Article published online: 2024-08-26

Giant Cystic Pneumocytoma in a Young Male: Rare Diagnostic Conundrum with Clinicoradiological and Histopathological Features

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Indian J Radiol Imaging 2025;35:192–195.

Abstract

Pulmonary sclerosing pneumocytoma is a rare benign neoplasm typically seen in middle-aged women. The exact preoperative diagnosis is quite challenging considering its nonspecific clinical and radiologic features along with complex histology. Moreover, obtaining an exact histopathological diagnosis can be difficult especially with the small biopsy specimens. Most patients are generally asymptomatic with incidental detection of peripheral, homogenous, solitary pulmonary nodule. It is essential to differentiate it from other mimickers including malignant lesions as limited surgical resection is curative in these cases without adjuvant therapy. We present a rare giant cystic variant of pneumocytoma, in a young male, which was initially mimicking inflammatory myofibroblastic tumor even on preoperative histology.

Keywords

- giant cystic pneumocytoma
- inflammatory myofibroblastic tumor
- lobectomy
- pulmonary sclerosing hemangioma
- “air gap sign”
- “welt vessel” sign

Introduction

Pneumocytoma is a rare neoplasm of the lung, typically seen in young to middle-aged women. The nonspecific clinicoradiological features, coupled with complex histology, make the exact preoperative diagnosis difficult. It is often impossible to differentiate it from other lung neoplasms. We present an atypical case of cystic pneumocytoma, in a young male, confirmed on postoperative histopathology. The common imaging findings of pneumocytoma and its histological features are detailed.

Case Presentation

A 31-year-old male patient presented with a history of occasional hemoptysis, cough, and chest pain for the last 3 months. He had a history of pulmonary tuberculosis 2 years ago, for which he completed the treatment regime. Chest radiograph showed well-defined, sharply marginated, homogeneous radio-opacity in the left mid-zone, with a broad base toward the pleura (►**Fig. 1A**). Ultrasonography of the chest showed a well-defined, predominantly cystic lesion in the left lower lung, underlying the costal pleura. Peripheral

article published online
August 26, 2024

DOI https://doi.org/10.1055/s-0044-1789244.
ISSN 0971-3026.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

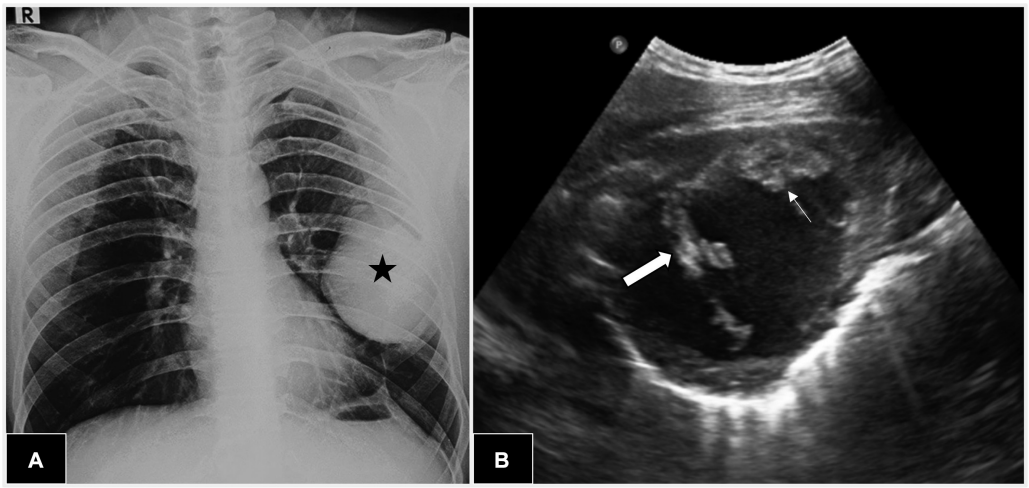

Fig. 1 (**A**) Chest radiograph showing a well-defined, sharply marginated, homogeneous radiopacity in the left mid-zone, with a broad base toward the pleura (*asterisk*). (**B**) On ultrasonography, the lesion showed soft-tissue components (*line arrow*) and a few thick internal septa (*thick arrow*).

