J Bras Pneumol. 2019;45(5):e20180412
http://dx.doi.org/10.1590/1806-3713/e20180412

Diffuse pulmonary lymphangiomatosis

Igor Biscotto[1,a], Rosana Souza Rodrigues[1,2,b], Danielle Nunes Forny[1,c], Miriam Menna Barreto[1,d], Edson Marchiori[1,e]

TO THE EDITOR:

A 14-year-old male with a history of pericardial effusion and pulmonary infiltrate presented to a routine medical visit with complaints of dyspnea. Physical examination revealed signs of pleural effusion (absence of breath sounds and dullness to percussion) in the lower part of the right hemithorax. No other abnormalities were observed. Chest x-ray and ultrasonography confirmed the presence of pleural effusion, and diagnostic thoracocentesis was performed. The analysis of the pleural fluid showed high levels of triglycerides (136 mg/dL), and chylothorax was diagnosed. A previously performed chest CT examination showed interlobular septal and peribronchovascular thickening, as well as pleural and mediastinal soft tissue infiltration (Figures 1A-C). The patient was hospitalized for further investigation, and pleural biopsy was performed. Microscopically, the lesion was characterized by the proliferation and dilatation of lymphatic channels, and showed immunopositivity for CD31 (Figure 1D), CD34, factor VIII-related antigen, actin, desmin, and vimentin. On the basis of the findings, the diagnosis of diffuse pulmonary lymphangiomatosis (DPL) was confirmed.

DPL is an extremely rare benign disease characterized by abnormal proliferation, dilatation, and thickening of lymphatic channels in the lungs, pleura, and mediastinal soft tissue. The disease can affect people of all ages, but it occurs predominantly in children and young adults, regardless of gender. Although the pathogenesis remains controversial, the disease seems to result from abnormal lymphatic development. The proliferative lymphatic aspect suggests a neoplastic etiology, and the structural disorganization indicates a hamartomatous origin. Most symptoms are mild; patients present with cough, shortness of breath, and hemoptysis (with or without chylous effusion), pleuropericardial effusion, and pneumothorax.[1-4]

The proliferation of lymphatic channels explains the most common thoracic imaging findings of DPL. On chest CT scans, the findings include thickening of the interlobular septa and bronchovascular bundles, patchy ground-glass opacities, diffuse infiltration of mediastinal and hilar soft tissue, and pleural effusion.[1,2,4] In our case, the imaging findings were thickening of the interlobular septa and bronchovascular bundles, mediastinal and pleural infiltration, and associated pleural effusion, all of which are compatible with DPL. The major differential diagnosis is pulmonary lymphangiectasia, a rare condition characterized by diffuse dilatation of the

