Radiology

Case 323: Minute Pulmonary Meningothelial-like Nodules

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Conflicts of interest are listed at the end of this article.

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History A 70-year-old woman with a 6-year history of asthma, a 12-year history of diabetes mellitus, and who did not smoke presented to the pulmonology clinic with dyspnea and cough. Chest CT performed 5 years earlier for similar symptoms revealed multiple pulmonary nodules. However, she was lost to follow-up before the work-up was concluded. Otherwise, her medical history was unremarkable. Family history included maternal endometrial cancer. Physical examination revealed partial oxygen saturation of 98%, respiratory rate of 18 breaths per minute, and heart rate of 77 beats per minute. Her breath sounds and other systemic findings were normal. Pulmonary function test results were as follows: forced expiratory volume in 1 second, 108% predicted (normal range, 80%–120%); total lung capacity, 72% predicted (normal range, 80%–120%); forced vital capacity, 101% predicted (normal range, 80%–120%); diffusing capacity for carbon monoxide, 69% predicted (normal range, 60%–120%); and forced midexpiratory flow, 85% predicted (normal range, 40%–160%). Complete blood count, erythrocyte sedimentation rate, C-reactive protein level, rheumatoid factor, and antinuclear antibody levels were within normal limits. The patient underwent volumetric thin-section CT of the chest using a multidetector CT scanner (Ingenuity Core 128; Philips Medical Systems) to evaluate lung nodules and pulmonary interstitium.

Part one of this case appeared 4 months previously and may contain larger images.

Imaging Findings

The initial unenhanced chest CT images obtained 5 years earlier showed randomly distributed small (≤6 mm) ground-glass nodules (Fig 1). High-resolution CT of the chest revealed numerous small ground-glass nodules with a random distribution in both lungs. Some of the nodules showed central lucencies with a ringlike appearance (Cheerio sign) (Fig 2) (1). The pulmonary nodules were essentially unchanged when compared with the chest CT images 5 years earlier. There was no mediastinal or hilar lymphadenopathy. The patient underwent a surgical lung biopsy. Histopathology revealed numerous bland spindle cell proliferations expanding the alveolar septa and resembling meningothelial cells with a whorl formation. Immunohistochemical staining was positive for progesterone receptors and epithelial membrane antigen but negative for synaptophysin (Fig 3). On the basis of the radiologic and histopathologic findings, the patient was diagnosed with minute pulmonary meningothelial-like nodules (MPMNs) and diffuse pulmonary meningotheliomatosis. The patient was observed clinically, without any additional treatment recommendations.

Discussion

MPMNs, also known as minute meningothelioid nodules, are a rare pathologic condition identified with increasing frequency and characterized by meningothelial-like cellular proliferation within the lung interstitium (2,3). The characteristic CT findings of MPMNs include multiple, small, and randomly distributed ground-glass nodules with central lucencies (ringlike appearance) (3–6).

The etiopathogenesis of MPMNs is unknown. It usually affects nonsmoking women in their sixth or seventh decade of life, as in the present case (4,5). MPMNs are usually incidentally discovered in surgical or autopsy lung specimens. Patients with MPMNs may be asymptomatic or may present with dyspnea or cough (4,5). MPMNs should be considered in the differential diagnosis of multiple pulmonary nodules (6), which includes pulmonary Langerhans cell histiocytosis (PLCH), multifocal lung adenocarcinoma, metastases, rheumatoid nodule, granulomatous polyangiitis, multifocal micronodular pneumocyte hyperplasia (MMPH), diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH), nonfibrotic hypersensitivity pneumonitis, and cavitary sarcoidosis (6,7).

On the basis of clinical findings alone, it can be challenging to distinguish these causes of multiple pulmonary nodules. Thin-section CT of the chest can help in diagnosing MPMN. Histopathologic examination and immunohistochemical staining are required to establish the definitive diagnosis.

PLCH can also cause multiple cavitary pulmonary nodules. However, it usually affects young male smokers and shows a predilection for the upper and mid lung, while the lung bases are often spared (8). Moreover, PLCH is usually progressive. Therefore, the long-term stability seen in this case is inconsistent with PLCH.

