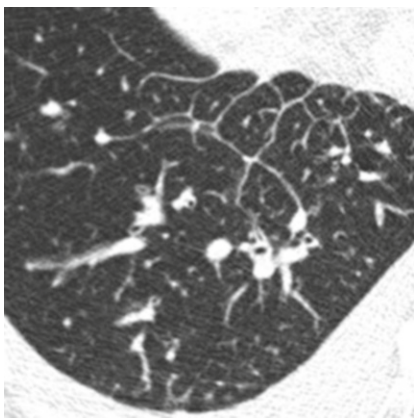
Septal Diseases

Radiology	Nicola Sverzellati Mario Silva	



G. Dalpiaz, A. Cancellieri (eds.), *Atlas of Diffuse Lung Diseases*,
DOI 10.1007/978-3-319-42752-2_4

Definition

Amyloidosis is a group of diseases caused by extracellular accumulation of abnormal misfolded autologous proteins (amyloid deposit), in a variety of organs and tissues. Current classification of amyloidosis is based on the type of fibrillar protein in the amyloid deposit (fibrillar amyloid light chain, AL, and serum amyloid A, AA, are the most common).

Amyloidosis can be primary or secondary in origin; hereditary forms are described but usually do not involve the chest. Localized and systemic forms of amyloidosis are described, with two main patterns of pulmonary involvement at HRCT, namely, nodular or diffuse. The interstitial diffuse form is more symptomatic than the nodular one.

Interstitial amyloidosis

Berk JL (2002) Pulmonary and tracheobronchial amyloidosis. Semin Respir Crit Care Med 23(2):155

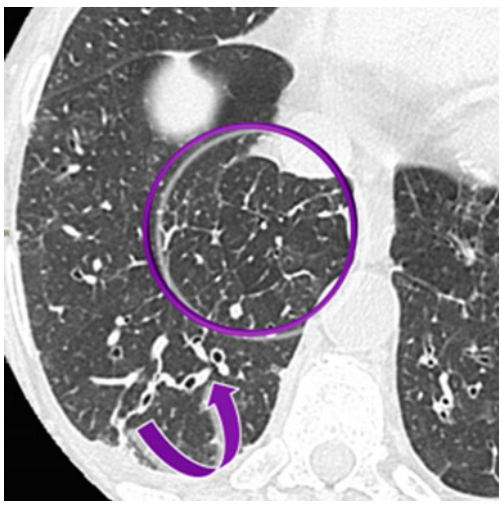
HIGH-RESOLUTION CT: HRCT

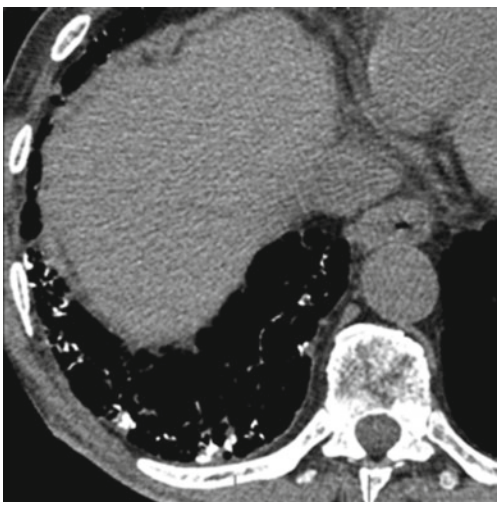
Key Signs

- Nodular interlobular septal thickening (beaded septum sign)
- Smooth interlobular septal thickening (O)
- Thickening of the bronchovascular bundles ( )
- Nodules (calcified in up to 50 % of cases) (see the image with mediastinal window)

Distribution

Usually symmetric and diffuse, but selective involvement with segmental distribution can be seen. Reticular opacities are predominantly subpleural and basal.





The beaded septum sign consists of nodular thickening of interlobular septa reminiscent of a row of beads. The beaded septum sign was initially described as a sign of lymphangitic spread of cancer although other diseases may be responsible of this sign (please also refer this sign in chapters "Septal Pattern" and "Case-Based Glossary with Tips and Tricks").

The reticular and nodular findings might be unspecific. The identification of coexisting nodules may help radiologists suggest the correct diagnosis. Nevertheless, pulmonary edema should always be considered in differential diagnosis, notably because it is frequent in subjects with myocardial amyloid deposits.

