



Title	Rare Diagnosis of a Multilobular Pulmonary Mass
Author(s)	Watabe, Yoshinobu; Ujiie, Hideki; Matsuno, Yoshihiro; Fukui, Hideaki; Fujiwara-Kuroda, Aki; Kato, Tatsuya; Hida, Yasuhiro; Kaga, Kichizo; Wakasa, Satoru
Citation	Chest, 160(1), E63-E67 <a href="https://doi.org/10.1016/j.chest.2021.01.034">https://doi.org/10.1016/j.chest.2021.01.034</a>
Issue Date	2021-07
Doc URL	<a href="http://hdl.handle.net/2115/86231">http://hdl.handle.net/2115/86231</a>
Rights	© 2021. This manuscript version is made available under the CC-BY-NC-ND 4.0 license <a href="http://creativecommons.org/licenses/by-nc-nd/4.0/">http://creativecommons.org/licenses/by-nc-nd/4.0/</a>
Rights(URL)	<a href="http://creativecommons.org/licenses/by-nc-nd/4.0/">http://creativecommons.org/licenses/by-nc-nd/4.0/</a>
Type	article (author version)
File Information	CHEST-20-4731_revision ver.3 Clean.pdf



[Instructions for use](#)

1 CHEST Imaging and Pathology for Clinicians

2 **(1) Title Page**

3 **Title:** Rare diagnosis of a multilobular pulmonary mass

4

5 **Authors:** Yoshinobu Watabe, MD,<sup>1</sup> Hideki Ujiie, MD, PhD, FCCP,<sup>1</sup> Yoshihiro Matsuno, MD,

6 PhD,<sup>2</sup> Hideaki Fukui, MD,<sup>2</sup> Aki Fujiwara-Kuroda, MD, PhD,<sup>1</sup> Tatsuya Kato, MD, PhD,<sup>1</sup> Yasuhiro

7 Hida, MD, PhD,<sup>1</sup> Kichizo Kaga, MD, PhD,<sup>1</sup> Satoru Wakasa, MD, PhD<sup>1</sup>

8

9 **Institutions and Affiliations:**

10 <sup>1</sup>Department of Cardiovascular and Thoracic Surgery, Faculty of Medicine and Graduate School  
11 of Medicine, Hokkaido University, Hokkaido, Japan

12 <sup>2</sup>Department of Surgical Pathology, Hokkaido University Hospital, Hokkaido University, Hokkaido,  
13 Japan

14

15 **Keywords:** Pulmonary lymphangioma, Cavernous lymphangioma, Video-assisted thoracoscopic  
16 surgery (VATS)

17 **Word Count:** 1543/1600

18 **Corresponding Author:**

19 Hideki Ujiie, MD, PhD, FCCP

- 1 Department of Cardiovascular and Thoracic Surgery, Hokkaido University Faculty and School
- 2 of Medicine, Kita 15, Nishi 7, Kita-ku, Sapporo, Hokkaido, 060-8638 Japan
- 3 Phone: +81-11-706-6042
- 4 Fax: +81-11-706-7612
- 5 Email: [Hideki.Ujiiie.MD@gmail.com](mailto:Hideki.Ujiiie.MD@gmail.com)
- 6

1 **CASE PRESENTATION:**

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

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

4

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

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

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

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

3

#### 4 ***What is the diagnosis?***

5 *Diagnosis:* Pulmonary cavernous lymphangioma

6

#### 7 **Discussion:**

##### 8 *Clinical Discussion*

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

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

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

7

#### 8 *Radiologic Discussion*

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

14 No definite enhancement was observed after intravenous administration of contrast material.

15 Magnetic resonance imaging (MRI) of lymphangiomas shows a signal similar to that of the  
16 muscle on T1-weighted images, with a marked signal increase on T2-weighted images that is  
17 greater than that of fat, thus reflecting the fluid content.<sup>10</sup> Only 2 cases underwent PET-CT,  
18 including the present case, and both cases showed slight accumulation.<sup>6</sup> However, these findings  
19 are not sufficiently characteristic to reliably differentiate lymphangioma from non-small cell lung

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

6

### 7 *Pathologic Discussion*

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



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

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

8

9 **Conclusions:**

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

14

15 **Acknowledgments:**

16 Financial/nonfinancial disclosures: None declared.

17 Other contributions: *CHEST* worked with the authors to ensure that the Journal policies regarding  
18 patient consent to report information were met.