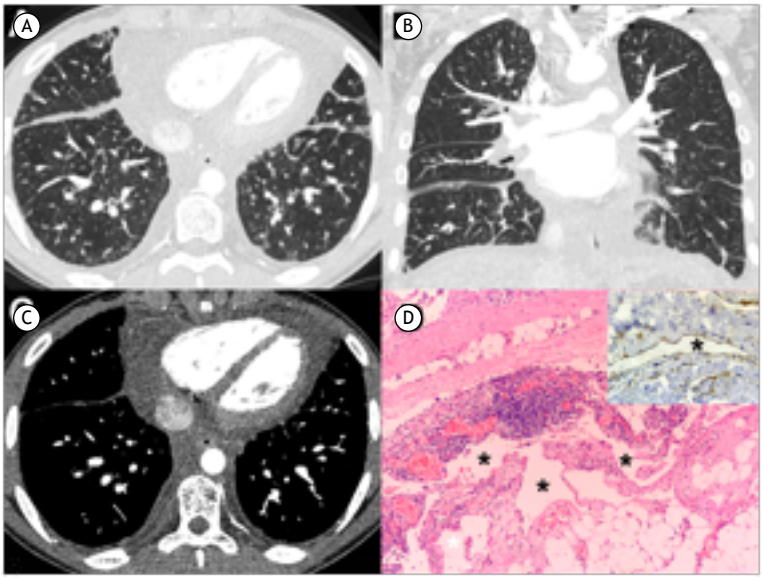

Figure 1. Contrast-enhanced reformatted axial (in A) and coronal (in B) chest CT images, as well as an axial image with mediastinal window settings (in C) showing peribronchovascular and interlobular septal thickening, associated with extensive pleural and mediastinal soft-tissue infiltration. In D, a photomicrograph showing diffuse proliferation of lymphatic channels (asterisks) along the pleura and immunopositivity of the endothelial cells in the lymphatic channels for CD31 (H&E and immunohistochemical staining; magnification, ×100).

1. Universidade Federal do Rio de Janeiro, Rio de Janeiro (RJ) Brasil.
2. Instituto D'Or de Pesquisa e Ensino, Rio de Janeiro (RJ) Brasil.
a. http://orcid.org/0000-0002-8088-5595; b. http://orcid.org/0000-0002-9952-3834; c. http://orcid.org/0000-0002-4297-5450;
d. http://orcid.org/0000-0002-8775-0458; e. http://orcid.org/0000-0001-8797-7380

pulmonary lymphatics. It is classified as congenital, presenting shortly after birth and being associated with high neonatal morbidity and mortality, or secondary, when there is evidence of pulmonary hypertension or venous obstruction. Although the chest CT findings of DPL and pulmonary lymphangiectasia are virtually identical, histopathologically, lymphangiomatosis is characterized by an increased number of variably sized lymphatic vessels. In contrast, microscopic examination reveals nonproliferative dilated lymphatic channels in cases of pulmonary lymphangiectasia.[5]

Biopsy with histological and immunohistochemical studies guarantees a definite diagnosis of DPL. Pathological examination shows the proliferation of complex, anastomotic, endothelium-lined spaces, with asymmetrically spaced bundles of spindle-shaped cells and collagen surrounding the endothelium-lined channels. On immunohistochemical staining, the endothelial cells in lymphangiomatosis cases are usually positive for D2-40, CD31, and factor VIII-related antigen.[3] Our patient showed positivity for CD31 and factor VIII-related antigen, among others, leading to the diagnosis of DPL.

No specific treatment for DPL is universally accepted. Current therapies are supportive and essentially palliative, aiming to relieve clinical symptoms. The disease is progressive and prognosis is generally poor. The evolution is often slow, with recurrent chylous effusion and mediastinal compression. Respiratory failure secondary to infection and accumulation of chylous fluid are the major causes of death among patients with DPL.[2,4]

REFERENCES

1. Raman SP, Pipavath SN, Raghu G, Schmidt RA, Godwin JD. Imaging of thoracic lymphatic diseases. AJR Am J Roentgenol. 2009;193(6):1504-13. https://doi.org/10.2214/AJR.09.2532
2. de Lima AS, Martynychen MG, Florêncio RT, Rabello LM, de Barros JA, Escuissato DL. Pulmonary lymphangiomatosis: a report of two cases. J Bras Pneumol. 2007;33(2):229-33. https://doi.org/10.1590/S1806-37132007000200020
3. Putta T, Irodi A, Thangakunam B, Oliver A, Gunasingam R. Young patient with generalized lymphangiomatosis: Differentiating the differential. Indian J Radiol Imaging. 2016;26(3):411-415. https://doi.org/10.4103/0971-3026.190416
4. Sun X, Shen W, Xia S, Wen T, Wang R. Diffuse Pulmonary Lymphangiomatosis: MDCT Findings After Direct Lymphangiography. AJR Am J Roentgenol. 2017;208(2):300-305. https://doi.org/10.2214/AJR.16.16589
5. Lim HJ, Han J, Kim HK, Kim TS. A rare case of diffuse pulmonary lymphangiomatosis in a middle-aged woman. Korean J Radiol. 2014;15(2):295-9. https://doi.org/10.3348/kjr.2014.15.2.295