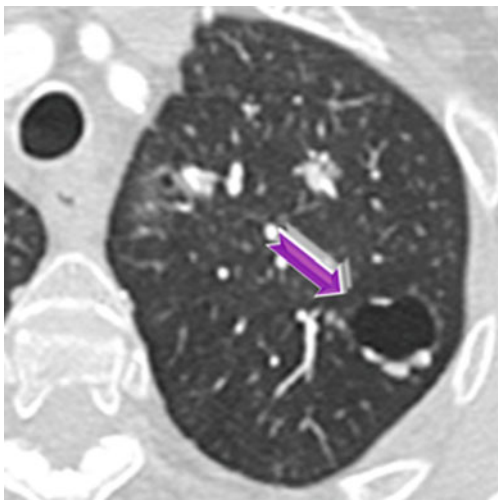
Pickford HA (1997) Thoracic cross-sectional imaging of amyloidosis. AJR Am J Roentgenol 168(2):351

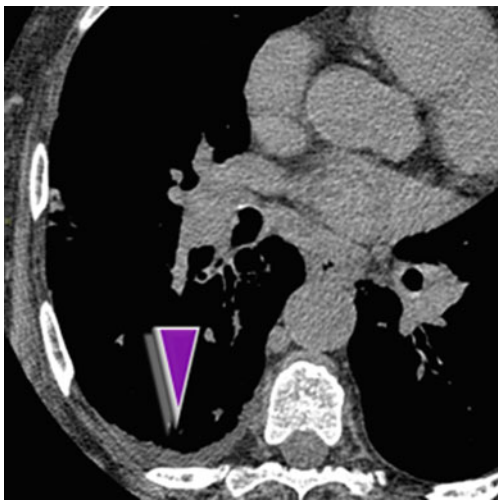
Ancillary Signs

- Ground-glass opacity.
- Patchy bilateral consolidations could show calcifications, some of them with punctate aspect.
- Lung cysts may coexist (➡), particularly in cases associated with lymphoproliferative disorders (e.g., LIP).

Non-parenchymal Signs

- Pleural thickening may be associated with pleural effusion (►).
- Hilar and mediastinal lymphadenomegaly with calcification is common in AL form of amyloidosis but uncommon in AA variant.
- Myocardial infiltration (wall thickening of the left ventricle with systolic and diastolic dysfunction and subendocardial or transmural late enhancement at MRI).





Differential diagnosis includes sarcoidosis because of beaded reticulation associated with lymph node enlargement with coarse calcifications. Also, it is important to differentiate between interstitial involvement from systemic amyloidosis and localized forms of diffuse alveolar septal amyloidosis, because the latter has more severe prognosis from pulmonary impairment.

Cordier JF (2009) Pulmonary amyloidosis in hematological disorders. Semin Respir Crit Care Med 26(5):502

Boydking A (2009) Localized interstitial pulmonary amyloid: a case report and review of the literature. Curr Opin Pulm Med 15(5):517–520

Course and Complications

- Treatment of underlying disease warrants resolution of interstitial involvement in the majority of cases of AA amyloidosis.
- AL amyloidosis related to hematologic disorders resolves in 30 % of cases treated with stem cell transplantation.

Clinical and radiological findings of the lung are usually secondary in pulmonary involvement from systemic amyloidosis. Cardiac involvement is a major prognostic factor; complications of cardiac involvement can overlap the pattern of interstitial amyloidosis. Assessment of myocardial involvement is suggested to provide comprehensive evaluation of cardiopulmonary involvement.

Czeyda-Pommersheim F (2015) Amyloidosis: modern cross-sectional imaging. Radiographics 35(5):1381

Definition

Erdheim-Chester disease (ECD) is a rare form of non-Langerhans cell histiocytosis, with systemic infiltration by CD68+ and CD1a– histiocytes without Birbeck granules. Diagnosis in adulthood is a distinctive feature of ECD compared to other forms of non-Langerhans histiocytosis. The clinical manifestation is heterogeneous due to the variability in organ involvement. However, long bones are primarily affected in 95 % of patients. Extra-osseous manifestation is also seen, particularly in the retroperitoneum (perirenal rind of soft tissue), central nervous system (sellar with diabetes insipidus or extra-sellar), and thorax (myocardium, pericardium, lung, mediastinum, pleura, and vessels).

