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Diffuse Pulmonary Lymphangiomatosis Involving Lung and Mediastinal Soft Tissue: A Rare Case in an Adult

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ABSTRACT

A 28-year-old female patient presenting with complaints of shortness of breath was diagnosed with diffuse pulmonary lymphangiomatosis based on radiological examinations and pathological analyses. This rare disease is characterized by the abnormal proliferation and dilation of lymphatic vessels. Although it is typically observed at younger ages in the literature, it can also be rarely diagnosed in adults. Our case emphasizes the importance of differential diagnosis for diffuse pulmonary lymphangiomatosis. The clinical, radiological, and pathological findings of the disease are discussed in detail.

Keywords: Diffuse pulmonary lymphangiomatosis, Mediastinal mass, Pathology, Case report

INTRODUCTION

Diffuse pulmonary lymphangiomatosis is an extremely rare pulmonary disease characterized by lymphatic proliferation of unclear etiology. Pulmonary lymphatic networks are responsible for transporting lymph fluid; however, in this disease, lymphatic vessels exhibit abnormal dilation and proliferation. Most cases occur in females under the age of 20, although it is also observed, albeit rarely, in adults. Clinically, the disease is characterized by prolonged shortness of breath, wheezing, and asthma-like symptoms (1). The diagnosis is typically made based on radiological imaging and histopathological evaluations. In this report, we evaluated the histopathological features of diffuse pulmonary lymphangiomatosis in light of the literature through the presentation of our case.

CASE REPORT

A 28-year-old female patient presented to the pulmonary diseases outpatient clinic complaining of shortness of breath. A chest X-ray revealed infiltrates predominantly concentrated in the lower and middle lobes of the lungs (Figure 1A). Thoracic computed tomography (CT) imaging showed an anterior mediastinal mass, interlobular and septal thickening, peribronchovascular thickening, and thin-walled subpleural cystic structures (Figure 1B-D).

For diagnostic purposes, a Video-Assisted Thoracic Surgery (VATS) procedure was performed. During VATS, chylous fluid and cystic structures were observed in the mediastinal region. Thin-walled subpleural cystic structures were identified in the lower lobes of the lungs (Figure 1E-F). Samples were taken from the lower lobes of the lungs and the mediastinum for diagnostic evaluation.

Pathological Examination and Diagnosis

Macroscopic examination revealed subpleural cystic structures in the parenchymal sample, with a maximum diameter of 5 cm, taken from the lower lobe of the right lung. The parenchymal cut surface appeared spongy with a pink-red coloration. In the mediastinum, fibrolipomatous tissue with a maximum diameter of 2 cm was observed.

Microscopic examination of serial sections showed preserved lung architecture. Notably, in the subpleural areas, cystic structures surrounded by flattened cells were observed, forming anastomosing networks. These structures were embedded in stroma containing oval or elongated fibroblast-like cells with nuclei of similar morphology. The described lesions were identified within the interalveolar septa (Figures 2A-D). The lesions extended to the subepithelial areas in the peribronchiolar region. The interstitial anastomosing cystic lesions mimicked emphysematous changes. No significant findings were observed in the lung parenchyma surrounding the lesions.

In the mediastinal tissue, isolated or grouped dilated spaces resembling fibrolipomatous structures were observed around major arteries and veins. These spaces were lined by endothelial-like cells but showed no significant accumu-

