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Case Report

Localized nodular pulmonary amyloidosis mimicking primary lung cancer associated with cystic airspaces: A case report ☆,☆☆

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ABSTRACT

Localized nodular pulmonary amyloidosis can form pulmonary nodules associated with cystic air spaces, but due to its rarity, it cannot be included in the differential diagnosis without appropriate knowledge. Among the differential diagnoses of nodules with cysts in the lungs is primary lung cancer, however, diagnosis based solely on imaging findings is challenging. A 59-year-old Japanese female was referred to our hospital for an abnormality noted on the chest radiograph of an annual health check. She had no history of smoking or medical issues. Chest computed tomography revealed a 1.2 cm pulmonary nodule with surrounding multilocular cystic air spaces in the superior lingular segment. We suspected it was a nodule of primary lung cancer arising in the pulmonary cyst and performed video-assisted thoracic surgery. As the intraoperative frozen examination after a wedge resection revealed fibrotic tissue without malignancy, we did not do any further resection. The histopathological examination of the permanent section revealed unstructured eosinophilic deposits positive for direct fast scarlet staining, which were consistent with amyloidosis. The surrounding pulmonary cysts contained the check valve made by amyloid deposition. Localized nodular pulmonary amyloidosis can give rise to pulmonary cysts and mimic primary lung cancer associated with cystic air spaces. It should be raised as a potential differential diagnosis for pulmonary nodules with cystic air space formation, particularly in patients without a smoking history.

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Introduction

Amyloidosis is a metabolic disorder characterized by the extracellular deposition of insoluble proteins known as amyloids, resulting in organ dysfunction [1]. In pulmonary amyloidosis predominantly categorized as localized amyloidosis, where amyloids deposit exclusively in specific organs, localized nodular pulmonary amyloidosis has been reported to be particularly associated with cystic formations [2]. but it is scarcely recognized by thoracic surgeons due to its rarity. On the other hand, pulmonary cysts commonly encountered in routine clinical practice are known to be potential sites for the development of lung cancer, and are particularly prevalent among heavy smokers [3]. The computed tomography findings of localized nodular pulmonary amyloidosis may resemble those of primary lung cancer, making preoperative diagnosis challenging, thus histological confirmation is imperative for definitive diagnosis. Herein we report a case of localized nodular pulmonary amyloidosis presented as pulmonary nodule with cystic formations mimicking primary lung cancer associated with cystic air spaces.

Case presentation

A 59-year-old Japanese female was referred to our hospital for an abnormality noted on the chest radiograph of an annual health check. The chest radiograph showed a nodular shadow with irregular and indistinct margins in the left lower lung field (Fig. 1). She had no history of smoking or medical issues. Chest computed tomography (CT) revealed a 1.2 cm pulmonary nodule with surrounding multilocular cystic air spaces in the superior lingular segment (Fig. 2). The serum tumor markers, antigens of fungi, and antibody to mycobacterium avium complex were negative. Although the transbronchial biopsy was inconclusive, the absence of changes on the follow-up CT scan 2 months later led us to suspect primary lung cancer arising in the pulmonary cyst. While a definitive diagnosis based solely on imaging examinations is challenging, CT-guided biopsy was omitted due to the risk of pleural dissemination, and video-assisted thoracic surgery was performed.

The thoracoscopic findings revealed a nodule with a pleural indentation in the left upper lobe (Fig. 3) and we performed a wedge resection of the lung for a pathological diagnosis. As the intraoperative frozen examination revealed fibrotic tissue without malignancy, we did not do any further resection.

The postoperative course was good and she was discharged 2 days after the operation. The histopathological examination of the permanent section revealed unstructured eosinophilic deposits (Fig. 4A) that were positive for direct fast scarlet (DFS) staining (Fig. 4B), exhibiting yellow-green birefringence by polarizing microscopy (Fig. 4C). These findings were consistent with amyloidosis. The surrounding pulmonary cysts contained the check valve made by an amyloid deposition (Fig.4D).

We conducted the following examinations to rule out systemic amyloidosis. The serum protein fraction was normal, and the urinary Bence Jones protein was negative. She did not exhibit ocular or oral dryness, and her serum autoantibody test was negative. Furthermore, her electrocardiogram and echocardiogram results were normal. As systemic amyloidosis was ruled out, we did not perform any additional examinations such as a biopsy of other organs or confirmation of the amyloid type by a specific antibody. Because she did not have lesions other than the resected lung, we diagnosed her with localized nodular pulmonary amyloidosis.