ECD

Campochiaro C (2015) Erdheim-Chester disease. Eur J Intern Med 26(4):223

Zaveri J (2014) More than just Langerhans cell histiocytosis: a radiologic review of histiocytic disorders. Radiographics 34(7):2008

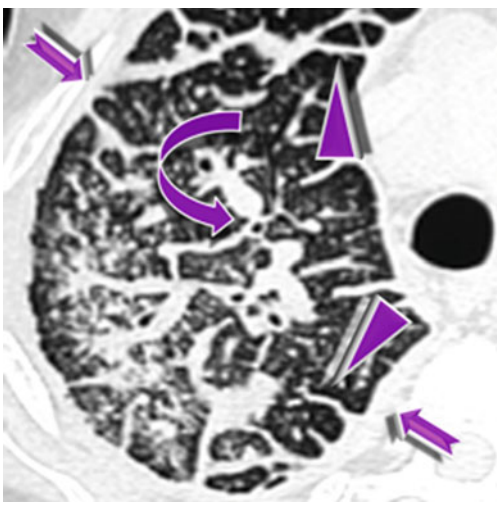
HIGH-RESOLUTION CT: HRCT

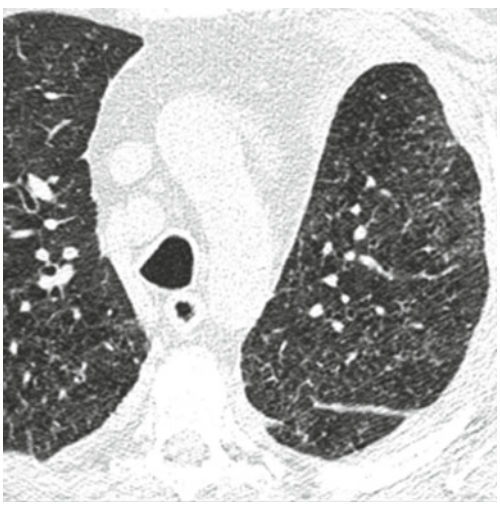
Key Signs

- Smooth thickening of interlobular septa (►)
- Smooth bronchovascular thickening (peribronchial cuffing) (↳)
- Smooth subpleural thickening (➡)
- Prominence of centrilobular structures

Distribution

Apical, anterior, and peripheral regions of the lungs are predominantly involved by symmetric smooth interlobular reticulation; also patchy or unilateral.





The thickening may be very marked assuming a “caricatural” aspect.

Pulmonary involvement is variable (14–54 % in different series), though it contributes significantly to symptoms and mortality. Pulmonary abnormalities may be due to either histiocytic infiltration or cardiogenic edema (from primary cardiac involvement).

Differential diagnosis includes lymphangitic carcinomatosis, as the differential diagnosis with systemic spread of neoplastic disease might be complicated in cases with atypical skeletal findings.

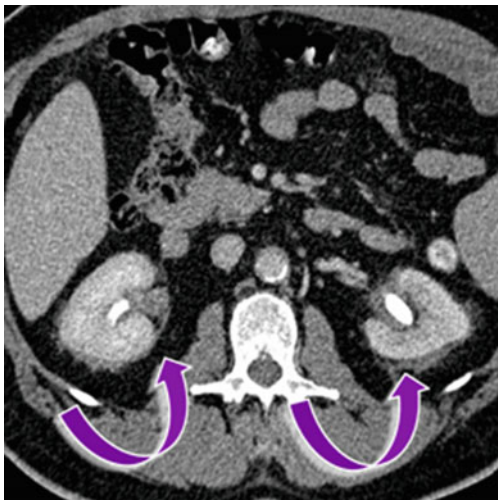
Arnaud L (2010) Pulmonary involvement in Erdheim-Chester disease: a single-center study of thirty-four patients and a review of the literature. Arthritis Rheum 62(11):3504

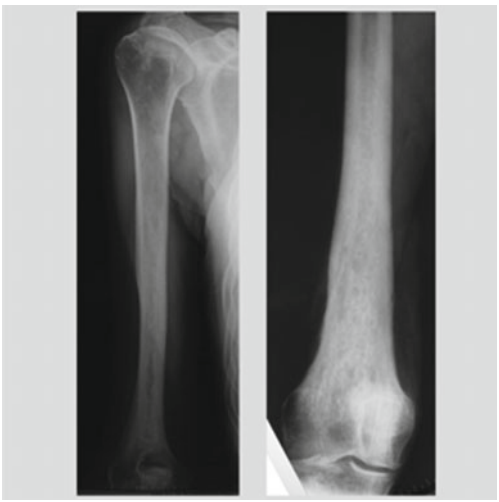
Ancillary Signs

- Variable ground-glass opacities or consolidation is seen in a small percentage of cases (please see image above).

