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CHEST Imaging and Pathology for Clinicians

(1) Title Page

Title: Rare diagnosis of a multilobular pulmonary mass

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CASE PRESENTATION:

A 57-year-old woman was admitted to our hospital for an abnormal chest shadow found during routine chest radiography. She did not have any respiratory symptoms. Her medical history included dyslipidemia. Her surgical history included conization for cervical cancer at age 38 years. She was a social drinker, ex-smoker of approximately 10 cigarettes per day (from ages 20 to 30 years), and denied recreational drug use. A review of systems yielded negative results. The woman was afebrile with no acute distress. The respiratory and cardiac portions of the physical examination indicated no abnormalities. Furthermore, her laboratory results indicated no abnormalities. Her chest radiogram showed an oval nodule in the left lower lung field. Non-contrast computed tomography (CT) indicated a 3.4- × 2.4-cm, well-demarcated, lobular solid mass in the lower lobe of the left lung without lymphadenopathy. The tumor was slightly enhanced from 18 HU to 36 HU on contrast-enhanced images (Figure 1). We subsequently performed positron emission tomography CT (PET/CT), which indicated slight accumulation in the mass and a maximal standardized uptake value (SUV max) of 1.59. There was no abnormal activity within the thoracic lymph nodes, and no extra-thoracic abnormalities were present. The patient subsequently underwent endobronchial ultrasound-guided transbronchial biopsy of the left B9 (EBUS-GS-TBB) using a 2.0-mm radial EBUS probe (Olympus, Tokyo, Japan) (Figure 2). Cytology results suggested lymphoid cell infiltration, and cytopathologic findings suspicious for bacterial infection or epithelioid granulomas were not pointed out.

Because of the location and mild uptake according to PET/CT, nontuberculous mycobacteriosis, actinomycosis, and mucinous neoplasm were considered the differential diagnoses. We decided that surgical resection was necessary to confirm the diagnosis.

The patient underwent video-assisted thoracoscopic (VATS) left lower lobectomy with lymph node dissection. The postoperative course was uneventful, and she was discharged home on postoperative day 4.

The macroscopic examination of formalin-fixed specimens revealed a solitary multilocular cystic lesion measuring 4.0 × 3.5 × 2.4 cm in the resected lung. According to the bacterial examination, the cyst contents comprised mucous fluid without bacteria. Each loculus was separated by a thin fibrous septum, and its inner surface appeared flat and smooth, thus indicating a cavernous appearance. No discernible nodules or evidence of hemorrhage were found (Figure 3). Additionally, lung parenchyma other than the aforementioned lesion appeared essentially normal, without any emphysematous or cystic changes.

Microscopic observation demonstrated that the inner surfaces of these cysts were sparsely lined by bland cuboidal cells in the monolayer (Figure 4A). Immunohistochemical (IHC) staining showed that these cells were positive for CD31, CD34, and podoplanin (D2-40) and negative for cytokeratin (AE1/AE3) (Figure 4B). There were no histopathological findings indicating pulmonary emphysema, interstitial pneumonitis, or lymphangioleiomyomatosis (LAM). Additionally, there was

no evidence of malignancy, which might cause secondary multilocular expansion of the peripheral structures.

What is the diagnosis?

Diagnosis: Pulmonary cavernous lymphangioma

Discussion:

Clinical Discussion

Lymphangiomas are rare, benign lymphatic malformations that are composed of cystically dilated lymphatic vessels, which are caused by a developmental defect or primary malformation of the lymphatic channels.[1] They are classified into three pathologic categories: lymphangioma simplex; cavernous lymphangiomas; and cystic lymphangiomas. Lymphangiomas can occur in any part of the body; the most common sites are the neck (75%) and axilla (20%). Although mediastinal lymphangioma is not uncommon (0.7% to 4.5%), especially in children, pulmonary lymphangioma is extremely rare. According to our literature search, only 17 cases, including the present case, have been reported in the international literature to date.[2]