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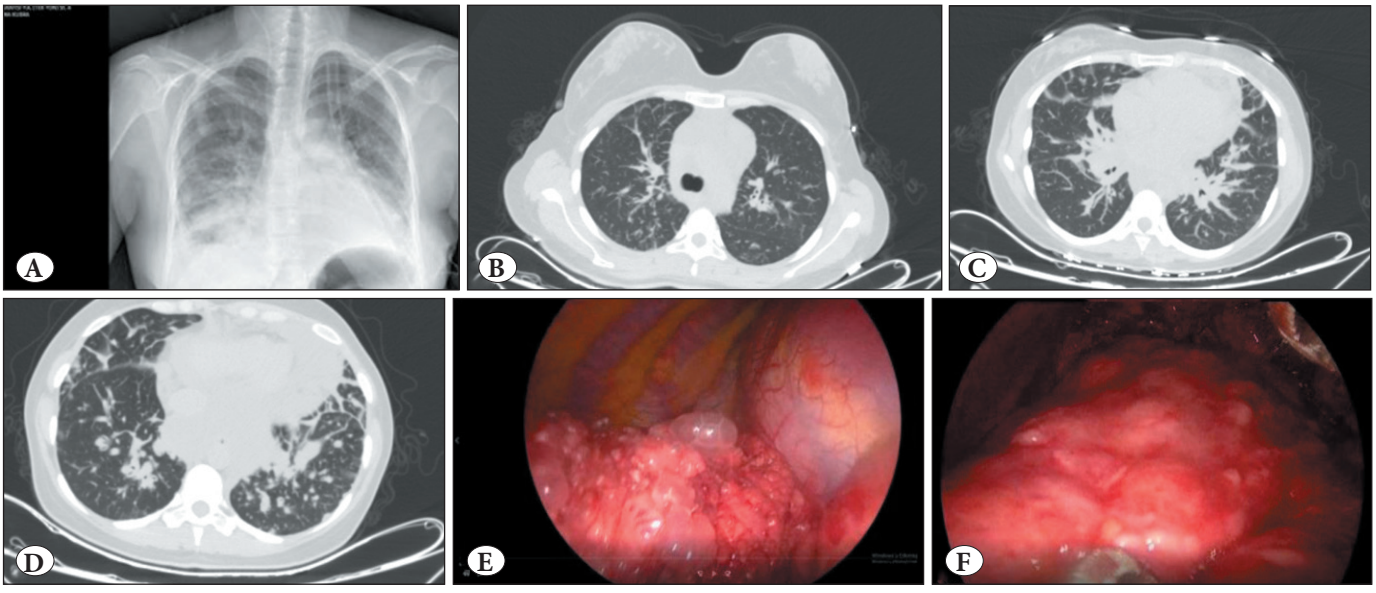

Figure 1: A) Increased opacity observed in the middle and lower lobes on chest PA radiograph. **B-D)** Thoracic computed tomography reveals irregular thickening predominantly in the peribronchiolar, septal, and subpleural regions of the lower and middle lobes. **E,F)** During Video-Assisted Thoracic Surgery (VATS), thin-walled cystic structures were identified on the visceral pleura.