Persistent multiple ground-glass nodules on follow-up CT scans may be associated with early-stage adenocarcinoma of the lung (6). While it can grow slowly, 5-year stability is inconsistent with malignancy. Similarly, pulmonary nodules associated with metastasis, rheumatoid

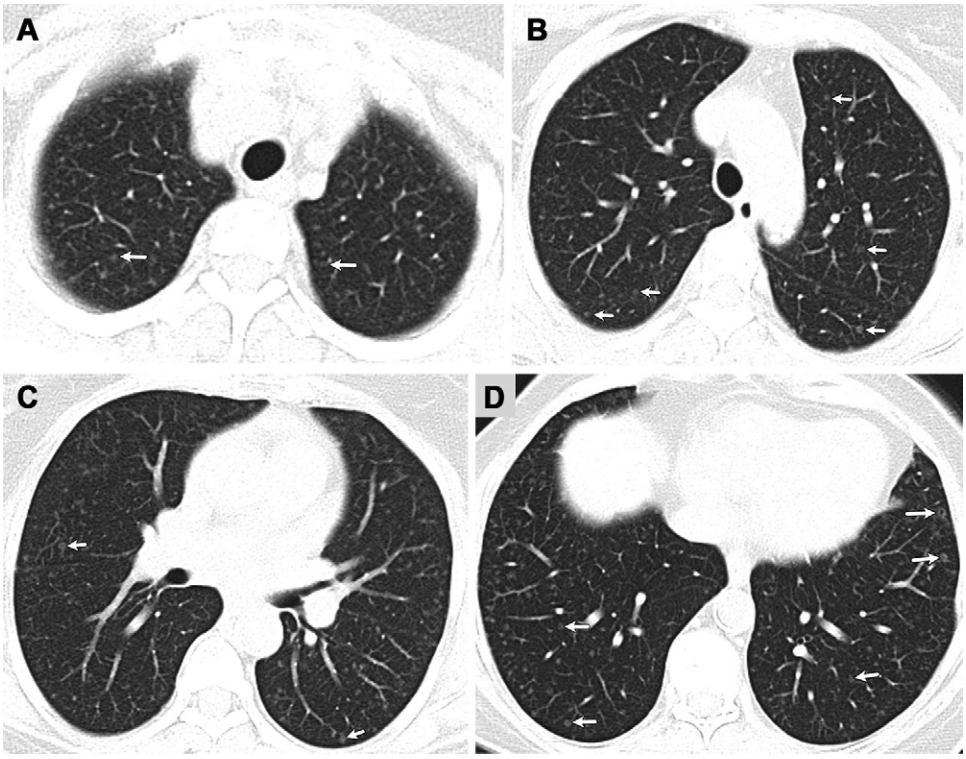

Figure 1: Axial unenhanced chest CT images obtained 5 years before current presentation. Selected images from **(A)** apices, **(B)** arcus aorta, **(C)** lingular bronchus, and **(D)** basal lung levels using lung window settings (16 × 1.5-mm collimation, 120-kV tube voltage, 130-mA tube current, 512 × 512 matrix, 1.5-mm section thickness). Images were also reconstructed with 1.0-mm section thickness. There are multiple, randomly distributed small (≤6 mm) ground-glass nodules. Note that some nodules include central lucencies (ringlike appearance) (arrows).