In terms of cavernous lymphangioma, only 8 cases have been reported.[3-8] An analysis of the complete series, including this case, indicated that the patient age ranged from 2 days to 59 years. The female-to-male ratio was 7:10. Half of the patients were asymptomatic, and the lesion

was found accidentally on chest radiography or CT; the rest caused a variety of symptoms such as cough, dyspnea, hemoptysis, retrosternal chest pain, pneumothorax, and respiratory distress.[9] There is a tendency for adult patients to be asymptomatic and for pediatric patients to exhibit symptoms. This may be because the size of tumor compared to the size of the thoracic cavity is larger in children than in adults. The maximum diameter ranged from 1.5 to 18 cm. The lesions were randomly distributed without any propensity for the right or left lung.

Radiologic Discussion

The most common finding of lymphangioma on CT is a uniformly cystic structure with smooth margins. Pulmonary lymphangiomas with a non-cystic appearance (lobular solid mass, as in the present case) appear to be rare. Most of the previous cases involved a poorly demarcated mass with uniform density. In contrast, the current case involved a well-demarcated, lobular, solid mass.

No definite enhancement was observed after intravenous administration of contrast material. Magnetic resonance imaging (MRI) of lymphangiomas shows a signal similar to that of the muscle on T1-weighted images, with a marked signal increase on T2-weighted images that is greater than that of fat, thus reflecting the fluid content.[10] Only 2 cases underwent PET-CT, including the present case, and both cases showed slight accumulation.[6] However, these findings are not sufficiently characteristic to reliably differentiate lymphangioma from non-small cell lung

cancer, bronchogenic cyst, and hemangioma..

There have been no reports of EBUS findings for pulmonary lymphangioma. In the present case, EBUS showed a low-echoic cystic mass. It seemed more similar to the macroscopic image because CT showed a solid mass. Therefore, EBUS imaging might be useful for diagnosing pulmonary lymphangiomas.

Pathologic Discussion

Several differential diagnoses should be addressed when localized multilocular cystic lesions of the peripheral lung are observed. Based on the macroscopic and histopathologic findings, in addition to the clinical information, pulmonary emphysema and LAM could be excluded. In cases of malignant neoplasms, primary lung or metastatic lesions might be the cause of cysts in the peripheral lung; however, this was not the case in the present case. Regarding vascular lesions, there might be difficulty differentiating lymphangiomas from hemangiomas. The lack of evidence of hemorrhage in this case strongly suggested that this lesion was not hemangiomatous. For this differential diagnosis, the detection of immunohistochemical markers is useful.[6] Among these, CD31, CD34, and podoplanin (detected by antibody D2-40) are widely used as markers of lymphangiomas, and a combination of these tests may increase the diagnostic accuracy.[5] CD31 and CD34 are relatively sensitive and specific markers of endothelial differentiation that are expressed in the majority of vascular tumors. Podoplanin is a cell surface sialoglycoprotein

expressed in the lymphatic endothelium and select epithelia. In this case, by performing IHC staining using anti-CD31 and CD34 antibodies and D2-40, we clearly confirmed that this lesion consisted of cavernous lymphatic dilation. A combination of IHC stains would increase the diagnostic accuracy when differentiating lymphangioma from hemangioma.

In terms of multilocular cyst formation, most lung lymphangiomas are characterized by a uni-cystic or pauci-cystic structure. A solitary lung lymphangioma with a cavernous appearance (as in the present case) seems to be rare.

Conclusions:

We encountered a rare case of pulmonary cavernous lymphangioma. Lymphangioma should be considered as the differential diagnosis of a pulmonary tumor. We confirmed the diagnosis from surgical resected specimen. Postoperative imaging showed no recurrence for 1 year after surgery.

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Figure Legends:

Figure 1. Axial and coronal sections of computed tomography (CT) images of the lung demonstrating a well-demarcated, lobular, solid mass (black arrows) in the lower lobe of the left lung measuring 3.4 x 2.4 cm in diameter.

Figure 2. EBUS showing a low-echoic lobulated mass. Transbronchial biopsy of the left B9 was performed.