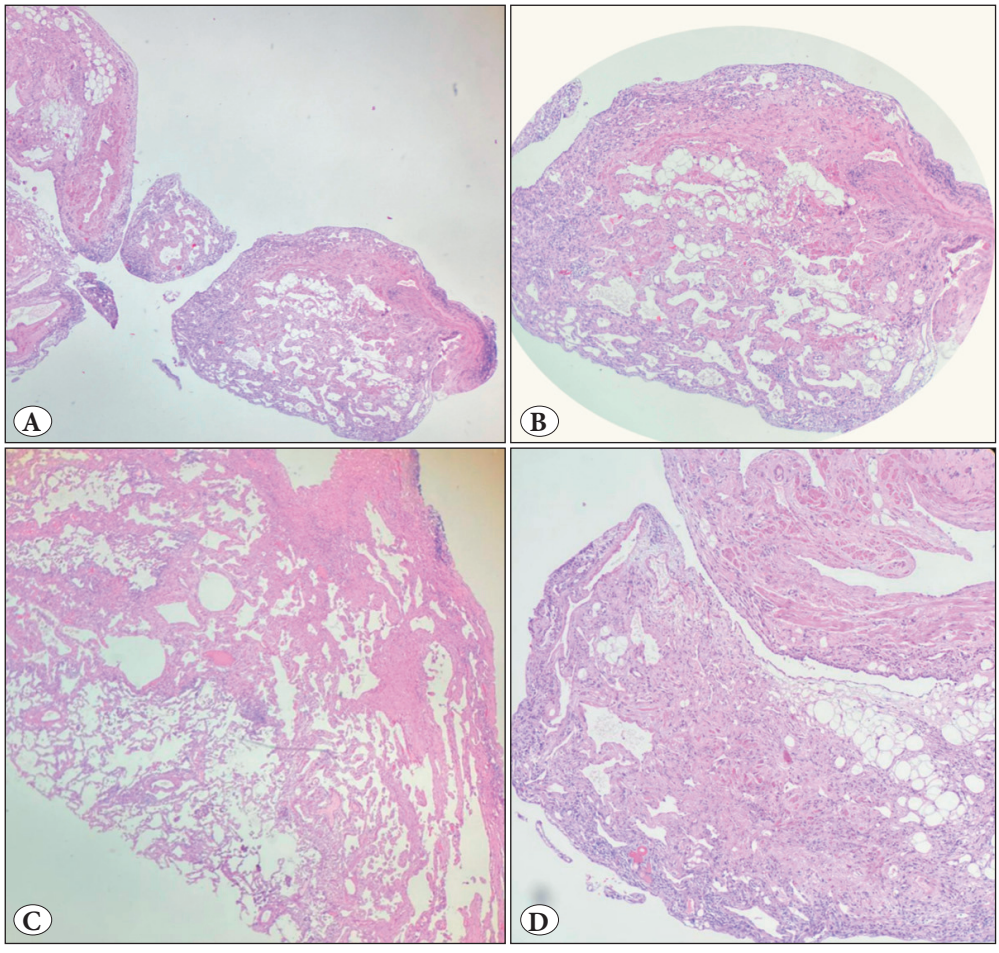

Figure 2: A,B) Lesion showing thin-walled, vessel-like proliferation with anastomosing structures lined by a single layer of flattened cells **(A)** H&E, X40; **(B)** H&E, X100. **C,D)** Dilated anastomosing vascular channels located in the visceral pleura, interlobular septa, and bronchovascular regions (H&E, X200).

lation within them. The nature and distribution of these lesions, as well as the involvement of both the lung parenchyma and mediastinum, strongly suggested a diagnosis of diffuse pulmonary lymphangiomatosis.

Immunohistochemical Study

In the described anastomosing structures, positive immunoreactivity for D2-40 (Figures 3A,B), CD31 (Figures 3C,D), and CD34 (Figure 3E) confirmed the endothelial origin of the cells. In perivascular cells, positive immunoreactivity for SMA (Figure 3F) and progesterone receptor (Figures 4B,C) was observed. Focal positivity was also noted with the estrogen receptor in these same cells. No immunoreactivity was detected with HMB45 in either endothelial cells or perivascular stromal cells.

While no immunoreactivity was observed in the lesions with the TTF-1 antibody, immunopositivity was present in the surrounding parenchymal alveolar epithelium (Figure 4A). These findings confirmed the diagnosis of diffuse pulmonary lymphangiomatosis.

DISCUSSION

Diffuse pulmonary lymphangiomatosis is an extremely rare disease characterized by lymphatic proliferation of unclear etiology. It is characterized by increased lymphatic vessel spaces surrounded by smooth muscle stroma around normal pulmonary lymphatic networks. Only case reports or small series have been documented (1).