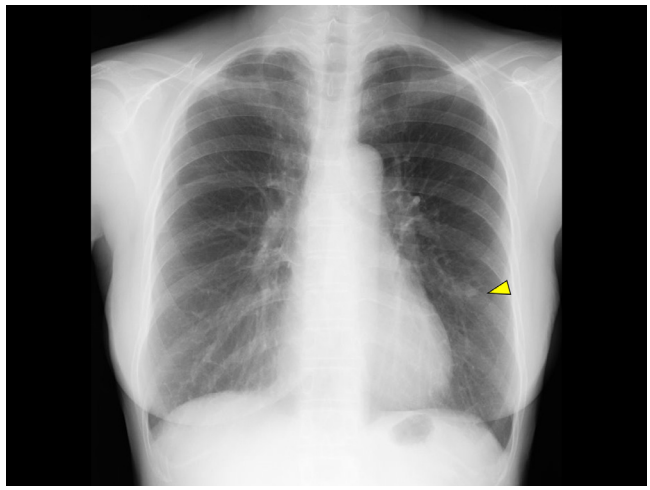

Fig. 1 – A chest radiograph revealed a nodular shadow in the left lower lung field (yellow arrowhead). The nodule exhibits irregular and indistinct margins, overlapping with the ninth rib.

Discussion

Amyloidosis is a metabolic disorder characterized by the deposition of insoluble proteins known as amyloids extracellularly, leading to organ dysfunction [1]. Amyloidosis a rare disease with an estimated incidence of approximately 10 cases per million patients each year [4]. It is classified into systemic amyloidosis, where amyloids deposit in multiple organs throughout the body [5], and localized amyloidosis, where amyloids deposit exclusively in specific organs [4]. In pulmonary amyloidosis, lesions are predominantly considered as localized amyloidosis, although they may possibly arise within the spectrum of systemic amyloidosis [6,7]. Pulmonary amyloidosis is classified into 3 categories based on the distribution of the amyloid deposition: 1) tracheobronchial amyloidosis, localized around the trachea and bronchi; 2) nodular pulmonary amyloidosis, characterized by the formation of tumorous nodules; and 3) diffuse alveolar septal amyloidosis, where amyloid deposits occur within the pulmonary interstitial walls and vascular media [4]. Many cases of nodular pulmonary amyloidosis, predominantly asymptomatic, are incidentally discovered through imaging examinations as shown in the present case [8].

Characteristic CT findings of pulmonary amyloid nodules include multiple, irregular nodules approximately 1-3 cm in size, often exhibiting calcifications, cavities, and cysts, and