Figure 3. Macroscopic finding of a 4.0- x 3.5- x 2.4-cm specimen. The cut surface demonstrates a dilated multi-cystic lesion.

Figure 4. A. Histologic analysis showing a cyst containing eosinophilic fluid. The cyst wall is lined with a single layer of endothelium. **B.** Immunohistochemical examination showed that the single layer of epithelial cells lining the cyst was positive for podoplanin and CD31.

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Figure 1

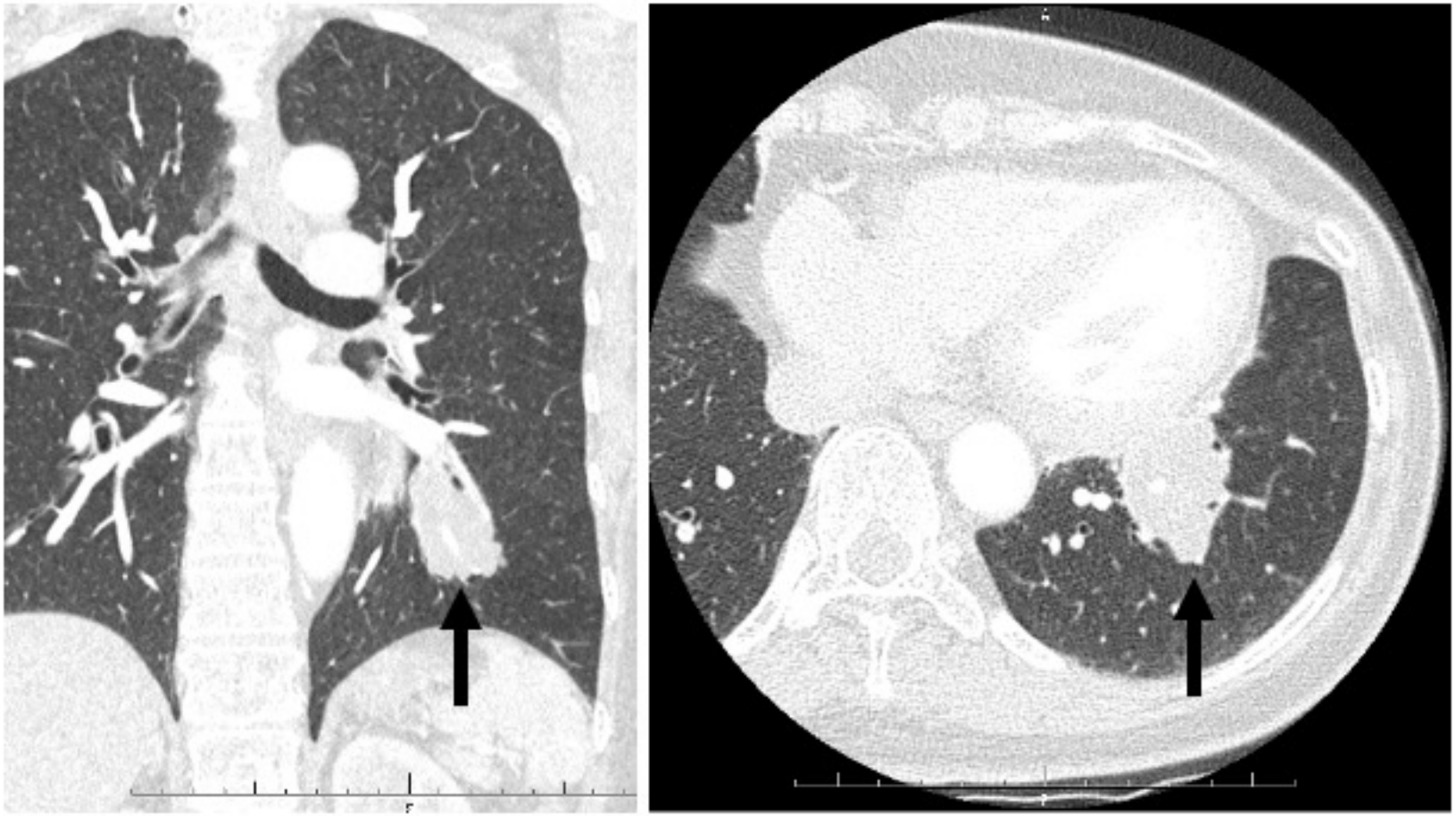
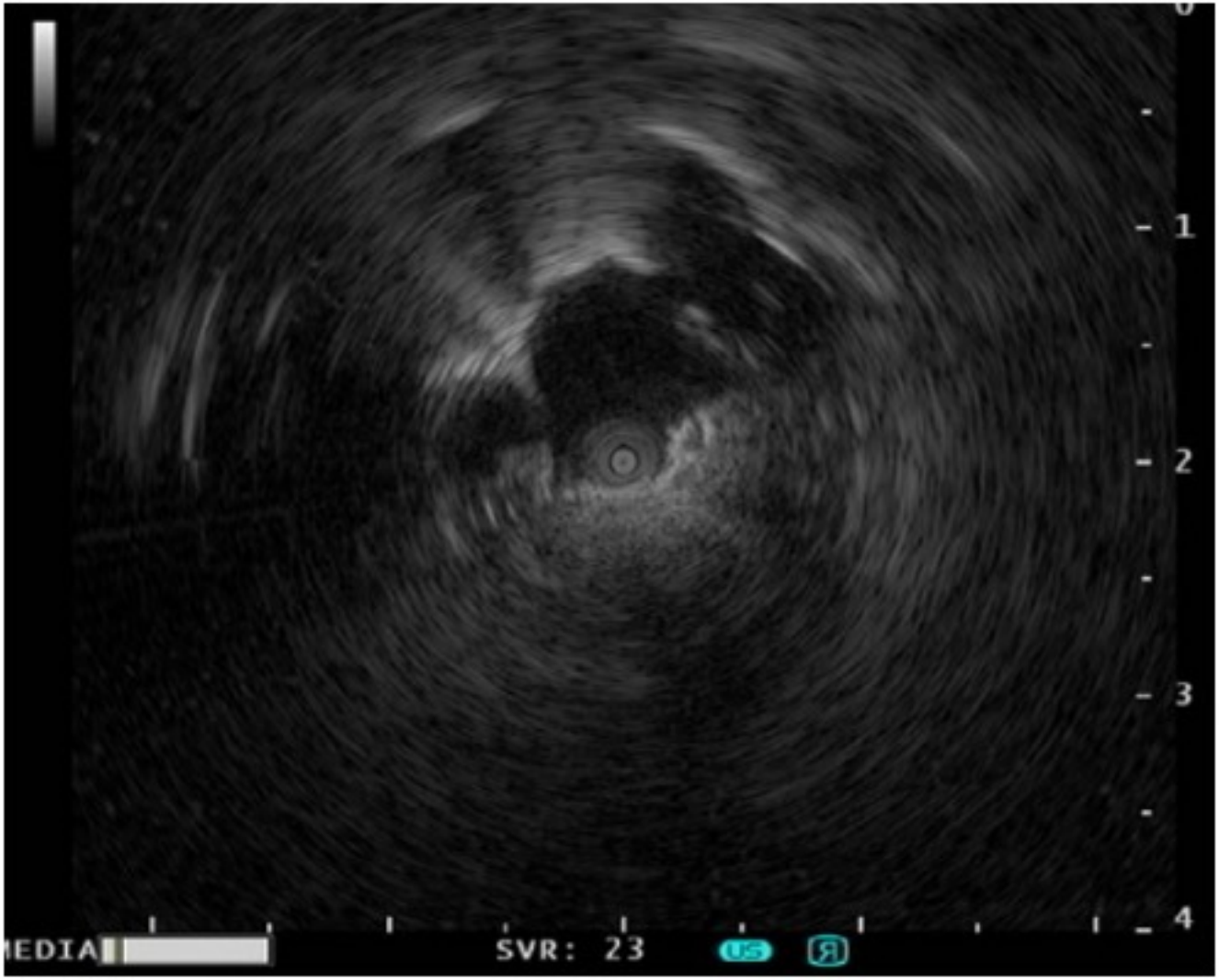


