

Diffuse Pulmonary Lymphangiomas Versus Lymphangiomyomatosis

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Case Presentation

A 26-year-old woman presented to the emergency room after a motor vehicle collision. Chest computed tomography (CT) performed at that time demonstrated a large pleural effusion, associated with a right upper lobe mass. A wedge excision and pleural decortication demonstrated multiple subpleural and septal lesions composed of prominent, variably dilated and anastomosing lymphatic channels, associated with fibrosis and patchy lymphocytic infiltrates.

On follow-up, the patient had progressive dyspnea associated with restrictive lung disease. Chest CT studies demonstrated bilateral ground-glass opacities, septal and pleural thickening, and recurrent chylous pleural and pericardial

effusions (Fig. 59.1). Four years after the initial diagnosis, the patient had a pregnancy during which her pulmonary function severely deteriorated, requiring a cesarean section at 29 weeks. Postoperatively, her respiratory status continued to worsen, ultimately leading to respiratory failure and death.

Autopsy revealed markedly enlarged lungs bilaterally, with extensive areas of pleural scarring. Other findings included marked ascites and additional lesions composed of similarly arranged lymphatic vessels involving the lungs (Fig. 59.2a–c), as well as the mediastinal and retroperitoneal soft tissues (Fig. 59.2d).

Her cause of death was attributed to respiratory failure due to **diffuse pulmonary lymphangiomas**.

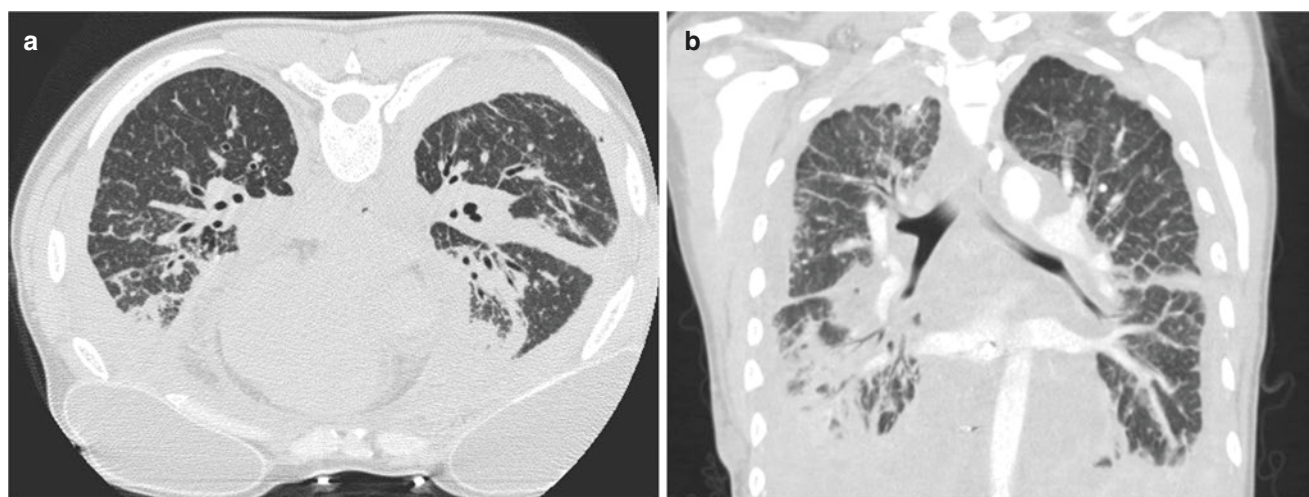


Fig. 59.1 CT imaging findings of diffuse pulmonary lymphangiomas commonly include extensive peribronchial/perivascular thickening, scattered ground-glass opacities, and pleural and pericardial effusion. (a) Axial view; (b) coronal view

