CASE REPORT

Atypical presentation of lymphangioleiomyomatosis as jugular vein thrombosis

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ABSTRACT. Lymphangioleiomyomatosis is a rare disorder of unknown origin that almost exclusively affects women of childbearing age. It is characterised by proliferation of abnormal smooth muscle cells (lymphangioleiomyomatosis cells) in the pulmonary interstitium and along the thoracic and abdominal lymphatics. Lymphangioleiomyomatosis may be associated with tuberous sclerosis complex. The most common manifestations of lymphangioleiomyomatosis are pulmonary symptoms, including progressive dyspnoea, recurrent pneumothoraces and chylous effusions. Extrapulmonary lymphangioleiomyomatosis as the initial presentation of the disease is highly unusual. We describe a patient with extrapulmonary lymphangioleiomyomatosis presenting as jugular vein thrombosis related to lower neck lymphangioleiomyoma. CT study showed bilateral lung cysts with left-sided hydropneumothorax and retroperitoneal lymphadenopathy. A left lower neck cystic lesion was seen with thrombosis of the adjacent left subclavian and internal jugular veins.

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Lymphangioleiomyomatosis (LAM) is a rare interstitial lung disease that affects women exclusively, typically during their reproductive years. A small percentage of patients have LAM in association with tuberous sclerosis complex (TSC). LAM is characterised by the abnormal proliferation of smooth muscle cells (LAM cells) in the lungs and in the thoracic and retroperitoneal lymphatics. Affected patients are at risk of developing renal hamartomas or angiomyolipomas. Patients with LAM characteristically present with chronic dyspnoea and cough and less commonly with spontaneous pneumothorax.

At radiography, LAM manifests with normal-to-large lung volumes and interstitial reticular opacities that may be subtle. Unilateral pneumothorax and unilateral or bilateral pleural effusions are frequent radiographic findings. CT and high-resolution CT demonstrate bilateral diffuse thin-walled cysts surrounded by normal lung parenchyma. CT may also demonstrate associated pleural effusion or pneumothorax, thoracic or abdominal lymphadenopathy and other abdominal abnormalities, including angiomyolipomas, lymphangioleiomyomas and ascites.

Manifestation of extrapulmonary LAM as an initial presenting symptom is rare. The most common forms of extrapulmonary LAM include renal angiomyolipoma, enlarged abdominal lymph nodes and lymphangioleiomyoma. Less commonly, ascites and hepatic angiomyolipoma may be present. If the diagnosis of extrapulmonary LAM precedes that of pulmonary LAM, the patient usually develops chest symptoms within one to two years.

Case history

A 40-year-old female patient presented to the emergency department with swelling of the left upper limb, and pain in the arm and left side of the neck and chest. There was no history of fever, trauma or oral contraceptive or any other drug intake, and there was no significant past history. On examination, the left upper limb was swollen and painful on compression; subcutaneous veins were prominent and peripheral pulses were palpable normally. High-resolution ultrasonography showed deep vein thrombosis of the left upper limb with echogenic thrombus in the left subclavian and internal jugular veins extending up to their confluence. A cystic lesion was seen in the left lower neck at the confluence of the two veins. The patient commenced anticoagulant medication and meanwhile was evaluated for the cause of venous thrombosis. There was no definite evidence of a systemic hypercoagulable state such as polycythaemia, protein C or protein S mutation. There was no breast lump on local examination, and there was no axillary lymphadenopathy. Ultrasonography of the bilateral breasts was normal. There were no malignant cells in the pleural fluid.

Contrast enhanced CT scan of the chest and neck was performed on a multidetector CT (MDCT). Thrombosis of the left internal jugular vein (IJV) was seen with a fluid density lesion juxtaposed to the lower end of left IJV at its confluence with the left subclavian vein (Figure 1), multiple superficial veins were outlined in the left upper limb (Figures 2 and 3). Lung window images showed innumerable, bilateral small, thin-walled lung cysts without intervening fibrosis and left-sided pneumothorax (Figure 4). Mediastinal window images revealed left pleural effusion (Figure 3) and aberrant

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Figure 1. Axial CT image of the lower neck showing thrombus in the lumen of the left internal jugular vein (IJV) with a thin-walled cyst in close approximation to the IJV posteriorly.

right subclavian artery (Figure 3) with common origin of the right and left common carotid arteries (not shown). Upper abdominal scans showed retroperitoneal lymphadenopathy (Figure 2). No renal or hepatic angiomyolipomas were seen, and no ascites was seen. The overall findings were compatible with LAM with left subclavian and jugular vein thrombosis related to cervical lymphangioleiomyoma complication.