Figure 2



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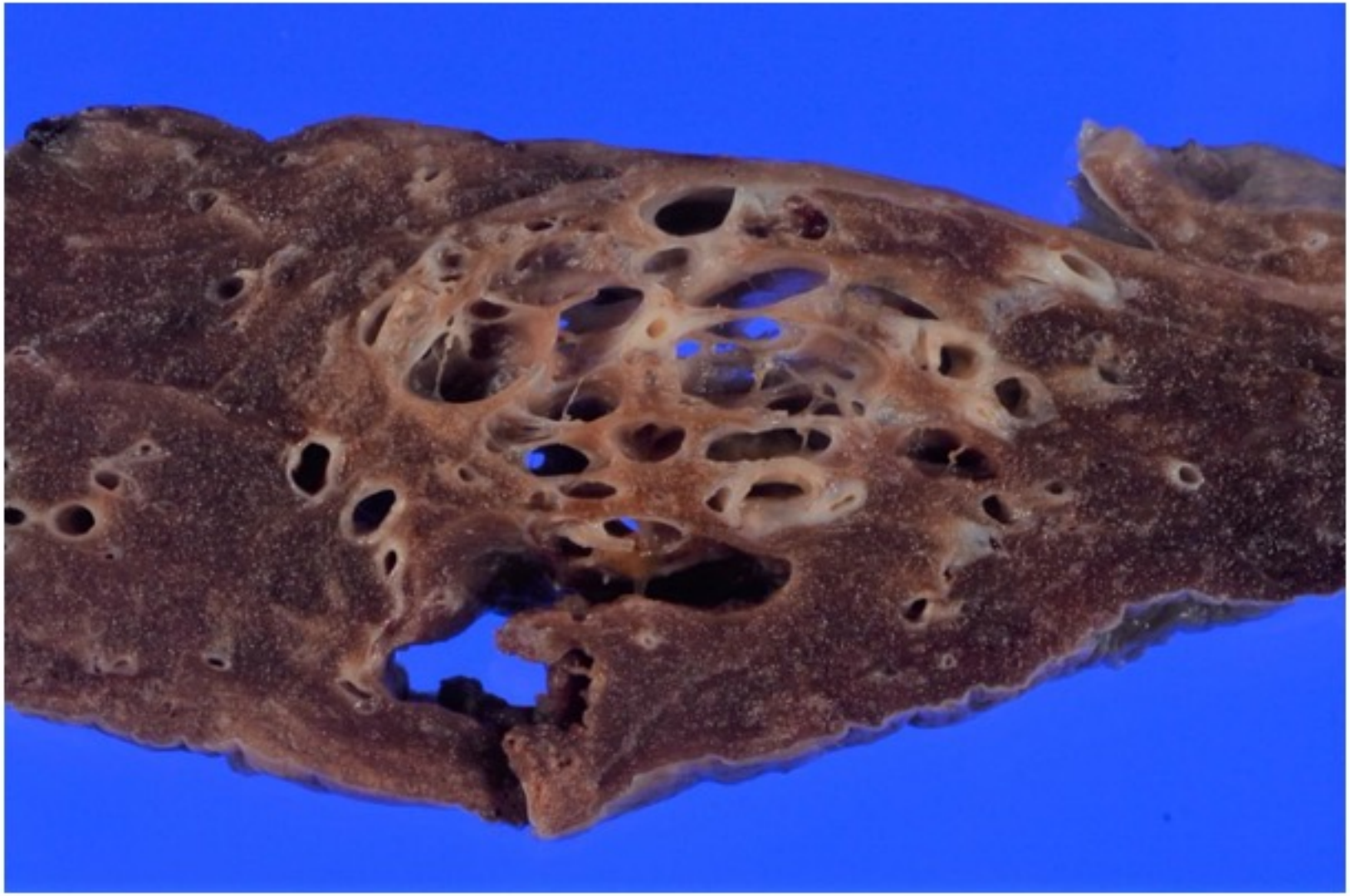