lobulated soft-tissue components and a few thick internal septa were present (►**Fig. 1B**), with no vascularity on Doppler sonography. There was no pleural effusion. Contrast-enhanced computed tomography (CT) was done for further characterization of the lesion. CT demonstrated a well-defined, peripherally enhancing cystic lesion measuring 8.5 cm × 7.5 cm in the superior lingula, with peripheral soft-tissue nodules. The solid component showed an attenuation of 65 to 75 HU, while the cystic areas showed an attenuation of 20 to 32 HU. The lesion was extending up to the costal pleural surface, with ill-defined fat planes at places. The major fissure was displaced posteroinferiorly. A branch of the left pulmonary artery coursing close to the lesion was prominent (►**Fig. 2**). There were no intralesional calcifications. The overlying ribs were unremarkable. Based on these findings, in a young male, the imaging-based

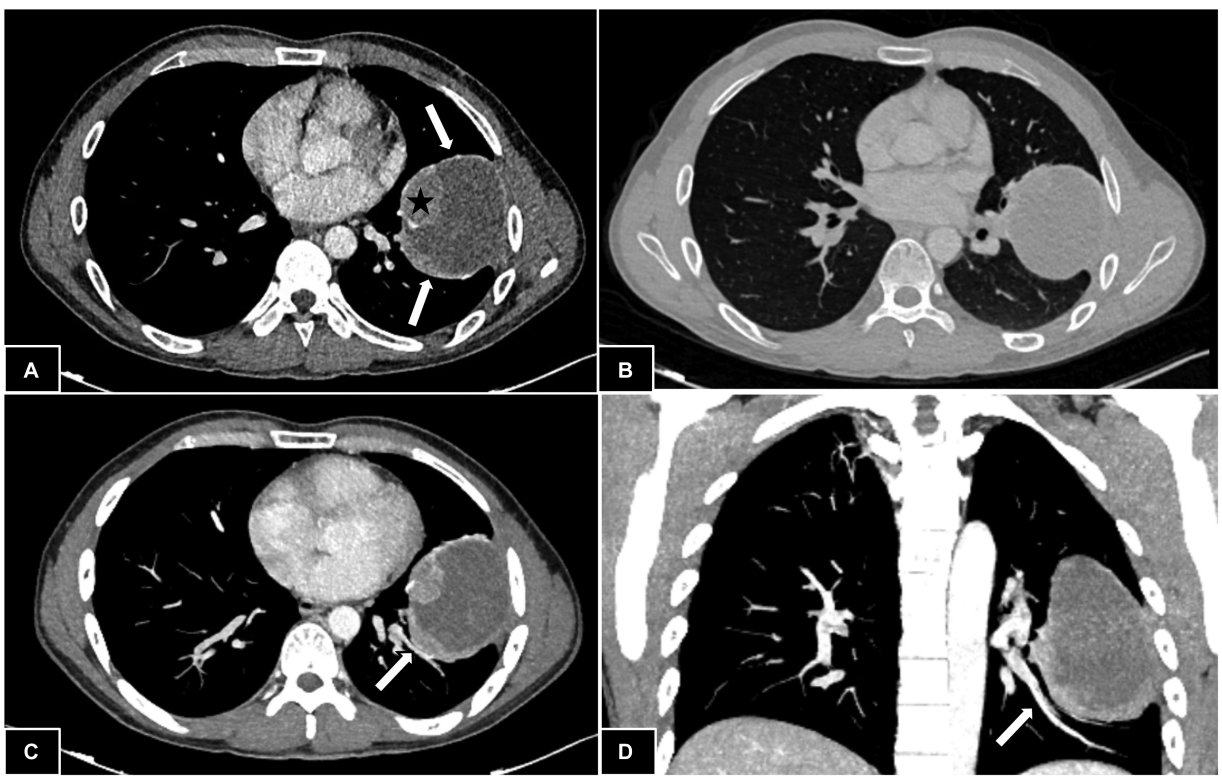

Fig. 2 (**A**) Axial computed tomography (CT) image (mediastinal window setting) shows a well-defined lesion in the superior lingula, which is predominantly cystic, with an enhancing nodule (*asterisk*). An enhancing "pseudocapsule" is seen (*white arrow*). Fat planes with the pleura are indistinct at places. (**B**) Axial image in the lung window setting showing the lesion. The overlying ribs are unremarkable. (**C**) Axial and (**D**) coronal maximum intensity projection (MIP) CT images showing the "welt vessel" sign (*arrows*).

differentials that were considered included inflammatory myofibroblastic tumor (IMT), sarcoma, and complicated bronchogenic cyst. CT-guided biopsy from the lesion showed spindle cells arranged in fascicular and storiform pattern. The cells were mildly pleomorphic with moderate cytoplasm. Surrounding areas showed lymphocytic and plasma cell infiltrate. These findings were suggestive of IMT.