19

1 **Figure Legends:**

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

5

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

8

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

11

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

15

16

17

1 **References:**

- 2 1. Hilliard RI, McKendry JB, Phillips MJ. Congenital abnormalities of the lymphatic system: a  
3 new clinical classification. *Pediatrics*. 1990;86(6):988-994.
- 4 2. Minato H, Kaji S, Kinoshita E, et al. Solitary intrapulmonary cystic lymphangioma in an  
5 infant: a case report with literature review. *Pathol Res Pract*. 2010;206(12):851-856.
- 6 3. Drut R, Mosca HH. Intrapulmonary cystic lymphangioma. *Pediatr Pulmonol*.  
7 1996;22(3):204-206.
- 8 4. Hamada K, Ishii Y, Nakaya M, Sawabata N, Fukuda K, Suzuki H. Solitary lymphangioma of  
9 the lung. *Histopathology*. 1995;27(5):482-483.
- 10 5. Nakajima J, Goto A, Takamoto S, Murakawa T, Fukami T, Kusakabe M. Invasive  
11 lymphangioma of the lung manifesting as a large pulmonary mass with hemoptysis: report  
12 of a case. *Surg Today*. 2007;37(5):418-422.
- 13 6. Shinohara S, Nakanishi R, Yasuda M, Tanaka F. Rapid growing pulmonary cavernous  
14 lymphangioma after chronic process for ten years. *Int J Surg Case Rep*. 2016;27:144-146.
- 15 7. Takemura T, Watanabe M, Takagi K, Tanaka S, Aida S. Thoracoscopic resection of a solitary  
16 pulmonary lymphangioma: report of a case. *Surg Today*. 1995;25(7):651-653.
- 17 8. Wilson C, Askin FB, Heitmiller RF. Solitary pulmonary lymphangioma. *Ann Thorac Surg*.  
18 2001;71(4):1337-1338.
- 19 9. Holden WE, Morris JF, Antonovic R, Gill TH, Kessler S. Adult intrapulmonary and

- 1            mediastinal lymphangioma causing haemoptysis. *Thorax*. 1987;42(8):635-636.
- 2    10.    Shaffer K, Rosado-de-Christenson ML, Patz EF, Jr., Young S, Farver CF. Thoracic
- 3            lymphangioma in adults: CT and MR imaging features. *AJR Am J Roentgenol*.
- 4            1994;162(2):283-289.
- 5