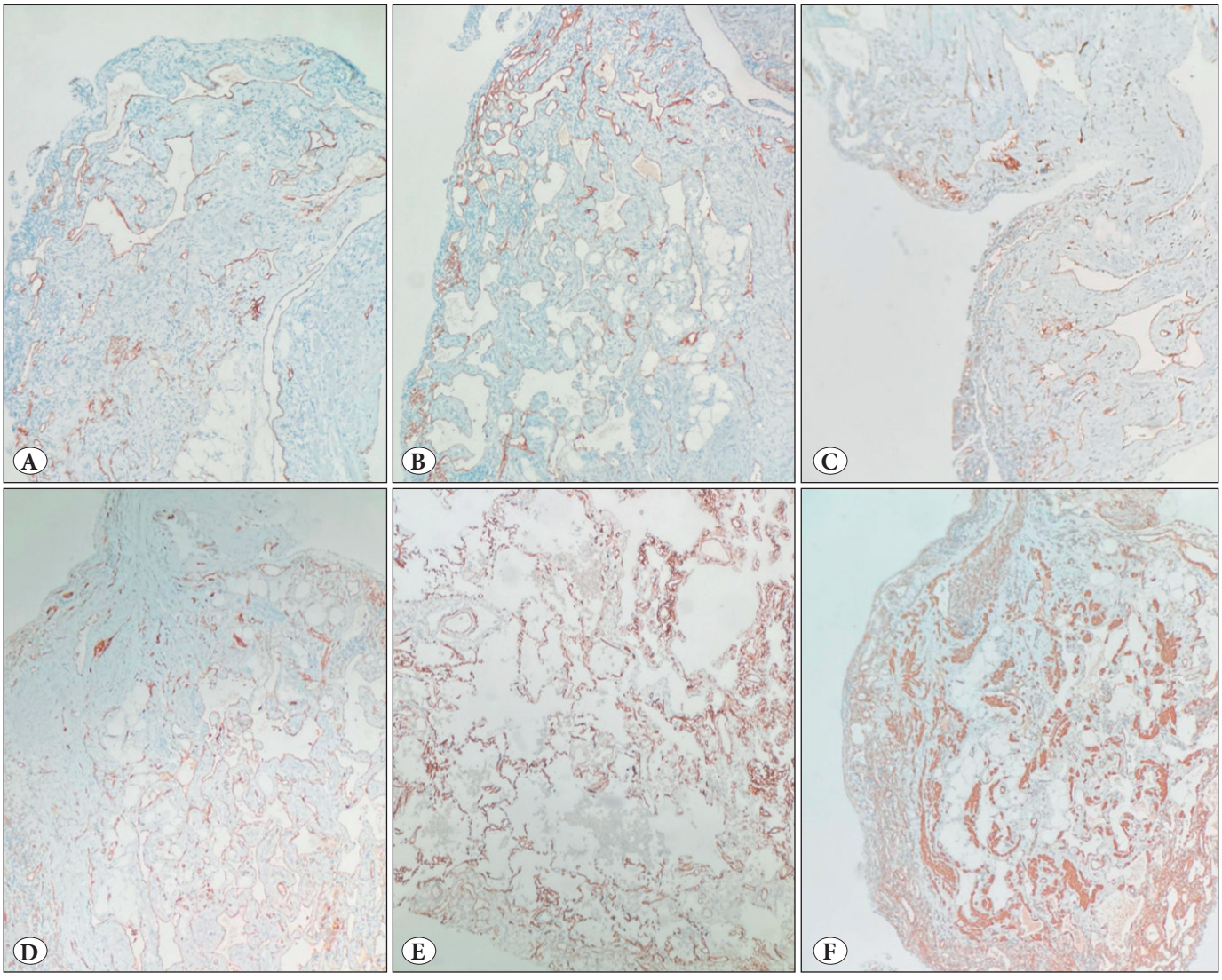

Figure 3: A-E) Positive immunohistochemical staining observed in the single-layered, flattened, endothelial cells using D2-40, CD31, and CD34 markers **(A,B)** D2-40, X100; **(C,D)** CD31, X100; **(E)** CD34, X200. **F)** Positive immunoreactivity in the perivascular spindle-shaped cells surrounding these endothelial cells using SMA immunohistochemical staining (SMA, X100).

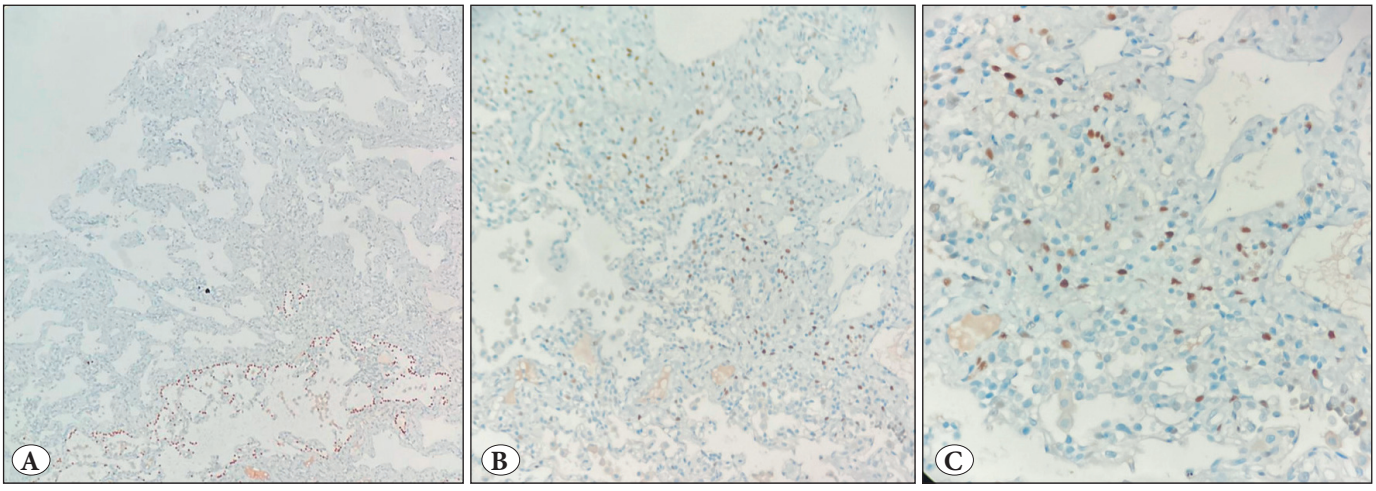

Figure 4: A) The histomorphological appearance of the dilated lymphatic channels resembles lung alveolar spaces, but TTF-1 is negative in these endothelial cells. Positive internal control staining of type 2 pneumocytes is observed (TTF-1, X100). **B,C)** Nuclear progesterone receptor positivity in perivascular cells **(B)** PR, X100; **(C)** PR, X200.

