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Case Report

Pulmonary light chain deposition disease: Case series and review of the literature ☆,☆☆

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ABSTRACT

Pulmonary light chain deposition disease is a rare entity characterized by immunoglobulin deposition within the lung parenchyma with pathologic features distinct from pulmonary amyloidosis. Here, the authors present the clinical presentation, associations, and radiologic features of pulmonary light chain deposition disease in a series of 4 patients as well as discuss the distinctions from amyloidosis. The present case series highlights the frequent presence of both cysts and nodules at CT. Clinically, lymphoma and/or autoimmune disease are often associated.

Introduction

Light chain deposition disease (LCDD) is a rare type of monoclonal immunoglobulin deposition first described by Randall et al in 1976 [1]. LCDD is characterized by the disorganized deposition of most commonly kappa light chains primarily in the kidneys, heart and liver requiring stringent pathologic examination for accurate differentiation from amyloid light-chain (AL) amyloidosis. Pulmonary involvement in LCDD was first noted by Kijner and Yousem et al in 1988 [2]. Although uncommon, pulmonary LCDD (PLCDD) should be considered part of the differential diagnosis of nodular and cystic lung disease. This work aims to describe the clinical and imaging findings of 4 pathology-confirmed cases of PLCDD as well as discuss differences with pulmonary amyloidosis. The clinical and imaging findings are summarized in Tables 1 and 2.

Case presentations

Case 1

A 56-year-old woman with a history of primary biliary cirrhosis and marginal zone lymphoma incidentally found in

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Table 1 – Summary of clinical findings in four patients with pathology-confirmed pulmonary light chain deposition disease (PLCDD).

Case	Age	Sex	Presentation	PMH	Smoking	Outcome	Biopsy type
1	56	F	Incidental PET/CT finding in workup of axillary lymphoma	PBC, extranodal marginal zone B cell lymphoma	Yes	Deceased	Surgical lung biopsy
2	51	F	Worsening dyspnea, nonproductive cough	SLE, RA, Sjogren's syndrome	Never	Alive	Surgical lung biopsy
3	69	F	Nasal congestion, fever, chest pain	Sjogren's syndrome, SLE, Hashimoto's thyroiditis	Yes, 46 pack years	Alive	Surgical lung biopsy
4	73	M	Incidental chest CT finding	SLE, SQCCA (tongue), CAD, HTN, hyperlipidemia	Never	Deceased	Surgical lung biopsy

CAD, coronary artery disease; F, female; HTN, hypertension; M, male, PBC, primary biliary cirrhosis; PMH, past medical history, RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SQCCA, squamous cell carcinoma.

Table 2 – Summary of CT findings in four patients with pathology-confirmed pulmonary light chain deposition disease (PLCDD).

	Cysts/nodules/ both?	Laterality	Craniocaudal predominance	Axial distribution (central, peripheral, peribronchovascular, random, other)	Cyst number (1-5, 6-15, >16)	Range of cyst size (<10 mm, 10-29 mm, >29 mm) and size of largest cyst	Other cyst findings
1	B	BL; B	Random; B	Random = nodules Cysts = peripheral	1-5	10-29 mm (11 mm)	-
2	B	BL; B	Lower; B	Random; B	>16	10-29 mm (24 mm)	Vessel coursing along cyst wall
3	B	BL; B	Mid; B	Central; B	1-5	10-29 mm (13 mm)	Vessel coursing along cyst wall
4	Nodules	L	Mid	Random; B	-	-	-
	Nodule number (1-5, 6-15, >16)	Range of nodule size (1-10 mm, 10-29 mm, >29 mm) and size of largest nodule	Nodule density (solid, semisolid, ground glass, mixed)	Most common nodule margins (spiculated, irregular, smooth, lobulated)	Nodule cavitation?	Other nodule findings	Other relevant CT findings
1	1-5	10-29 mm (21 mm)	Solid	Lobulated	None	-	Left axillary LAD
2	>16	10-29 mm (12 mm)	Solid	Irregular	None	Some lobulated	Few reticular and ground glass opacities in the upper lungs
3	1-5	>29 mm (34 mm)	Solid	Irregular	None	Air-bronchograms	Paraseptal emphysema, apical scaring, mild bronchiectasis, dependent atelectasis
4	1-5	10-29 mm (22 mm)	Solid	Lobulated	None	-	-

B, both; BL, bilateral; L, left; LAD, lymphadenopathy; mm, millimeter.

a left axillary lymph node. She had a history of second-hand smoke exposure and occasional smoking. Physical examination was unremarkable. FDG ([^{18}F] fluorodeoxyglucose)-PET/CT for lymphoma work up revealed a metabolically active nodule in the right middle lobe (Fig. 1). Pulmonary function testing revealed moderately decreased diffusion capacity. Right middle lobectomy showed findings consistent with an extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) and extensive congo-red negative extracellular deposits comprised of kappa immunoglobulin light chains on mass spectroscopy consistent with light chain deposition disease (Fig. 2). Bone marrow biopsy was normal.