Figure 1

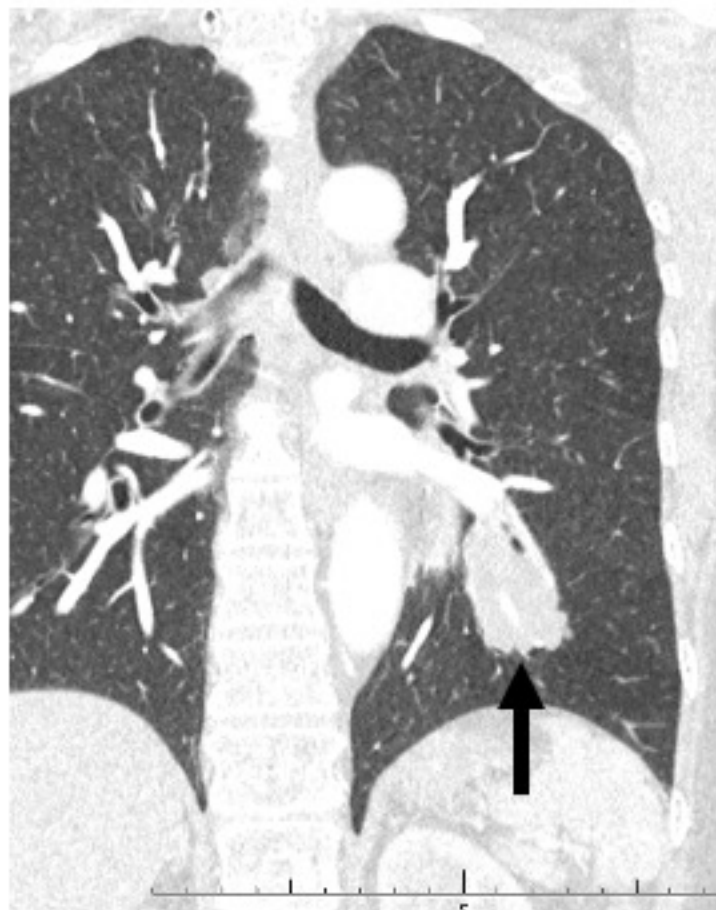


Figure 2

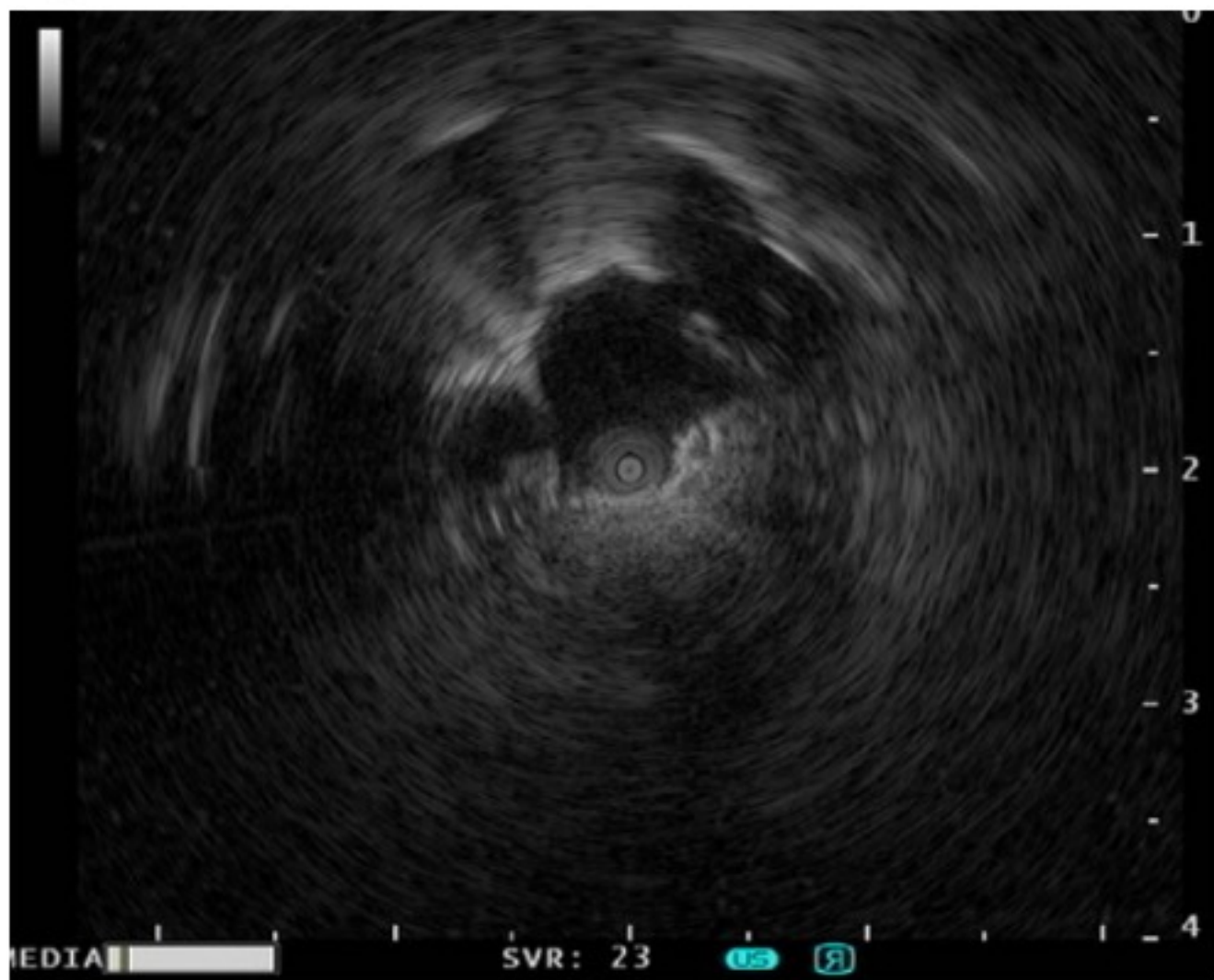