Non-parenchymal Signs

- Pericardial effusion (up to tamponade); smooth or nodular pericardial thickening.
- Pleural thickening with late enhancement after injection of contrast agent.
- "Hairy kidney" from retroperitoneal fibrosis (☟) can be seen at bottom slides of thoracic scans (30 % of cases); urologic complications are rather common due to encasement of ureters from retroperitoneal fibrosis.
- Symmetric osteosclerosis of long bones, typically periarticular in lower limbs (tibia and distal femur).
- "Coated aorta" due to periaortic infiltration.
- Gadolinium-enhanced lesions of the central nervous system.





✓ The systemic involvement is a key feature of ECD that needs to be assessed when pulmonary and cardiac signs are seen at chest CT. Skeletal and retroperitoneal findings are therefore of paramount importance to target the differential diagnosis.

📖 Wittenberg KH (2000) Pulmonary involvement with Erdheim-Chester disease: radiographic and CT findings. AJR Am J Roentgenol 174(5):1327

Dion E (2004) Imaging of thoracoabdominal involvement in Erdheim-Chester disease. AJR Am J Roentgenol 183(5):1253

Course and Complications

- Serial imaging of the involved organ is warranted (3–6 months) to monitor pharmacological treatment, notably at its beginning.
- FDG-PET is helpful to assess disease activity.
- Worsening of cardiopulmonary abnormalities are among the most frequent life-threatening complications.

📖 Haroche J (2012) Erdheim-Chester disease. Curr Opin Rheumatol 24(1):53

Yahng SA (2009) Erdheim-Chester disease with lung involvement mimicking pulmonary lymphangitic carcinomatosis. Am J Med Sci 337(4):302

De Filippo M (2009) Erdheim-Chester disease: clinical and radiological findings. Radiol Med 114(8):1319

Definition

Lymphangitis carcinomatosis (LC) is caused by the infiltration of pulmonary lymphatics by neoplastic cells. The primary tumor is most frequently located in the bronchial tree, breast, pancreas, stomach, colon, and prostate. Invasion of lymphatics may vary according to the site of primary tumor: direct spread from intrathoracic neoplasms, retrograde diffusion from hilar lymph nodes for upper abdomen tumors, and contiguity from hematogenous metastasis

Pulmonary lymphangitic carcinomatosis (PLC), LC

Biswas A (2015) Getting the whole picture: lymphangitic carcinomatosis. Am J Med 128(8):837

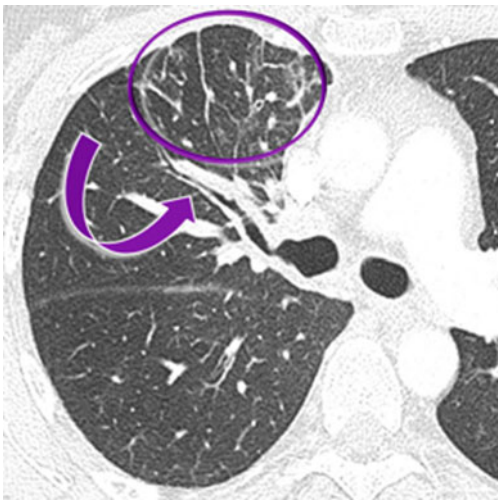
HIGH-RESOLUTION CT: HRCT

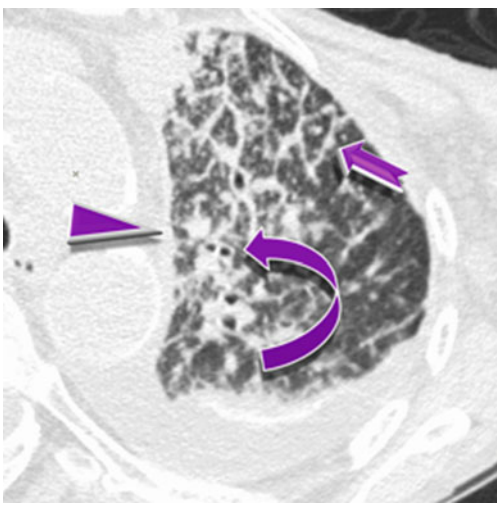
Key Signs

- Smooth interlobular septal thickening (O)
- Nodular interlobular septal thickening (beaded septum sign) (➡)
- Smooth or nodular peribronchovascular interstitial thickening (peribronchial cuffing) (⇳)
- Smooth or nodular thickening of fissures or pleural surface (►)