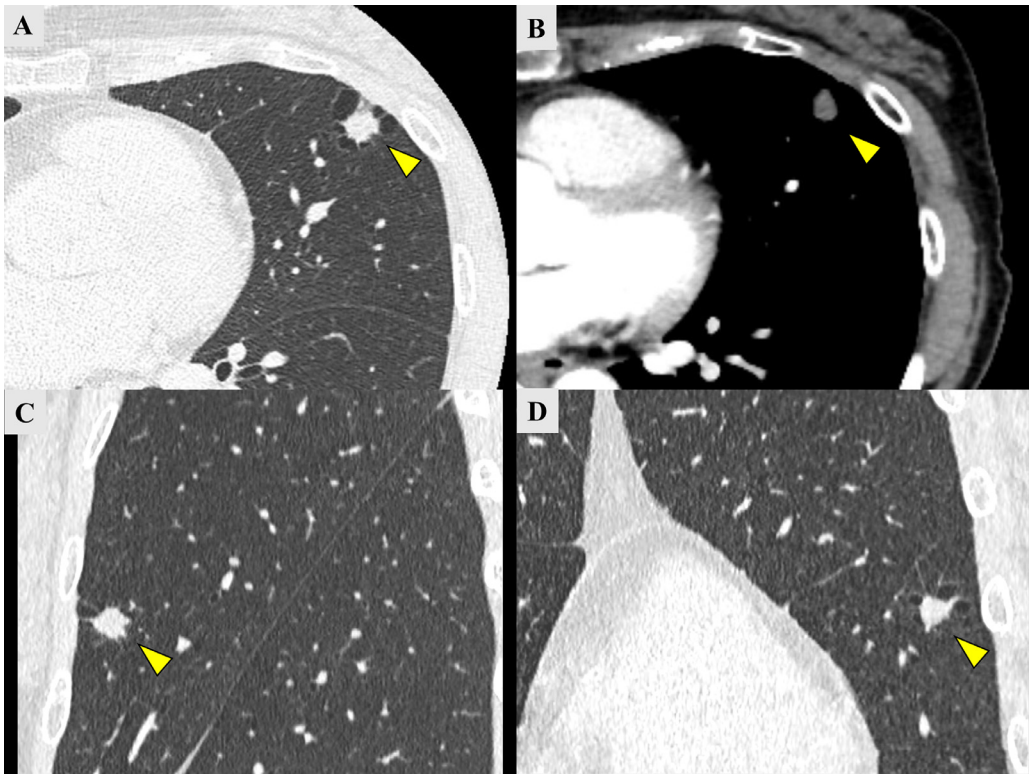

Fig. 2 – Chest computed tomography revealed an irregularly margined solid nodule measuring 1.2 cm with surrounding multilocular cystic air spaces in the superior lingular segment (yellow arrowhead). The axial lung window is shown in (A), the contrast-enhanced mediastinal window in (B), the sagittal lung window in (C), and the coronal lung window in (D). The nodule is located subpleurally but is not in contact with the visceral pleura, and it is devoid of ground-glass opacities (A, C, D). No enhancement effect or calcification is observed within it (B).

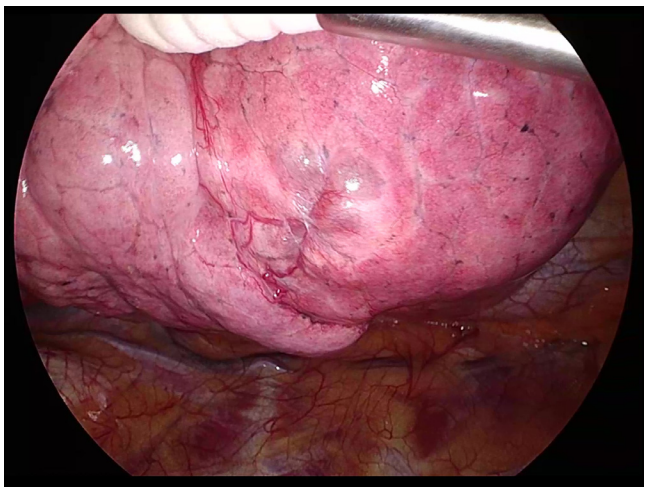

Fig. 3 – The thoracoscopic findings revealed a nodule with a pleural indentation in the superior lingular segment. Angiogenesis and multilocular cysts were observed around the pleural indentation. No exposure of the lesion was noted from the pleural surface.

occasionally demonstrating a tendency toward a gradual enlargement [9,10]. Mechanisms underlying cyst formation in pulmonary amyloidosis involve 1) a check-valve mechanism resulting from a narrow airway due to inflammatory cell infiltration and amyloid deposition, 2) pulmonary vulnerability due to the deposits, and 3) ischemia related to vascular constriction [2]. In this case, a histopathological examination confirmed a check-valve mechanism at the border between the nodule and cyst, suggesting that an amyloid deposition was the likely cause of the cyst formation.

Primary lung cancer associated with cystic airspaces, known as emphysematous cysts, is occasionally encountered in routine clinical practice. These cysts are recognized as potential sites for the development of lung cancer. Factors contributing to carcinogenesis from cystic walls include: 1) squamous metaplasia of cystic walls, 2) scarring of the cystic walls, and 3) prolonged exposure to carcinogenic substances within lung cysts [3,11–13]. The characteristic presentation involves lung cancer originating from the wall of emphysematous cysts, particularly prevalent among heavy male smokers around the age of 60, predominantly located in the upper lobe of the lungs [14,15].