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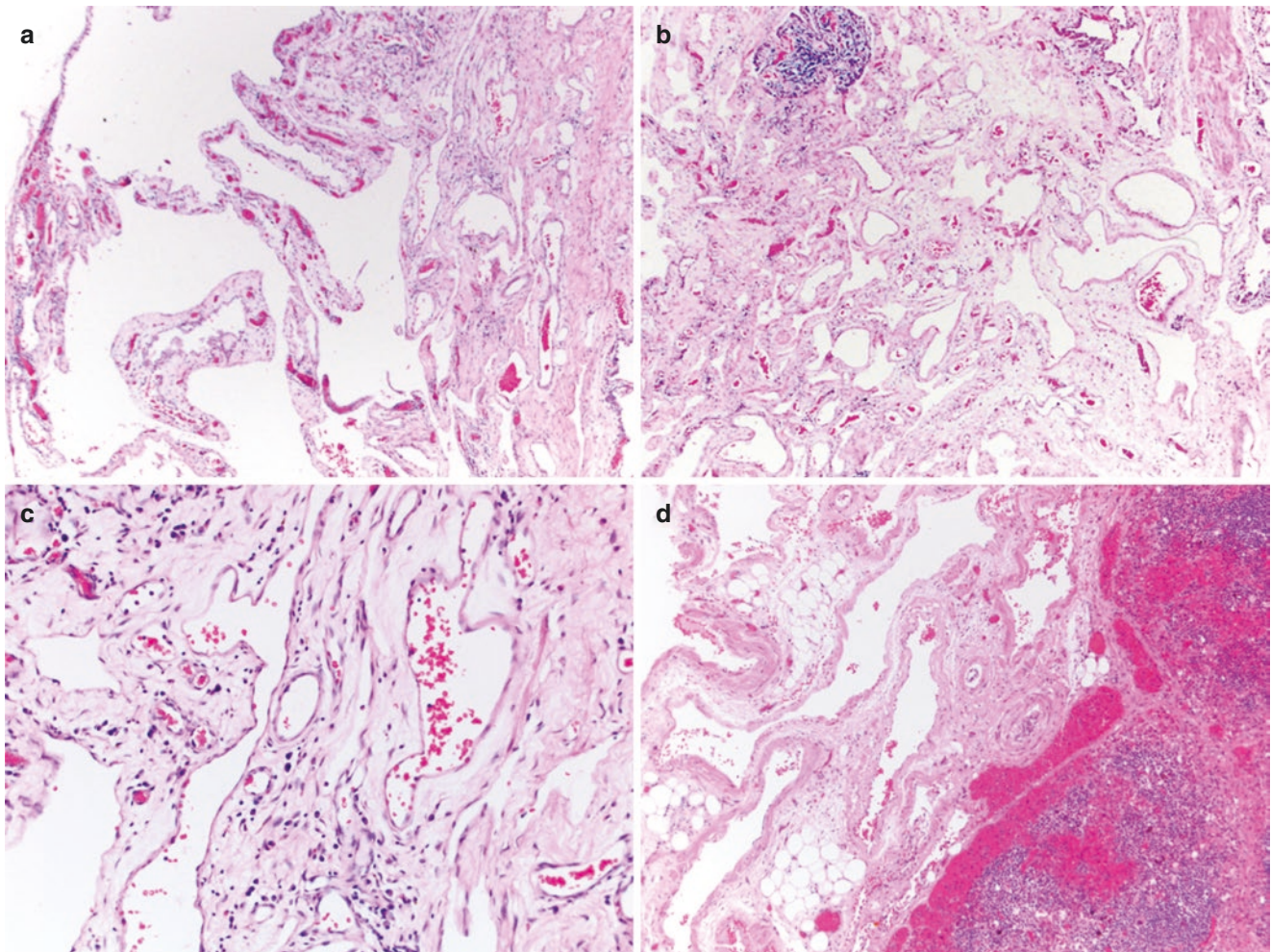