Distribution

Bilateral distribution is as common as unilateral involvement. If bilateral, abnormalities are asymmetric. Possible nongravity-dependent distribution (O)





Pulmonary edema represents the main differential diagnosis. Coexisting perilymphatic nodules and nonsymmetric or nongravity-dependent distribution of the septal lines are features more consistent with lymphangitis (in axial CT image, note the anterior nongravity-dependent septal thickening O).

Other disorders may also mimic lymphangitis carcinomatosis: pulmonary leukemia, eosinophilic pneumonia, veno-occlusive disease, and metabolic disorders are indeed characterized by predominant interlobular septal thickening. Thickened interlobular septa may be spurious in other disorders (e.g., infections, sarcoidosis, etc.), which, however, display other more distinctive CT features.

The beaded septum sign consists of nodular thickening of interlobular septa reminiscent of a row of beads. The beaded septum sign was initially described as a sign of lymphangitic spread of cancer although thoracic sarcoidosis in literature has been called the "great mimic" and can manifest with various patterns on HRCT like nodular septal thickening simulating the lymphangitic carcinomatosis. Other diseases responsible of this sign are amyloidosis and lymphoproliferative diseases (lymphoma, leukemia); please also refer to beaded septum sign in chapters "Septal Pattern" and "Case-Based Glossary with Tips and Tricks."

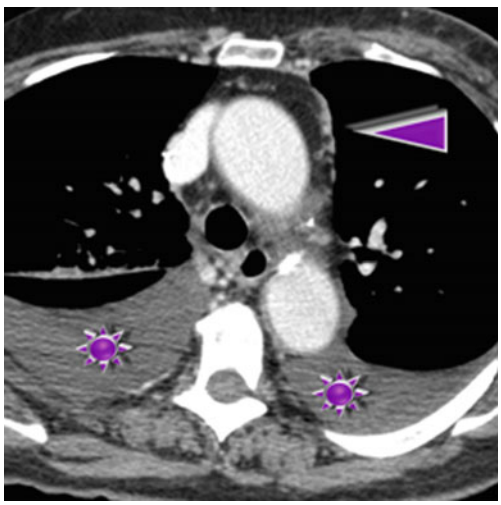
Honda O (1999) Comparison of high resolution CT findings of sarcoidosis, lymphoma, and lymphangitic carcinoma: is there any difference of involved interstitium? J Comput Assist Tomogr 23(3):374

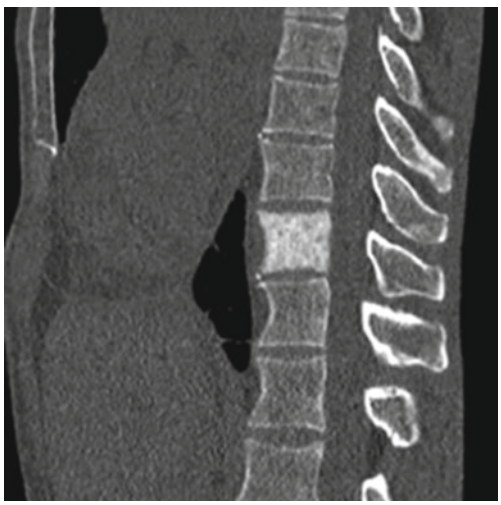
Ancillary Signs

- Intralobular septal thickening
- Patchy GGO
- Wedge densities located in the periphery of the lung, usually small in size (one or few contiguous lobules)

Non-parenchymal Signs

- Pleural effusion (✸)
- Pleural thickening, also nodular (►)
- Hilar and mediastinal lymphadenopathy
- Association with systemic metastasis (e.g., lytic and or sclerotic skeletal lesions)





Johkoh T (1992) CT findings in lymphangitic carcinomatosis of the lung: correlation with histologic findings and pulmonary function tests. AJR Am J Roentgenol 158(6):1217

Course and Complications

- Interlobular septal and bronchovascular bundle thickening and pulmonary nodules may increase in extent and size.
- CT signs of lymphangitic carcinomatosis may reduce after chemotherapy.
- Pleural and pericardial involvement may complicate lymphangitic carcinomatosis.