In summary, emphysematous cysts caused by smoking serve as the originating site for primary lung cancer, whereas amyloidosis by itself contributes to cystic formation irrespective of smoking. Nodular pulmonary amyloidosis may present radiological features akin to primary lung cancer, posing diagnostic challenges on imaging examinations. Therefore, when identifying lung nodules associated with cystic air spaces,

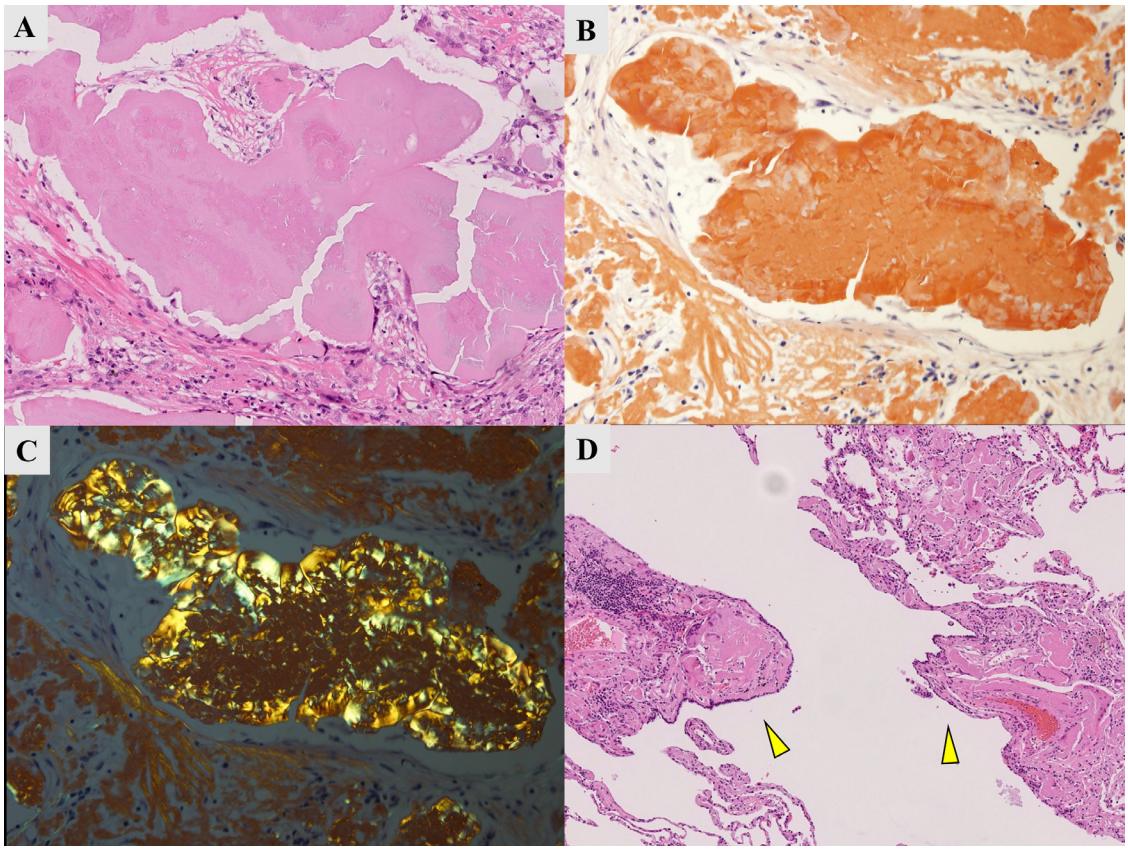

Fig. 4 – Hematoxylin and eosin (HE) staining (×20) revealed unstructured, faintly eosinophilic deposits within the nodules (A). The deposits showed positive staining with direct fast scarlet (B) and exhibited Yellow-green birefringence by polarized microscopy (C). The diagnosis of amyloidosis was established based on these findings. At the boundary between the nodules and cysts, a check-valve structure formed by an amyloid deposition was observed (HE ×4, marked with yellow arrowheads in D). This check-valve structure was considered as the causative factor for cystic formation.

nodular pulmonary amyloidosis should be raised as a differential diagnosis, particularly in patients without a smoking history.

Conclusion

Localized nodular pulmonary amyloidosis can result in cystic formation and mimic primary lung cancer associated with cystic air spaces. It should be raised as a potential differential diagnosis for pulmonary nodules presenting with cystic air space formation, particularly in patients without a smoking history.

Patient consent

Written informed consent for the publication of this report was obtained from the patient.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2024.05.068.

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