Transthoracic ultrasound: an essential diagnostic tool in a very rare case of thoracic lymphangiomatosis

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Abstract
Thoracic lymphangiomatosis (proliferation of anastomosing lymphatic vessels, of different sizes, in pulmonary, pleural and mediastinal regions) is an extremely rare disorder occurring mostly in childhood. We present a diffuse pulmonary lymphangiomatosis (DPL) case in a young adult female patient in which repeated surgical biopsies were inconclusive and transthoracic ultrasound-guided (TUS) biopsy led to the diagnosis. Even histologically, DPL is very difficult to differentiate from other lymphatic diseases such as lymphangioma and lymphangiomomyomatosis, requiring an experienced pathologist and proper immunohistochemistry staining. This case highlights the importance of TUS-guided biopsies in the armamentarium of imagistic techniques in this very rare case

Keywords: diffuse pulmonary lymphangiomatosis; guided biopsy; transthoracic ultrasonography

Introduction
Thoracic lymphangiomatosis (TL), an extremely rare lymphatic disorder which occurs mostly in childhood, is described as a proliferation of different size anastomosing lymphatic vessels in the pulmonary, pleural and mediastinal lymphatic territories [1-5].

There are few reports and little research regarding TL due to its rarity, most of them being single cases or a small case series. Since the etiopathogenetic mechanisms are not fully deciphered, there is not yet available a specific therapy [2].

We present a TL case in a young adult female patient, with an unclear diagnosis for a long time and finally established through percutaneous transthoracic ultrasound (TUS)-guided biopsy.

Case report
A 23-year old woman, with no particular history, was admitted in the Thoracic Surgery Department in 2013 and diagnosed with idiopathic left chylothorax with stage III secondary left pleural sterile empyema. Left thoracotomy, visceral decortication and pleurectomy were performed, with good recovery after the surgery. In March 2016 she was hospitalized with dyspnea and fatigue. The CT-scan showed a large mediastinal mass (120 mm longitudinal diameter) and a surgical biopsy was performed revealing a macroscopically, a loculated...
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The patient was re-admitted in July 2016 with right chylothorax and pericardial effusion. A third surgical intervention was performed with thoracic duct ligation and surgical biopsies. The histopathological report described dilated lymphatic and venous channels, totally excluding malignancy. The patient had a temporary favorable evolution after surgery.

In December 2017, the patient was admitted in our Department, with dyspnea and fatigability, shortness of breath and important hepatosplenomegaly accompanied with grade 2 thrombocytopenia (platelets = 80 000/mm³). The CT-scan revealed a 150/130/220 mm mediastinal mass of cystic appearance, bilateral pleural effusions, pleural thickening (fig 1a,b), and diffuse thickening of the interlobular septa and bronchovascular bundles, mainly on the left side. The hepatosplenomegaly was also described but no specific lesions were found. TUS was performed revealing a large mediastinal mass, with septa of various thickness and multiple loculated fluid collections (fig 1c,d). A percutaneous TUS-guided biopsy was performed from a thickened septum using a left parasternal approach. The histological examination described findings specific for lymphangiomatosis (fig 2). No malignant cells were identified. Laboratory workup excluded multiple causes of hepatosplenomegaly and were considered to be manifestations of the disease. The respiratory symptomatology was under a feeble control with intermittent bronchodilators. Pulmonary transplantation was recommended and the patient was referred to a specialized tertiary care center for listing.

Discussion

“Lymphangiomatosis” is a very rare condition characterized by the proliferation of lymphatic ducts [1-5]. This condition is distinguished from other lymphatic diseases exactly by its proliferative character [4,5]. This disease may mimic also malignancy with severe, debilitating symptoms and aggressive behavior. In adult patients lymphangiomatosis can also masquerade as interstitial lung disease or recurrent infections [6].