Case 2

A 51-year-old woman with a history of systemic lupus erythematosus (SLE), rheumatoid arthritis and Sjogren's syndrome

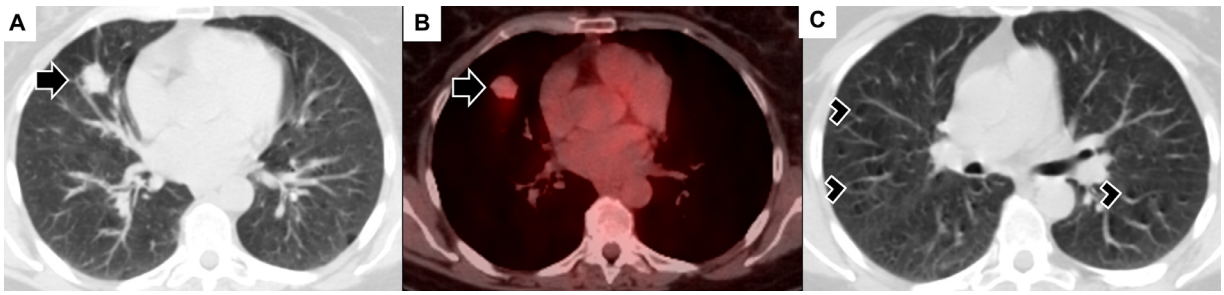

Fig. 1 – Imaging findings in a 56-year-old woman with pulmonary light chain deposition disease and MALT lymphoma (case 1). (A) Axial slice from a low dose non-contrast chest CT obtained as part of an FDG PET/CT examination demonstrates a dominant 2.1 x 2.4 x 1.2 cm solid lobulated pulmonary nodule in the right middle lobe (arrow) which showed mild FDG avidity (B). (C) Additional axial slice from the same low dose non-contrast chest CT demonstrates multiple pulmonary cysts in a slightly peripheral predominant distribution in both lungs (arrowheads).

who presented with worsening dyspnea and nonproductive cough. The patient had no smoking history. On physical examination, the patient demonstrated diffuse inspiratory squeaks and bibasilar crackles. Pulmonary function testing revealed mild to moderate restrictive physiology and moderate reduction in diffusing capacity. Chest radiographs showed subtle patchy bilateral interstitial opacities which persisted over multiple months. The patient was further assessed with a contrast-enhanced CT of the chest which revealed multiple bilateral cysts (>16) and nodules (>16) with a lower craniocaudal predominance and random axial distribution (Fig. 3). Cysts ranged from 10 to 29 mm in size and a vessel coursed along at least one cyst wall. Nodules ranged from 10 to 29 mm in size and were most often of solid and irregular morphology. Additional CT findings included reticular and ground-glass opacities in the upper lungs. The patient underwent a left lower lobe wedge resection which revealed congo red negative extracellular deposits comprised of kappa immunoglobulin light chains on mass spectroscopy consistent with light chain deposition disease. Bone marrow biopsy was normal.

Case 3

A 69-year-old woman with a history of SLE, Hashimoto's thyroiditis, Sjogren's syndrome and a 35 pack year history who presented with an episode of nasal congestion, fevers, and chest pain. No hemoptysis or sputum production. Physical examination showed bibasilar crackles, left greater than right. Pulmonary function testing revealed mild reduction in diffusion capacity. Chest radiograph demonstrated an opacity in the medial right midlung (Fig. 4A). Further evaluation with contrast-enhanced chest CT (Figs. 4B and C) showed a 2.0 × 2.0 × 1.3 cm pulmonary nodule in the medial segment right middle lobe in addition to right middle lobe bronchiectasis. The patient underwent a right middle lobectomy which revealed congo red negative extracellular deposits comprised of kappa immunoglobulin light chains on mass spectroscopy consistent with kappa restricted light chain deposition disease as well as findings of a low-grade B-cell lymphoma. Bone marrow biopsy was normal.