In most cases, the disease can affect multiple organs. The most commonly affected organs include the bones, liver, and spleen (2). When multiple organs are involved, lesions can also be detected in the lung parenchyma. Symptoms of the disease include progressive or long-standing shortness of breath and wheezing, which may mimic asthma. Hemoptysis can also occur (3). In advanced stages of the disease, chyloptysis may be seen due to stagnation of lymphatic flow. Rare complications include chylous ascites, chylopericardium, and protein-losing enteropathy (4). The complaints and findings in our case are consistent with those described in the literature.

Thoracic CT findings include thickening of the interlobular septa and bronchovascular regions, irregular ground-glass opacities, widespread infiltration in the mediastinum and hilum, and pleural effusion (5,6). In our case, similar findings were observed, although significant pleural effusion was not detected. Differential diagnoses based on radiology include pulmonary lymphangioleiomyomatosis and lymphangiectasia.

Diffuse pulmonary lymphangiomatosis is typically a progressive disease with a poor prognosis. Patients often experience recurrent chylous accumulations and mediastinal compression. Respiratory failure, caused by chylous fluid accumulation in the lungs and pleura or by infection, can result in death (7).

Pathological evaluation of lymphangiomatosis reveals proliferation characterized by anastomosing lymphatic vessels lined with endothelium and cystic spaces. In immunohistochemical studies, endothelial cells in lymphangiomatosis are positive for D2-40, CD31, and Factor VIII-related antigens. Additionally, the spindle cells in the stromal tissue between the anastomosing vascular structures are positive for SMA but negative for HMB-45. In contrast, spindle cells in lymphangioleiomyomatosis are positive for both SMA and HMB-45 (8).

The histopathological findings in our case are consistent with diffuse pulmonary lymphangiomatosis. Lymphangioleiomyomatosis, a condition included in the differential diagnosis, was excluded based on the absence of cystic structures lined with endothelium and the lack of HMB-45 antibody reactivity. While lymphangiomatosis can occur in both men and women, lymphangioleiomyomatosis is significantly more common in women (9).

Although the chest CT findings of lymphangiomatosis and pulmonary lymphangiectasia are often similar, histopathologically, lymphangiomatosis is characterized by an increased number of lymphatic vessels of varying sizes. In contrast, microscopic examination of pulmonary lymphangiectasia cases reveals dilated but non-proliferating lymphatic channels (9,10).

In our case, the lymphatic anastomosing channels, particularly in the subpleural areas, may be confused with emphysema. TTF-1, which demonstrates positive immunoreactivity in the adjacent parenchyma but negative in lymphangiomatous areas, is an important biomarker. For less experienced pathologists, emphysema should be considered in the differential diagnosis.

Most treatments for this disease are palliative (2). However, thoracic surgery, radiotherapy (RT), chemotherapy, and experimental treatments such as doxycycline sclerothera-

py, anti-vascular endothelial growth factor (VEGF) agents, interferon α-2b, and propranolol have been explored (11).

CONCLUSION

This case reflects the challenges in diagnosing diffuse pulmonary lymphangiomatosis. The diagnosis was established through a combination of clinical, radiological, and pathological findings. Since diffuse pulmonary lymphangiomatosis is generally a progressive disease with a poor prognosis, early diagnosis and appropriate therapeutic approaches are of critical importance.

When compared to the literature, the immunohistochemical reactions and clinical findings observed in this case have strengthened the diagnosis. The rarity of such cases, combined with the diversity of clinical presentations, makes diagnosing this disease particularly challenging.

Conflict of Interest
No conflicts of interest are declared.

Authorship Contributions
Concept: **HNU, EC,** Design: **HNU, EC,** Data collection and/or processing: **HNU, EC,** Analysis and/or interpretation: **HNU, EC,** Writing: **HNU, EC, SGB,** Approval: **HNU, EC, SGB.**

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