Lymphangitic carcinomatosis may happen through different pathways and usually progress by contiguity with involvement of interlobular septa (beaded reticulation), intralobular interstitium (ground-glass or small consolidations with geometric shape, sometimes into the crazy-paving pattern), and peribronchovascular bundle.

Follow-up: radiation therapy in oncologic patients can be a confounding factor because lung damage from radiation therapy and lymphangitic carcinomatosis look alike. The differential diagnosis can be based on the spatial distribution because diffuse lung abnormalities outside the radiation volume and bilateral distribution increase the level of confidence toward lymphangitic carcinomatosis.

Larici AR (2011) Lung abnormalities at multimodality imaging after radiation therapy for non-small cell lung cancer. Radiographics 31:771

Definition

Pulmonary edema is classified as cardiogenic (increase in interstitial fluid from high pulmonary hydrostatic pressure) or noncardiogenic (increase in interstitial fluid from high vascular permeability). Interstitial edema is characterized by infiltrates in the interstitial spaces of the lung, mostly in the loose peribronchovascular tissues and the interlobular septa.

PE

In more severe cases of pulmonary edema, the fluid accumulation is in the alveoli (please see PE, alveolar).

Komiya K (2013) Comparison of chest computed tomography features in the acute phase of cardiogenic pulmonary edema and acute respiratory distress syndrome on arrival at the emergency department. J Thorac Imaging 28:322

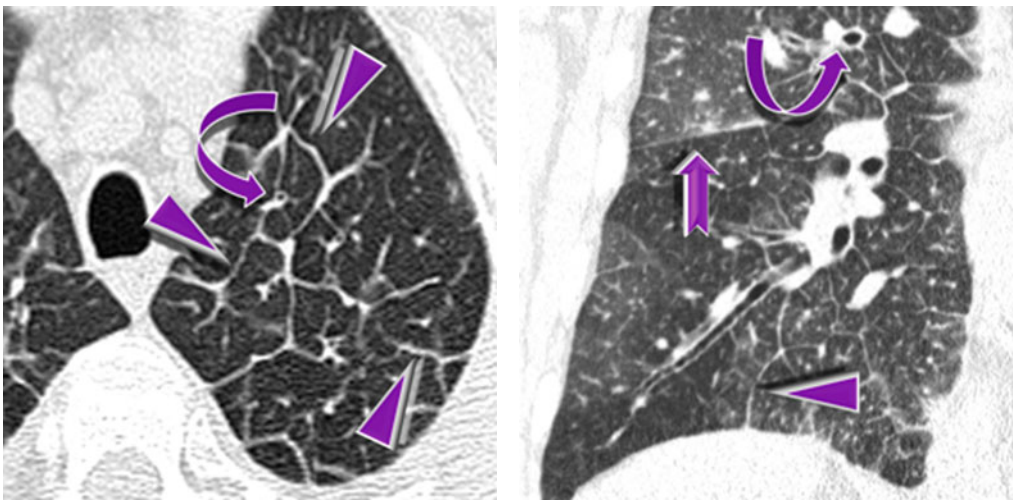
Key Signs

HIGH-RESOLUTION CT: HRCT

- Smooth thickening of interlobular septa (►)
- Smooth bronchovascular thickening (peribronchial cuffing) (⇘)
- Smooth subpleural thickening, easy visible at the fissural level (➡)
- Ground-glass opacity (GGO), patchy or lobular

Distribution

In most patients, pulmonary edema has a diffuse and random distribution, with some lobes more severely affected than others.



The absence of distortion of lung parenchyma and the more linear, smooth septal thickening, despite extensive involvement, helps to differentiate cardiogenic interstitial edema from fibrosing interstitial lung diseases.

In permeability edema vessels are not dilated and diffuse septal lines are rarely observed, whereas they are often the major feature associated with cardiogenic edema.

Scillia P (2004) Computed tomography assessment of lung structure and function in pulmonary edema. Crit Rev Comput Tomogr 45(5–6):293

Milne EN (1985) The radiologic distinction of cardiogenic and noncardiogenic edema. Am J Roentgenol 144:879

In papillary muscle rupture from myocardial infarction, acute mitral valve regurgitation causes pulmonary edema with selective involvement, usually the right upper lobe. Moreover, monolateral edema may be due to prolonged lateral decubitus.