Case 4

A 73-year-old man with a history of SLE, squamous cell carcinoma of the tongue status post resection, hyperlipidemia, hypertension and coronary artery disease status post coronary artery bypass grafting incidentally found to have two solid lobulated pulmonary nodules in the left upper and left lower lobes on a non-contrast chest CT (Fig. 5). The patient had no smoking history. Physical examination was unremarkable. Pulmonary function testing demonstrated increased airway resistance but was otherwise normal. The patient underwent surgical resection of the 2 nodules with each revealing a kappa-light chain restricted plasmacytoma with congo-red negative extracellular deposits comprised of kappa immunoglobulin light chains on mass spectroscopy consistent with light chain deposition disease. Bone marrow biopsy was normal.

Discussion

Pathologically, LCDD is defined by disorganized deposition of non-amyloid light chain immunoglobulins most commonly with a kappa light chain predominance leading to disruptive accumulation of proteinaceous material along basal membranes, collagen or elastic fibers [3]. Isolated PLCDD is characterized by disease exclusively present in the lung parenchyma. Although the specific etiology of isolated PLCDD remains elusive, Colombat et al described 3 such cases with confirmed pulmonary B cell clones with a restricted immunoglobulin repertoire of similar heavy and light chain CDR3 sequences, suggestive of a possible antigen-driven primary lymphoid proliferation [4]. However, the exact pathophysiologic mechanisms keeping disease localized to the lung remain to be discovered. Misdiagnosis of PLCDD as AL amyloidosis; a separate disease of light chain monoclonal immunoglobulin deposition, is possible due to the shared macroscopic characteristics of both conditions. In contrast to amyloid, the amorphous material in LCDD does not show the apple green birefringency under polarized light which is characteristic for amyloid de-