The patient underwent left upper lobectomy via a posterolateral thoracotomy. The cut surface of the mass showed two cystic spaces filled with hemorrhagic material and clots. The surrounding pleura and lung parenchyma showed areas of hemorrhage. Postoperative histopathology (►**Fig. 3**) showed cysts with predominantly denuded lining epithelium. The cyst wall showed loosely arranged round to oval-shaped cells with bland chromatin. There were areas of hemorrhage with hemosiderin-laden macrophages and cholesterol clefts, admixed with inflammatory cells. Adjacent alveolated lung parenchyma showed hemorrhage and macrophages in the alveoli. Immunohistochemistry (IHC) was reactive for thyroid transcription factor 1 (TTF-1), and non-reactive for cytokeratin 7 (CK-7) and anaplastic lymphoma kinase (ALK). Few round cells in the cyst wall were reactive for smooth muscle actin (SMA). These features were suggestive of cystic variant of sclerosing pneumocytoma. The patient had an uneventful postoperative period and is on follow-up.

Discussion

Pneumocytoma was described as a tumor of vascular origin and was earlier known as pulmonary sclerosing hemangioma. However, due to its proven origin from type II pneumocytes, it is categorized as an adenoma, in the classification of lung tumors proposed by the World Health Organization (WHO) in 2015.[1] It is a rare tumor of the lung, accounting for 0.2 to 1% of benign pulmonary tumors and is predominantly seen in middle-aged women.[2] While most patients are asymptomatic, the common presenting symptoms include cough, hemoptysis, and chest pain.

On radiograph, pneumocytoma appears as a sharply marginated round or ovoid, homogenous opacity. CT findings are nonspecific; however, it appears as a well-defined, solitary, homogenous nodule or mass, usually smaller than 3 cm in size. Smaller lesions show homogenous enhancement, whereas larger lesions are predominantly composed of nonenhancing areas, which likely represent intralesional hemorrhage.[3] Pleural attachment is common and this is described as a reliable imaging feature.[3] Few pointers have been described, which, if present, should raise the suspicion of pneumocytoma on cross-sectional imaging.[3–5] The "welt vessel" sign or "overlying vessel sign" refers to an engorged vessel adjacent to the lesion. The vessel, however, does not penetrate the lesion. The lesion is also described to have an enhancing "pseudocapsule" made of the compressed lung parenchyma. The "air gap sign" refers to the crescent-shaped low-attenuation area surrounding the mass, devoid of lung markings, appreciated on the lung window setting. Although not seen in the current case, it has been shown to have a higher specificity on imaging.[6] There are a few hypotheses explaining this sign. Bahk et al[7] postulated that the hyalinization of undifferentiated alveolar mesenchymal cells encases the bronchioles and leads to distension of the distal air spaces. Sagara et al[8] suggested that peritumoral hemorrhage and airway communication could result in air space around the tumor, which on microscopy was surrounded by hemosiderin-laden macrophages. Matsuyama et al[9] suggested that peritumoral hemorrhage and tumor contraction lead to the air gap sign. The ground-glass attenuation surrounding the lesion is referred to as the "halo sign" and represents peritumoral hemorrhage.[6]

Although nonspecific, the majority of pneumocytomas are fluorodeoxyglucose (FDG) avid, and the maximum standard uptake value (SUVmax) correlates with the tumor size. The higher FDG avidity of large tumors may lead to a false diagnosis of malignancy.[10] Various studies have reported mean SUVs in the range of 0.6 to 4.7.[10–12]

Rarely, the tumor can be bilateral and present as multiple random nodules. Although typically categorized as a benign tumor, instances of potentially malignant pneumocytomas