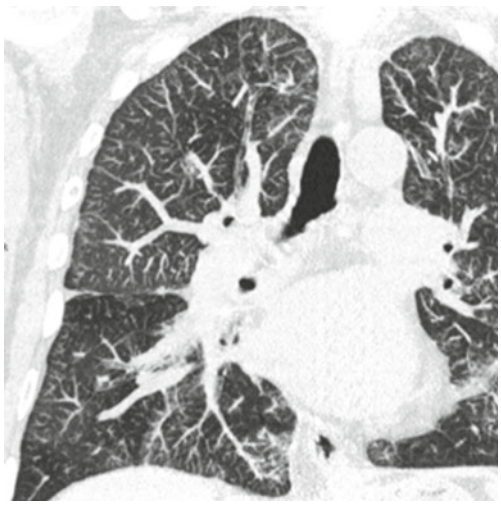
Gurney JW (1989) Pulmonary edema localized in the right upper lobe accompanying mitral regurgitation. Radiology 171(2):397

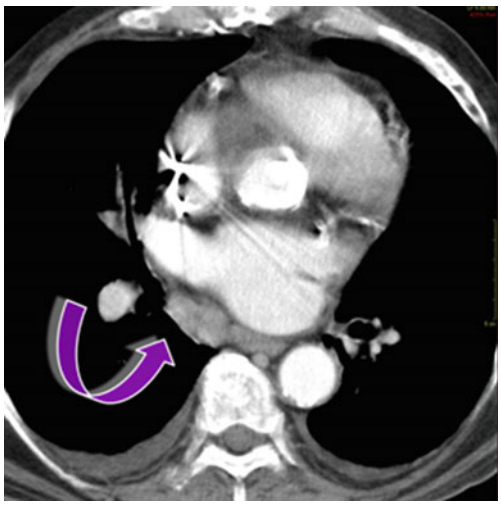
Ancillary Signs

- Possible crazy paving
- Low-density ill-defined centrilobular nodules
- Transient subpleural curvilinear opacities (possibly representing engorged lymphatics)

Non-parenchymal Signs

- Pleural effusion, more commonly bilateral
- Enlargement of pulmonary veins up to the left atrium and left cardiac chambers
- Enlarged mediastinal lymph nodes in nearly up to 50 % of cases ( )
- Haziness of mediastinal fat





Course and Complications

- Cardiogenic edema generally resolves with reduction of fluid overload.
- In cases of chronically elevated pulmonary venous hypertension, interstitial fibrosis-like changes might be expected on CT.

Marano R (2015) Comprehensive CT cardiothoracic imaging: a new challenge for chest imaging. Chest 147(2):538

Definition

Pulmonary veno-occlusive disease (VOD) is a rare disease characterized by narrowing of pulmonary venules and small veins caused by intimal fibrosis. Such abnormalities are associated to *postcapillary* pulmonary arterial hypertension (PAH).

VOD, pulmonary veno-occlusive disease (PVOD)

Montani D (2009) Pulmonary veno-occlusive disease. Eur Respir J 33:189

Mandel J (2000) Pulmonary veno-occlusive disease. Am J Respir Crit Care Med 162(5):1964

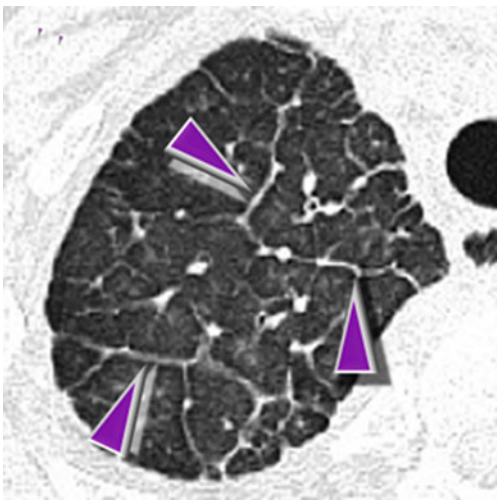
HIGH-RESOLUTION CT: HRCT

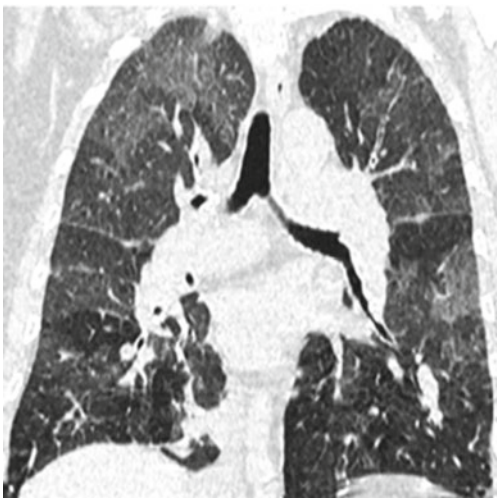
Key Signs

- Smooth thickening of interlobular septa (►)
- Ground-glass opacity, patchy or lobular (see coronal image below)

Distribution

Patchy involvement of both lungs with nondependent distribution; septal thickening may be diffuse over time.