Fig. 59.2 (a, b) Histologic features of diffuse pulmonary lymphangiomas include multiple lesions composed of variably dilated lymphatics with a lymphangitic distribution, accompanied by fibrosis and variable lymphocytic aggregates (H&E, 40 \times). (c) The lesional vessels

are lined by cytologically bland lymphatic endothelium (H&E, 200 \times). (d) Extrapulmonary lesions may be seen in DPL; in this particular case in the retroperitoneum, it is associated with lymph nodes (H&E, 40 \times)

Final Diagnosis: Diffuse Pulmonary Lymphangiomas

What Are the Clinical Features of Diffuse Pulmonary Lymphangiomas (DPL) and How Do They Differ from Lymphangiomyomatosis (LAM)?

Diffuse pulmonary lymphangiomas (DPL) is a rare condition characterized by diffuse prominence of lymphatic vessels within the lung parenchyma (lymphangiomas) [1]. It typically arises in children and young adults, with no significant difference between sexes [1, 2]. Rare cases of DPL have been reported in middle-aged adults [3, 4]. DPL is a typically aggressive disease which presents with a wide variety of clinical manifestations; these range from mild wheezing and

productive cough to severe respiratory failure associated with infiltrative disease and recurrent pleural effusions [1]. The content of the expectoration and pleural effusion are often chylous [1, 2]. DPL is often associated with other lymphatic abnormalities and involvement of other organs in up to 75% of cases [5]. The clinical prognosis of DPL is poor, and death by respiratory failure is common [2, 6, 7].

On the other hand, LAM shows a marked preference for women of reproductive age. Somewhat similarly to DPL, LAM typically presents with dyspnea, spontaneous pneumothorax, and ultimately respiratory failure. Involvement of venous and lymphatic vessels can lead to other less common clinical manifestations, such as hemoptysis, pulmonary hypertension, and chylothorax [8–10]. This entity is also discussed in Chap. 58 (Lymphangiomyomatosis versus Benign Metastasizing Leiomyoma).

How Can Radiologic Studies be Used to Distinguish DPL from LAM?

The most common radiologic manifestations of DPL are distinctive, although not entirely specific. The most CT findings are smooth septal and peribronchovascular thickening and diffusely increased attenuation of mediastinal fat. Other common findings include bilateral patchy ground-glass opacities, pleural and pericardial effusion, pleural thickening, and lymphadenopathy [6, 11]. Representative CT images are seen in Fig. 59.1.

In contrast, the CT imaging appearance of LAM typically consists of multiple air-filled cysts of variable size, distributed throughout the entirety of the lung parenchyma (Fig. 59.3). Other common pulmonary findings include reticulated opacities, pneumothorax, increased lung volumes, and pleural effusions [12–14].

What Are the Pathologic Features of DPL and LAM? How Can Immunohistochemistry be Used to Distinguish These Two Entities?

DPL is histologically characterized by the presence of complex anastomosing thin-walled lymphatic vessels, which are present throughout the lung parenchyma and pleura, with a subpleural, septal, and peribronchovascular distribution (Fig. 59.2a, b). The lesional vessels are lined by cytologically bland endothelial cells (Fig. 59.2c) and may be associated with fibrosis and increased hemosiderin-laden macrophages. True infiltration of the lung parenchyma is usually not seen in DPL [5, 7, 15].

On the other hand, LAM is characterized by the presence of solid nodules or multiple cysts throughout the lung parenchyma, lined by cytologically bland spindle to epithelioid perivascular cells (PEC) (Fig. 59.4). These lesions show a similar anatomic distribution to lymphangiomas, given their close association with lymphatic structures, with a peribronchial, septal, and subpleural location [8, 16].

Immunohistochemical stains can be useful to further differentiate DPL from LAM, since the latter has a characteristic immunophenotype, with expression of smooth muscle actin, HMB45 (Fig. 59.4), and estrogen and progesterone receptors (Fig. 59.4) (PR more commonly than ER) in a majority of cases [17–19]. In addition, immunoreactivity for β -catenin in a membranous and cytoplasmic pattern has been described in a majority of cases of LAM [17].