Figure 3





Figure 4A

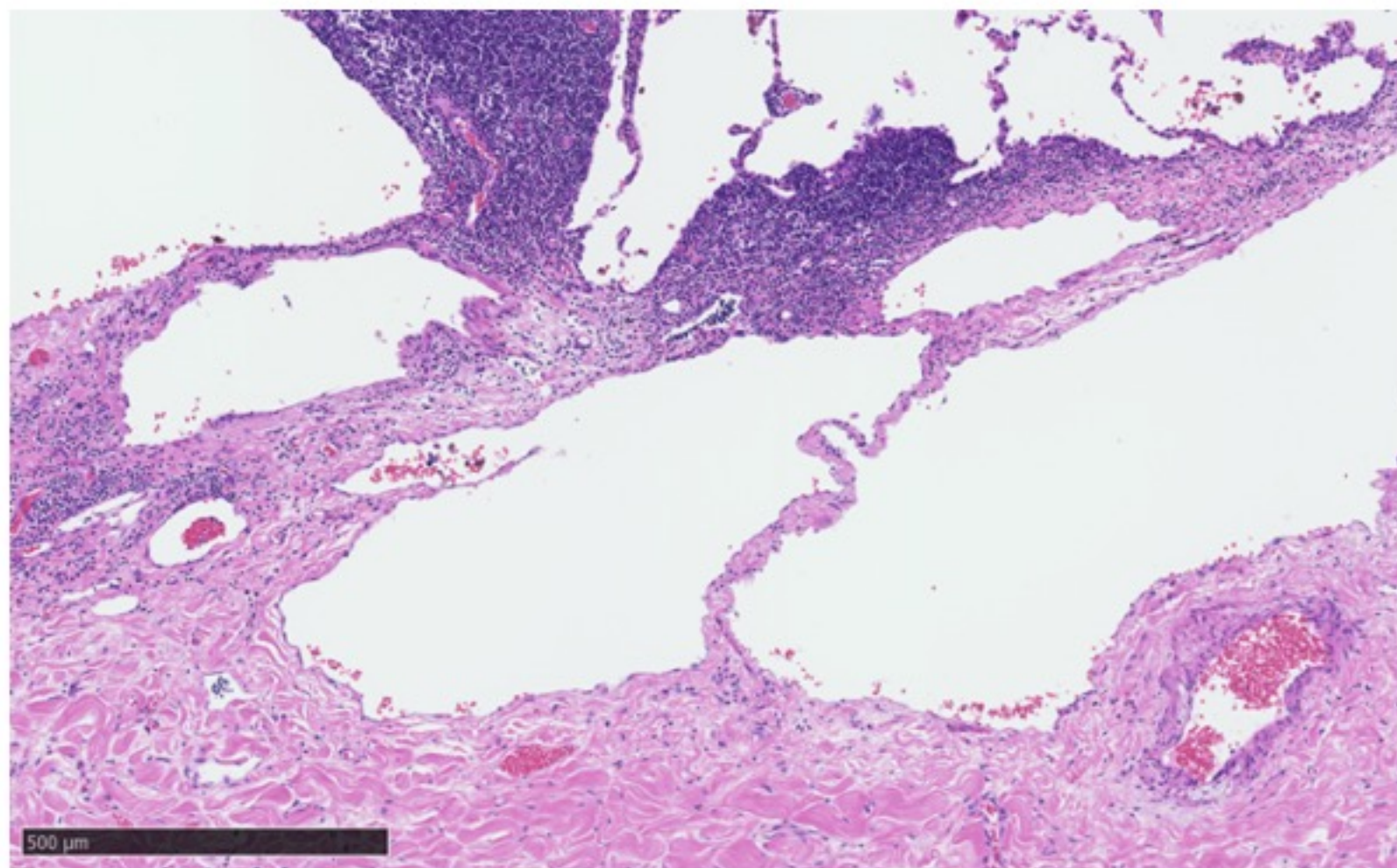




Figure 4B