In our case, TUS described similar aspects as the CT findings, which means that at least a thorough follow up by US might be of interest in these patients. As it has
been shown before, TUS is a valuable tool for the prevascular and posterior mediastinal located masses in contact with the thoracic wall [7]. Also, it can guide biopsies which can be extremely important when other options are contraindicated, such as in the cases of patient with allergies to contrast agents. Diagnosis of lymphangiomatosis can be established on transbronchial or surgical biopsy but, in our case, despite 3 surgical biopsies had been performed, the diagnosis was not established, probably due to the lack of appropriate immunohistochemical staining and clinical suspicion. On the other hand, in this particular case, a less invasive diagnostic method was of major importance and led to the final diagnosis, taking into account the altered respiratory status, that posed a greater anesthetic risk if a fourth intervention would have been performed. Another important issue is represented by the potential severe complications of open biopsy in patients with TL as mentioned in the literature [8], which supports the need of a minimal invasive diagnostic approach, such as a US-guided biopsy. Concomitant with the advances of endoscopic ultrasound FNA, which is feasible even for paraesophageal lung tumors [9], it is obvious that the intrathoracic organs benefit from another technique that can procure minimally invasive biopsies.

Histologically, TL is difficult to be differentiated from other lymphatic diseases such as lymphangioma and lymphangiomyomatosis [5]. The key to recognizing these conditions is the lymphangitic distribution of abnormal lymphatics, with dilation in lymphangiectasis and anastomosing proliferation in lymphangiomatosis, with the presence of endothelial markers such as CD31, factor VIII-related antigen and D2-40 on immunohistochemistry staining [2,4].

Precise diagnosis is crucial for further treatment, and though the imaging findings are quite characteristic [10], they are not sufficiently specific to avoid a biopsy [1,2,6].

Imaging methods have the best chances for guiding the diagnosis, doubled, classically, by transbronchial or open lung biopsy. In our case, TUS biopsy contributed decisively to the diagnosis, being the first presented case diagnosed in this manner, to our knowledge. Therefore, TUS can represent a non-invasive, largely accessible tool in diagnosis and follow-up of the patients with TL.

In conclusion this case highlights the difficulties in the diagnosis of TL and the utility of TUS-guided biopsy. This type of approach should be used more often in the armamentarium of imagistic techniques in clinical practice.

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References
1. Blei F. Lymphangiomatosis: clinical overview. Lymphat Res Biol 2011;9:185-190.
2. Satria MN, Pacheco-Rodriguez G, Moss J. Pulmonary lymphangiomatosis. Lymphat Res Biol 2011;9:191-193.
3. Faul JL, Berry GJ, Colby TV, et al. Thoracic lymphangiomas, lymphangiectasis, lymphangiomatosis and lymphatic dysplasia syndrome. Am J Respir Crit Care Med 2000;161:1037-1046.
4. Brown M, Pysher T, Coffin CM. Lymphangioma and congenital pulmonary lymphangiectasis: a histologic, immunohistochemical, and clinicopathologic comparison. Mod Pathol 1999;12:569-575.
5. Radhakrishnan K, Rockson SG. The clinical spectrum of lymphatic disease. Ann N Y Acad Sci 2008;1131:155-184.
6. Boland JM, Tazelaar HD, Colby TV, Leslie KO, Hartman TE, Yi ES. Diffuse pulmonary lymphatic disease presenting as interstitial lung disease in adulthood. Am J Surg Pathol 2012;36:1548-1554.
7. Chira RI, Chira A, Mircea PA, Valean S. Mediastinal masses-transsthoracic ultrasonography aspects. Medicine (Baltimore) 2017;96:e9082.
8. Harnisch E, Sukhai R, Oudesluys-Murphy AM. Serious complications of pulmonary biopsy in a boy with chylopericardium and suspected pulmonary lymphangiomatosis. BMJ Case Rep 2010;2010:bc0820092206.
9. Chira RI, Chira A, Ichim VA, et al. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of paraesophageal lung tumors - diagnostic yield and added value. Med Ultrason 2019;21:377-381.
10. El Hajj L, Mazieres J, Rouquette I, et al. Diagnostic value of bronchoscopy, CT and transbronchial biopsies in diffuse pulmonary lymphangiomatosis: case report and review of the literature. Clin Radiol 2005;60:921-925.