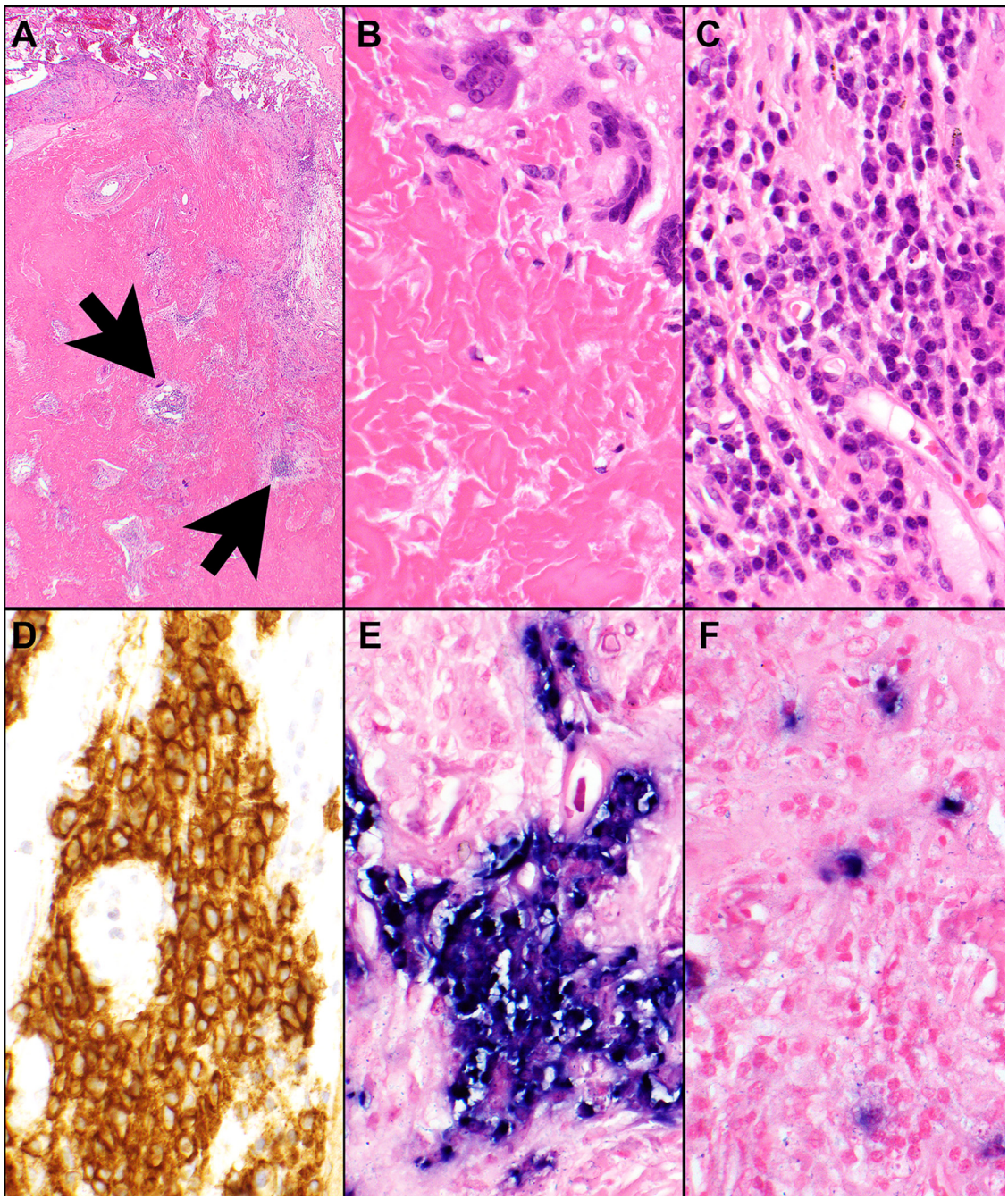

Fig. 2 – Pathology findings in a 56-year-old woman with pulmonary light chain deposition disease and extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) (case 1). (A) On low magnification there is circumscribed pink amorphous material within alveolated parenchyma. Scattered clusters of inflammatory cells are within the amorphous material (arrows). (B) Scattered multinucleated giant cells are associated with the amorphous material. (C) The inflammatory infiltrates (arrow A) are predominantly comprised of plasma cells as confirmed by CD138 immunotest (D) with scattered lymphocytes. (E) The plasma cells are kappa light chain restricted. (F) Only rare plasma cells show lambda light chain expression. Magnification, H&E x 2 (A), x 400 (B, C), CD138 x 400 (D), in situ hybridization kappa (E) and lambda (F) x 400.

posits. AL amyloidosis is also characterized by crystal violet metachromaticity on histochemical stains, P-component presence, and nonbranching 8-10 nanometer fibrils on electron microscopy (EM). In contrast, EM of LCDD deposits is characterized by an amorphous appearance. Moreover, in LCDD, deposits will be congo-red negative and mass spectrometry will not reveal the protein composition that is typical of amyloid [5].

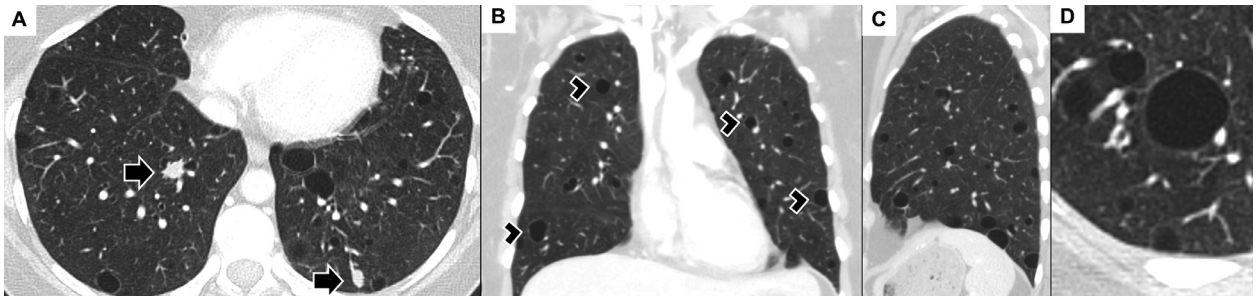

Fig. 3 – Imaging findings in a 51-year-old woman with pulmonary light chain deposition disease (case 2). Axial (A) and coronal (B) contrast-enhanced chest CT slices demonstrate multiple scattered solid irregular pulmonary nodules (arrows) and pulmonary cysts (arrowheads). Sagittal slice through the left (C) lung demonstrates a lower craniocaudal predominance. Small field of view axial slice (D) demonstrates a vessel coursing along a cyst wall.