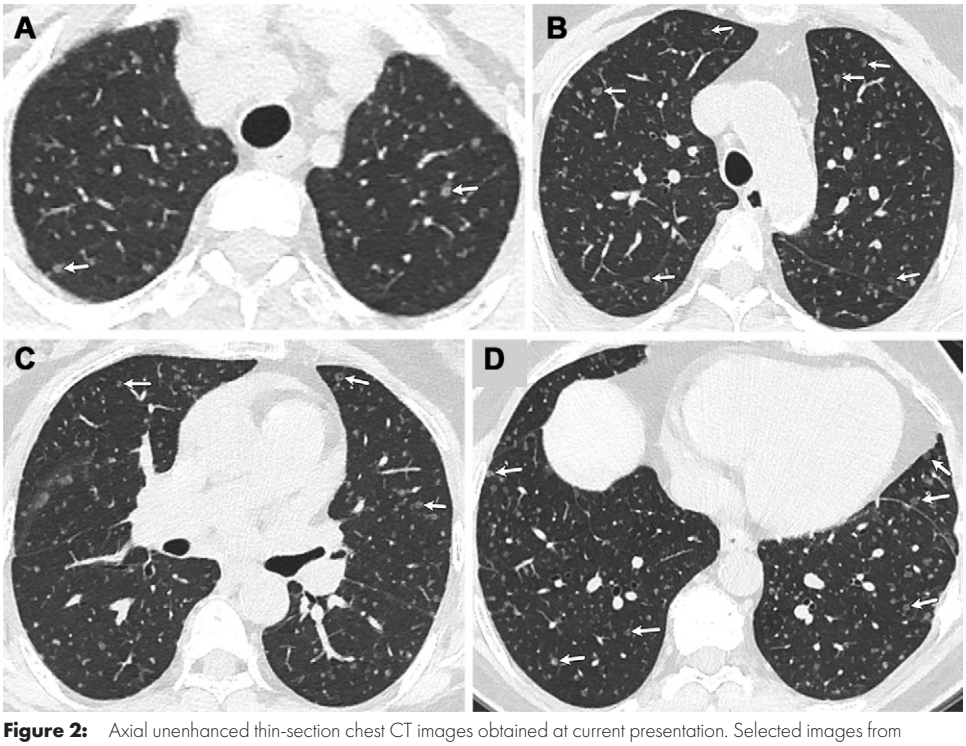

Figure 2: Axial unenhanced thin-section chest CT images obtained at current presentation. Selected images from **(A)** apices, **(B)** arcus aorta, **(C)** lingular bronchus, and **(D)** lower lung using lung window settings (64 × 0.625-mm collimation, 100-kV tube voltage, 350-mA tube current, 512 × 512 matrix, and 1.0-mm section thickness). Images were also reconstructed with 0.5-mm section thickness using a high-spatial-frequency algorithm. There are multiple, randomly distributed small (≤6 mm) ground-glass nodules. Again, some of the nodules include central lucencies (ringlike appearance) (arrows).

nodule, and granulomatous polyangiitis are not expected to remain stable for 5 years (6). Moreover, the patient had normal laboratory findings inconsistent with rheumatoid arthritis, granulomatous polyangiitis, or infection.

MMPH is a rare cause of multiple pulmonary nodules and is seen frequently in patients with the tuberous sclerosis complex. Hisopathologically, MMPH is characterized by benign hamartomatous proliferation of type II pneumocytes, often occurring concurrently with pulmonary lymphangioleiomyomatosis (8). Chest CT shows randomly distributed, well-defined small ground-glass nodules and thin-walled, well-defined, scattered round lung cysts. Although pulmonary nodules in MMPH can be stable for many years, as in the present case, central lucency is not an expected CT finding (8). Moreover, the present case did not have lung cysts consistent with lymphangioleiomyomatosis at CT and did not have a clinical history of tuberous sclerosis complex.

DIPNECH is a disease of unknown origin characterized by abnormal proliferation of pulmonary neuroendocrine cells secreting hormones, causing airway inflammation and fibrosis, which may result in constructive bronchiolitis (9). In patients with DIPNECH, uniform nodules are seen throughout both lungs and have well-defined margins on chest images. These nodules do not grow or change over time. Moreover, CT usually shows mosaic attenuation due to air trapping with thickened bronchial walls, which is absent in the present case. While DIPNECH is commonly seen in nonsmoking middle-aged women, central lucency is not an expected CT finding in DIPNECH nodules (9).

Nonfibrotic hypersensitivity pneumonitis (HP), previously known as subacute HP or extrinsic allergic alveolitis, is characterized by an immune-mediated inflammation of the bronchi and peribronchiolar lung tissue caused by inhalation of organic or nonorganic allergens (10). Histopathologically, HP is characterized by poorly defined noncaseating granulomas, cellular bronchiolitis, and giant cells in the pulmonary interstitium or alveoli. Radiologically, HP is characterized by small (<5 mm) centrilobular ground-glass nodules with indistinct borders, mosaic attenuation with air trapping, and patchy areas of ground-glass opacity. Ground-glass nodules in the nonfibrotic HP may contain a small central lucency caused by air in a patent bronchiole and can mimic MPMN radiologically (10). However, unlike MPMN, in nonfibrotic HP, the nodules are smaller and more numerous, and the subpleural lung is spared. While patients with MPMN are generally asymptomatic, nonfibrotic patients with HP usually have signs of small airway disease, and CT usually shows evidence of air trapping.