What Other Lesions Should I Consider in the Differential Diagnosis of DPL?

Other lymphatic vascular lesions may be histologically difficult to distinguish from DPL. These include solitary lymphangiomas and lymphangiectasis. The former consist of solitary, typically well-circumscribed lesions composed of abundant lymphatic vessels, lined by cytologically bland endothelial cells, and containing lymph within their lumen. These lesions may be solid or cystic, with capillary and/or cavernous architecture, and are commonly associated with prominent lymphoid aggregates [5]. In small biopsies, and in the absence of clinical and imaging correlation, these lesions may be histologically indistinguishable from DPL.

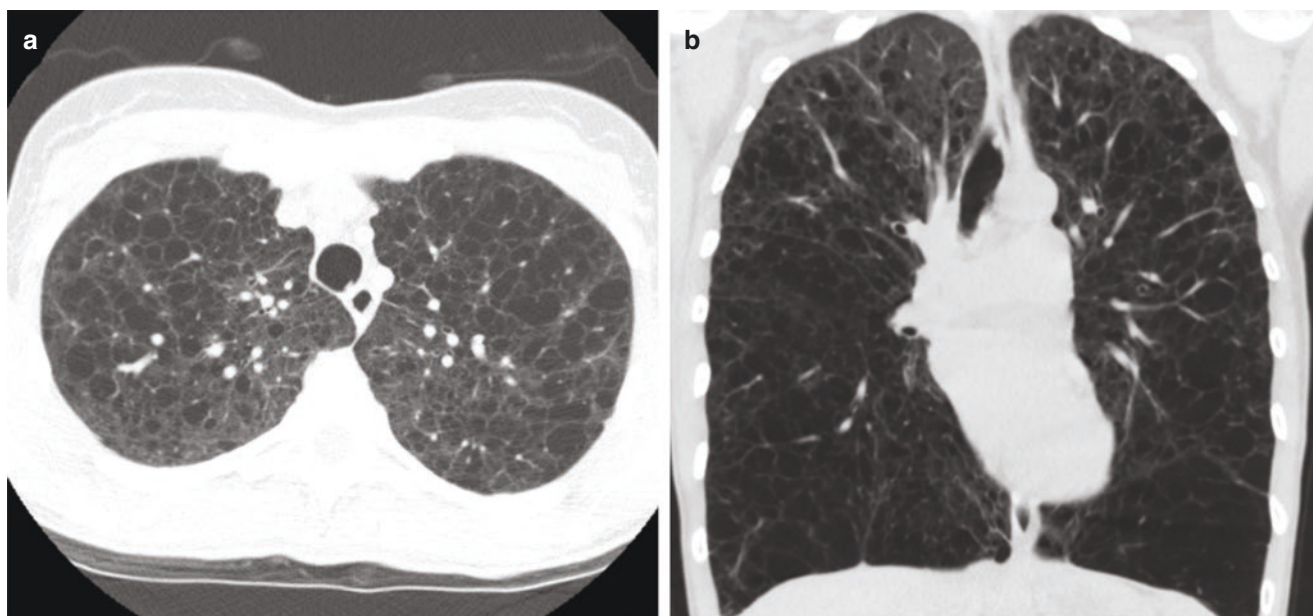


Fig. 59.3 CT imaging findings of lymphangiomyomatosis are typically characterized by the variable presence of thin-walled pulmonary cysts, without a predilection for a specific region, and often distrib-

uted in a homogeneous manner throughout the lungs. (a) Axial view; (b) coronal view