Histologic correlation with CT findings has shown that thickened interlobular septa corresponded to the presence of septal fibrosis and venous sclerosis. GGO may be related to alveolar wall thickening or pulmonary edema.

The diagnosis is challenging and multidisciplinary (including pulmonary function test, hemogasanalysis, and right-heart catheterization); the presence of key signs provides good diagnostic accuracy in the appropriate clinical scenario. However, lung biopsy may be required to confirm diagnosis. PVOD is associated with extremely poor prognosis.

Frazier AA (2007) Pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis. Radiographics 27:867

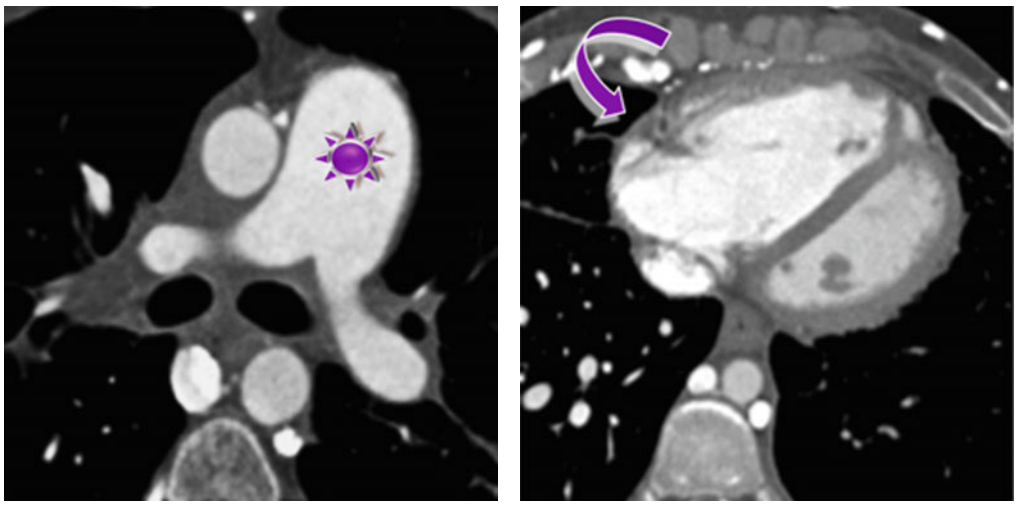
Miura A (2013) Different sizes of centrilobular ground-glass opacities in chest high-resolution computed tomography of patients with pulmonary veno-occlusive disease and patients with pulmonary capillary hemangiomatosis. Cardiovasc Pathol 22(4):287

Ancillary Signs

- Centrilobular ground-glass opacities
- Late-phase alveolar consolidation caused by edema, hemorrhage, or infarction

Non-parenchymal Signs

- Cardiovascular signs consistent with pulmonary hypertension, e.g., enlargement of pulmonary arteries (✸) and right-heart chambers (↻) with normal pulmonary veins and normal left cardiac chambers.
- Mediastinal lymph node enlargement.
- Pleural and pericardial effusion may be seen.



Early PVOD may show scant parenchymal findings that are easy to overlook. In addition, it may be observed in association with other conditions such as connective tissue disease.

Mineo G (2014) Pulmonary veno-occlusive disease: the role of CT. Radiol Med 119:667–673

Course and Complications

Interlobular septal thickening increases in extent. Ground-glass opacity and pleural effusion may appear and mimic pulmonary edema associated with pulmonary hypertension.

Thickened interlobular septa are more frequently associated with PVOD rather than pulmonary capillary hemangiomatosis (PCH), the latter being characterized by larger centrilobular ground-glass opacities.

Rossi A (2014) Rare causes of pulmonary hypertension: spectrum of radiological findings and review of the literature. Radiol Med 119(1):41