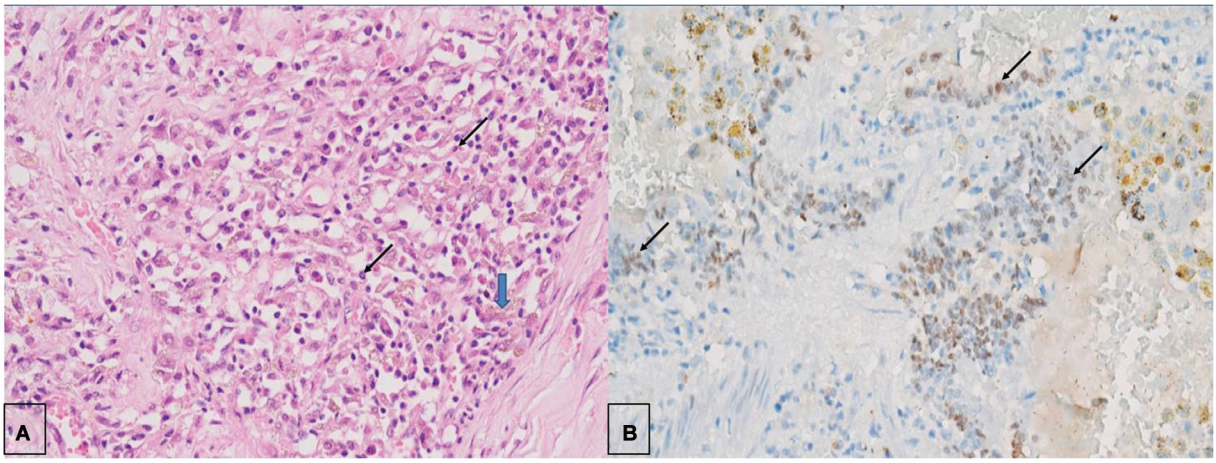

Fig. 3 Histopathology of the excised specimen. (**A**) Sclerosing pneumocytoma showing solid and cystic pattern with tubules lined by cuboidal cells (*black thin arrows*) and surrounding stromal cells. Inflammatory cells and hemosiderin (*blue thick arrow*) are also noted (H&E, ×400). (**B**) The cuboidal cells lining the tubules show positivity for TTF-1 (*black arrows*; TTF-1 immunostain, ×400). TTF-1, thyroid transcription factor 1.

have been reported. Large tumor volume increases the possibility of malignancy. Other associated findings include mediastinal lymphadenopathy, endobronchial invasion, and skeletal metastases.[13–17]

The nonspecific appearance of pneumocytoma on CT makes the radiological diagnosis elusive. Owing to its peripheral location and heterogeneous appearance, it can be misdiagnosed as an adenocarcinoma, and CT texture analysis can be used in differentiating the two.[18] In endemic areas, tuberculosis is an important differential diagnosis, especially in the presence of lymphadenopathy.[19] Giant, isolated pneumocytomas mimic sarcoma, teratoma, and IMT, as in the current case. Pleuropulmonary IMTs present in young males. They are solitary tumors with a predilection for the peripheral lung. They can attain a large size and there may be associated pleural invasion and overlying rib erosion.

Aspiration cytology and frozen sections may be inconclusive, and histopathology provides the definitive diagnosis. The tissue morphology is complex and comprises of four components (hemangiomalike areas, adenoid papillary areas, solid cellular areas, and fibrosclerotic areas) and two tumor cell types (cuboidal and stromal cells). Tumors with atypical histology may be misdiagnosed as papillary or solid subtype of lung adenocarcinoma, or as a neuroendocrine tumor.[20] In fact, IMTs also show spindle cells on histopathology. However, IHC clinches the diagnosis: pneumocytomas are positive for TTF-1 and epithelial membrane antigen (EMA) in surface cuboidal cells and round interstitial cells.[21] Cystic variant of pneumocytoma is rare and is accompanied by hemorrhage in at least a third of the cases.[22]

Asymptomatic patients with incidentally detected lesions can be followed up with serial imaging. When symptomatic, limited surgical resection of the tumor is advocated. However, due to nonspecific imaging features and a confusing histological appearance, many patients undergo lobectomy. Postoperative histopathology is crucial for diagnosis, as in our case.

Funding
None.

Conflict of Interest
None declared.

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