pulmonary adenocarcinoma. Surgery was performed, and it was pathologically confirmed to be PAP. Inoue et al. [7] reported the case of a 71-year-old male with PAP, who presented with a few focal GGOs with ill-defined margins without septal thickening in the subpleural areas of the bilateral lungs. Since they had not changed in shape after 4 months, lung cancer was suspected. Eventually, this lesion was also proven to be PAP by surgery.

Kita et al. [8] reported the case of a 59-year-old male with PAP, who presented with partly solid nodules with irregular margins in the subpleural area and near the hilum of the middle lobe. The nodules had increased in size compared with a CT scan performed 5 years earlier, and were resected. As a result, these lesions were also proven to be PAP.

Concerning our case, there were multiple focal GGOs in the peripheral areas of the lung, which had clear and straight boundaries and a lobular distribution. Moreover, a crazy-paving-like appearance was seen within the GGOs on TSCT. The GGO in the right lung apex increased in size and became denser, while the other 2 GGOs in right upper lung decreased in size and became fainter. A previous study found that the TSCT findings of PAP are closely correlated with severity of respiratory condition [9]. Considering that all 3 of the above-mentioned patients and our patient had no or mild symptoms, focal GGOs may indicate an early-stage or mild case of PAP.

Neoplastic lesions, including atypical adenomatous hyperplasia, adenocarcinoma in situ, and mucosa-associated lymphoid tissue lymphoma also show multiple GGOs on TSCT. It is often difficult to differentiate these disorders from PAP. However, localized GGOs with a crazy-paving-like appearance and a lobular distribution, and the regression of GGOs may be indicative of PAP. In such cases, anti-GM-CSF antibody testing may be considered.

Conclusion

PAP usually shows widespread GGOs on whole lung, but it rarely shows localized GGOs. Lobular distribution and the regression of GGOs may be indicative of PAP.

Patient consent

We confirm that we have obtained written, informed consent from the patient for the publication of this case report. The patient has been thoroughly informed about the details that will be published and understands the implications of the publication. The written consent is stored securely and is available for review by the editorial team upon request.

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