Figure 4A

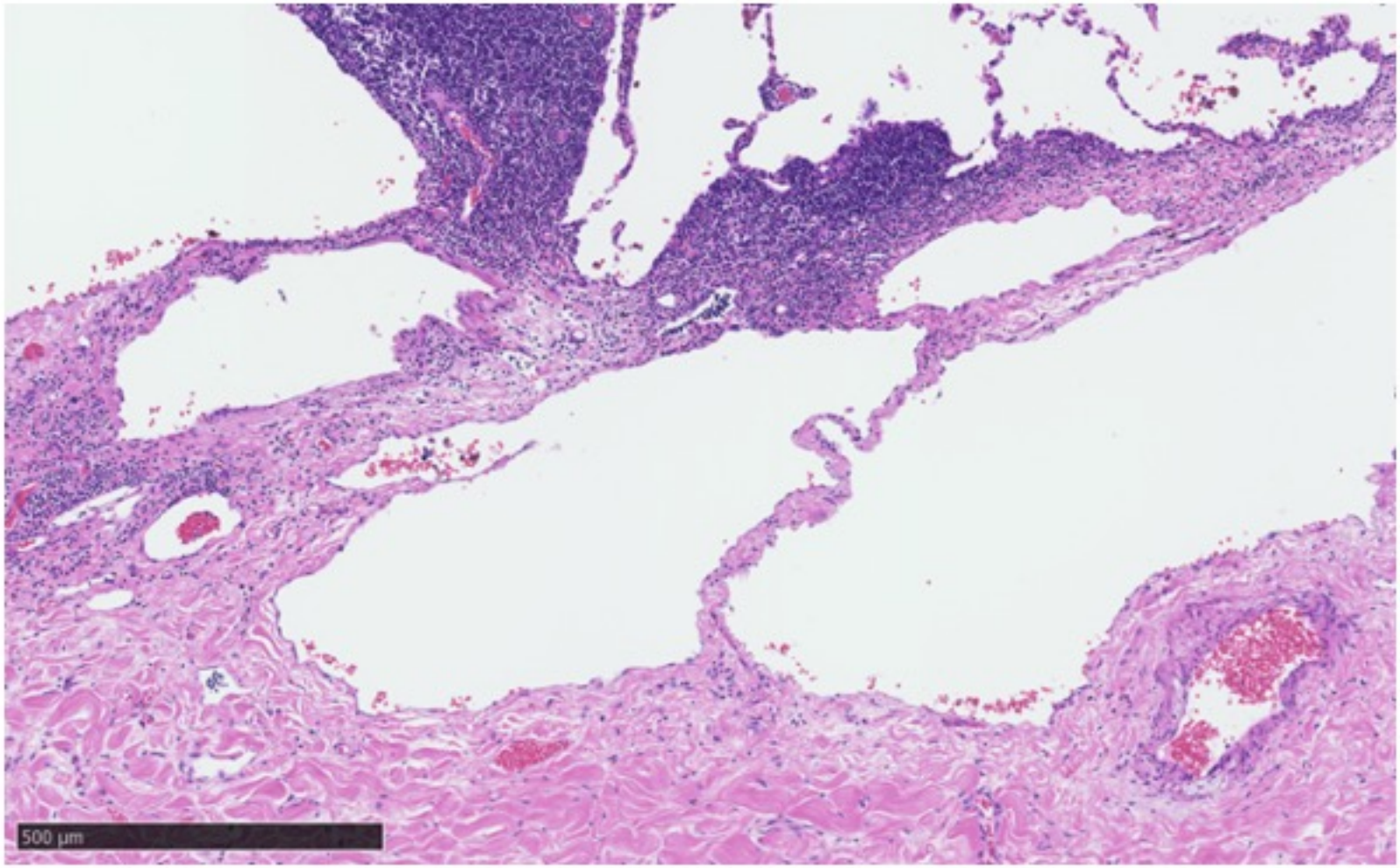

Figure 4B