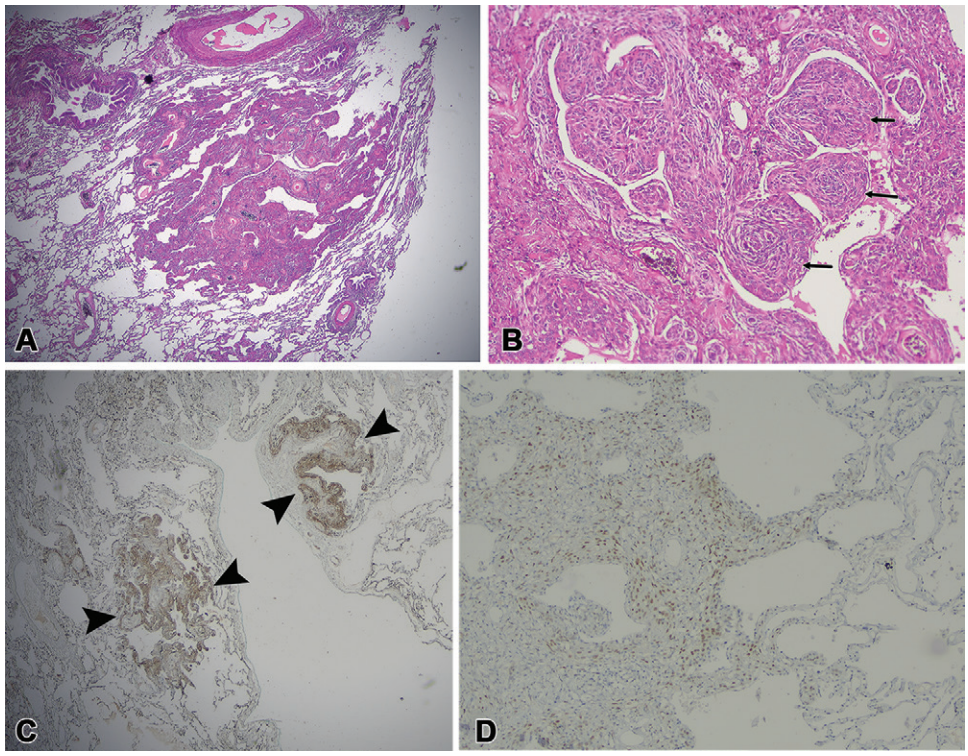

Figure 3: Right lower lobe lung biopsy specimen. **(A)** Photomicrograph shows numerous foci of cellular proliferation expanding the alveolar septa. (Hematoxylin-eosin stain; original magnification, ×20.) **(B)** Photomicrograph shows numerous cellular proliferations expanding the alveolar septa and resembling meningothelial cells with a streaming arrangement in syncytial sheets and whorl formation (arrows). (Hematoxylin-eosin stain; original magnification, ×100.) **(C)** Immunohistochemical staining for epithelial membrane antigen shows positive staining (arrowheads). (Original magnification, ×20.) **(D)** Immunohistochemical staining for progesterone receptors shows positive staining. (Original magnification, ×100.)

Pulmonary cavitary sarcoidosis (PCS) is a rare manifestation of sarcoidosis. The prevalence of PCS has been reported as 2.2%, and cavitary lesions are usually seen in patients with severe and active sarcoidosis (7). Radiologically, PCS is generally characterized by thin-walled, multiple, and multiloculated cavitary lesions with the upper lobe predominance, and rarely can septae inside the cavity be found. In PCS cases, the pericavitary space is often affected by nodules, micronodules, ground-glass opacity, consolidation, or fibrosis (7). However, the lung parenchyma surrounding the nodules was normal in the present case. Hours et al (7) reported the median diameter of cavitary lesions in patients with PCS was 20 mm (range, 11–100 mm). However, unlike PCS, the nodules in the present case were much smaller and did not contain apparent cavitation.

In conclusion, this patient had nonspecific respiratory symptoms and randomly distributed ground-glass nodules with central lucencies that were stable over 5 years, suggesting a benign process. The CT appearance and long-term stability favored a diagnosis of MPMNs, confirmed at histopathology. Thin-section CT of the chest helps in diagnosing MPMN and its differentials.

Disclosures of conflicts of interest: F.U. No relevant relationships. **E.K.** No relevant relationships. **F.B.** No relevant relationships. **G.A.** No relevant relationships.

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Congratulations to the 59 individuals and nine resident groups that submitted the most likely diagnosis (minute pulmonary meningothelial-like nodules) for Diagnosis Please, Case 323. The names and locations of the individuals and resident groups, as submitted, are as follows:

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