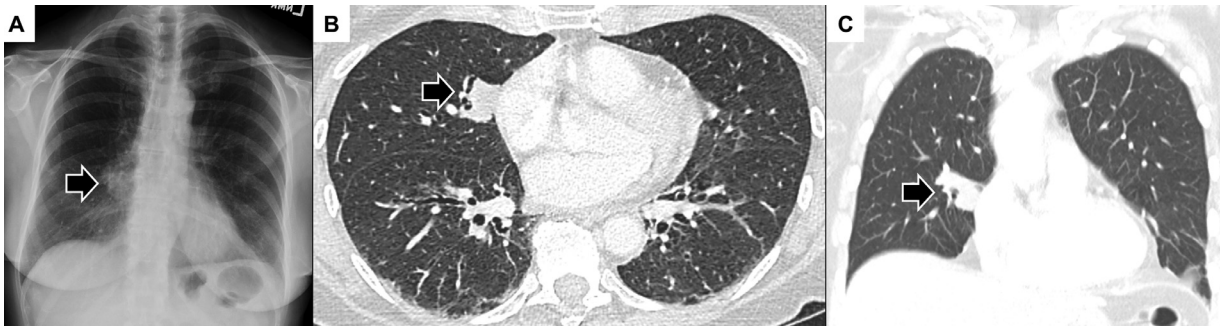

Fig. 4 – Imaging findings in a 69-year-old woman with pulmonary light chain deposition disease (case 3). (A) Chest radiograph reveals a round opacity at the central right midlung (arrow). Axial (B) and coronal (C) contrast-enhanced chest CT slices demonstrate a 2.0 x 2.0 x 1.3 cm pulmonary nodule in the medial segment right middle lobe (arrow).

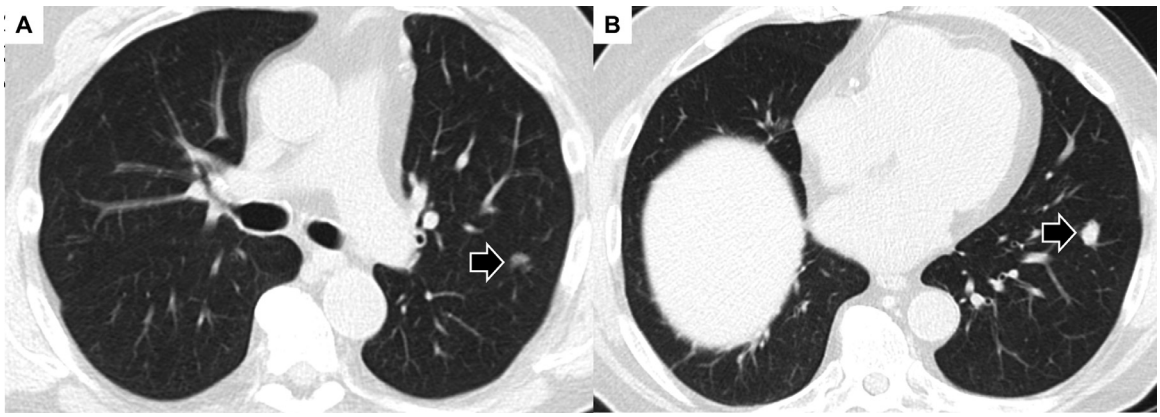

Fig. 5 – Imaging findings in a 73-year-old man with pulmonary light chain deposition disease (case 4). Axial (A and B) noncontrast chest CT slices demonstrate 2 solid lobulated pulmonary nodules (arrows) with a middle craniocaudal distribution in the left upper and left lower lobes.

Systemic LCDD has been described to have a male predominance, seen in patients between 35 and 76 years and associated with B cell neoplasms such as lymphoma, Waldenstrom macroglobulinemia and chronic lymphocytic leukemia (CLL) [6]. Although the kidneys tend to be the most frequently affected organ by systemic LCDD, pathology confirmed deposits have been found in the liver, heart, peripheral nerves, gastrointestinal tract, and skeletal muscles with resulting symptoms due to disruption of organ function, leading to a heterogeneous clinical presentation [7].

Histologically, PLCDD has nodular and diffuse forms [5]. Nodular PLCDD is characterized by well-circumscribed localized nodular light chain deposits with lymphocytic infiltrates and foreign body giant cells (Fig. 2) [3,8]. Historically, most cases of nodular PLCDD have been found incidentally on lung biopsies of otherwise healthy patients, although moderate

respiratory symptoms have been reported upon presentation [5,9,10]. Approximately 50% of patients with nodular PLCDD have an associated lymphoproliferative disorder or plasma cell dyscrasia [5,10].