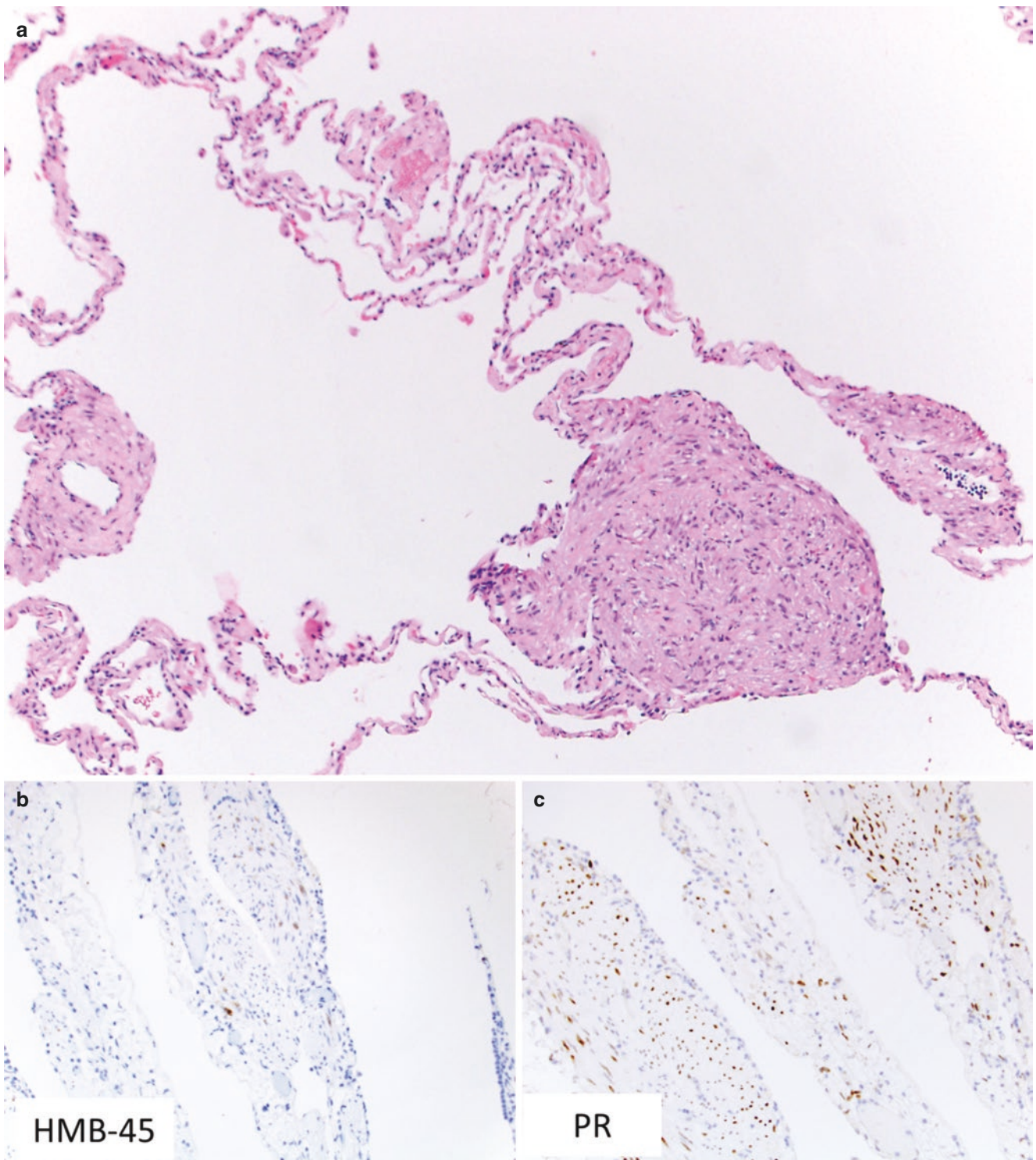


Fig. 59.4 Histologic findings in LAM. (a) Notice the presence of myoid cells within the cyst lining (H&E, 100 \times), which show focal expression of (b) HMB-45 and (c) variable progesterone receptor (PR) (IHC DAB, 100 \times)

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