Diffuse PLCDD is a histologic pattern characterized by diffuse basement membrane thickening of both respiratory and vascular tissues within the lung parenchyma [5]. Large airway involvement has also been described [9]. Light chain infiltration may either be secondary to systemic disease or localized to the lung [9]. Diffuse PLCDD tends to have a poorer prognosis when compared to the other PLCDD types often necessitating lung transplantation following clinical presentation which tends to involve chronic respiratory symptoms with an obstructive airflow pattern [5,9]. Similar to nodular disease, lymphoproliferative disorders, and plasma cell dyscrasias may be associated with diffuse PLCDD [5,11]. It is important to be aware that pulmonary amyloidosis also has nodular and diffuse forms. Bhargava et al suggested that making a pathologic distinction between the diffuse forms of PLCDD and pulmonary amyloidosis may not be of great clinical significance given the poor prognosis of patients with either disease [5]. On the other hand, distinguishing between the nodular forms of PLCDD and pulmonary amyloidosis carries significant clinical value as nodular PLCDD has a much stronger association with lymphoproliferative and/or plasma cell dyscrasias as well as an association with development of renal failure [5].

Literature describing the radiologic manifestations of PLCDD is scarce. Sheard et al described the thoracic CT findings in 9 cases of PLCDD [12]. In their study, Sheard et al described nodules as commonly present (8/9) and universal presence of cysts (9/9) with nodules tending to be randomly distributed (3/6), between 2 and 5 in number (4/8), and on average 10 mm in diameter while cysts also tended to be randomly distributed (6/9) and measuring on average 10 mm [12]. More recently, Wei et al described a series of 4 PLCDD patients with CT findings which showed both nodules and cysts present in all with nodules ranging from 1-2 in number to 6-14 mm in size with a frequent peripheral distribution (3/4) while cysts ranged from 8 to 15 mm in size and were randomly distributed [13]. The aforementioned findings in both studies generally concur with those noted in this series. The most common nodule morphology in the present study was solid and irregular or lobulated, which differs from the well circumscribed morphology frequently encountered by Sheard et al and fits with the irregular morphology found in half of patients described by Wei et al. The finding of a vessel traversing a cyst wall observed in multiple cases in this series has also been previously described in patients with PLCDD [12,13].

It is worth noting that there is a diffusely cystic CT pattern of PLCDD with no nodules which was first described by Colombat et al in a series of 3 cases [14]. Interestingly, this form of purely cystic PLCDD tends to affect young females [4]. Recruitment of macrophages to light chain deposits leading to excessive production of matrix metalloproteinases (MMPs) with resulting elastin destruction and rupture of alveoli and bronchioles has been proposed as a possible mechanism for cyst formation in this patient population [8,11,15].

Given the rarity of PLCDD, consideration in daily clinical practice is most likely to be part of a differential diagnosis including other entities that may present with multiple cysts or multiple cysts and nodules. These diseases include but are not limited to lymphangioleiomyomatosis (LAM), pulmonary langerhans cell histiocytosis (PLCH), lymphocytic interstitial pneumonia (LIP), and amyloidosis [11,13]. LAM tends to present with a diffuse bilateral distribution of cysts in young females. PLCH often presents in young adult smokers with upper and middle lung predominant irregular nodules which may cavitate over time. LIP has a slight female predilection and presents with diffuse ground-glass opacities with centrilobular nodules and thin-walled cysts in a random distribution. Amyloidosis may present with cysts and nodules.

This study is limited by its retrospective nature and exclusion of cases with confirmed PLCDD lacking thoracic CT imaging prior to tissue diagnosis. The number of potential cases to be included in this study was also limited by the inherent rare nature of this disease as well as the relatively recent widespread adoption of cross-sectional imaging, as evidenced by all CT examinations being from 2008 to 2020. Additionally, the range of slice thickness encountered likely limited the ability to detect smaller findings in some patients, particularly case 1 in which the CT images were obtained from an FDG PET/CT examination. Despite these limitations, our findings generally concur with those previously reported by other authors.

In conclusion, we present a series of four PLCDD cases with thoracic CT examinations prior to tissue biopsy. In our series, ages ranged from 51 to 73 years old with a 3:1 female to male ratio. Lymphoma and autoimmune disease were common. Both cysts and nodules were present in most patients. Craniocaudal distribution of cysts and nodules were most often in the middle with one case having a clear lower predominance and no case having an upper predominance. There was no clear pattern of axial distribution of cysts or nodules. All nodules were solid and either irregular or lobulated. Number of cysts and nodules varied widely from 1-5 to >16.

Patient consent

All patients part of this case series provided written authorization for use of their medical information.

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