Discussion

LAM is a rare, progressive cystic lung disease that primarily affects women, and can result in respiratory failure and the need for lung transplantation. Smooth muscle cell infiltration of the lung results in destruction of lung architecture; dilatation of distal airspaces; and obstruction of lymphatics, blood vessels and airways [1].

Figure 2. Axial CT image through the upper abdomen showing low attenuation retroperitoneal lymphadenopathy around aorta and inferior vena cava and reaching up to the renal hilae. No renal or hepatic mass lesion is seen. Multiple superficial veins are outlined in the left upper limb.

Figure 3. Axial mediastinal window through the chest shows aberrant right subclavian artery passing posterior to the oesophagus; left-sided pleural effusion is seen. Extensive superficial collateral veins are seen in the left upper limb.

Most reported cases of this disease occur in white women of childbearing age with a mean age of 34 years. Hormonal factors may play a role in the pathogenesis and clinical course of LAM, and menstruation, pregnancy and exogenous oestrogen (including use of oral contraceptives) may exacerbate symptoms [1]. The most common presenting symptom in patients with LAM is dyspnoea, reported in up to 59% of affected women [1]. Less frequent presenting symptoms include chest pain, haemoptysis and wheezing [1]. Pulmonary function studies usually demonstrate obstructive lung disease characterised by a reduction in the forced expiratory volume in 1 s (FEV_1) and the FEV_1 -to-forced vital capacity (FEV_1/FVC) ratio [1]. Pulmonary radiographic abnormalities in patients with LAM have been reported as reticular, reticulonodular and miliary opacities or pulmonary cysts [1]. These manifestations may precede, accompany or post-date other thoracic manifestations of

Figure 4. Axial lung window CT image showing multiple, small bilateral thin-walled lung cysts with normal intervening lung parenchyma. Left-sided small pneumothorax is seen anteriorly with pleural fluid (effusion) posteriorly and in the oblique fissure.

the disease, including pneumothorax and chylous pleural effusion. The CT manifestations of LAM are distinctive, characterised by numerous thin-walled cysts surrounded by normal lung parenchyma and distributed diffusely and bilaterally [2]. The high-resolution CT features of LAM are distinct from those of other diffuse lung diseases, such as pulmonary Langerhan's cell histiocytosis, emphysema and idiopathic pulmonary fibrosis. LAM is distinctively characterised by a diffuse distribution of cysts and does not typically spare the lung bases, and the intervening lung parenchyma in LAM is usually normal. Pulmonary imaging findings alone are diagnostic when diffuse bilateral thin-walled pulmonary cysts are demonstrated in women of child-bearing age [1, 2].

Patients with LAM often exhibit extrapulmonary manifestations of the disease and, in some rare cases, may present because of symptoms related to extrapulmonary involvement. Approximately 15–57% of patients with LAM have renal angiomyolipomas, which are often small and symptomatic. Other extrapulmonary manifestations of LAM include chylous ascites (in up to one-third of patients), uterine leiomyoma and lymphaticocouretic and lymphaticovenous communications. LAM may also affect the liver and pancreas. Abdominal and pelvic lymphangioleiomyomas are described [3].

LAM can occur without other disease ("sporadic" LAM) or in association with TSC [4]. TSC is an autosomal-dominant genetic disorder with pulmonary, renal and lymph node findings similar to those of LAM. For many years, it has been debated whether LAM represents a forme fruste of TSC. Although histological and clinical features may be identical in women with LAM and patients with TSC-associated pulmonary involvement, there are reported differences. Patients with TSC-associated LAM, compared with patients with sporadic LAM, generally experience a longer delay between onset of symptoms and diagnosis of pulmonary disease, exhibit chylothoraces less frequently and are more likely to present with gradual onset of dyspnoea. Renal angiomyolipomas are found in 40–80% of patients with TSC but occur in 8–57% of patients with sporadic LAM. Patients with LAM do not have the brain and skin findings associated with TSC (cortical tubers, subependymal nodules, retinal hamartomas, facial angiofibromas or periungual fibromas) [4]. Ours was a case of sporadic LAM as there were no cutaneous or central nervous system (brain) manifestations.

The four major abdominopelvic abnormalities described in patients with LAM include renal angiomyolipoma (AML), lymphadenopathy, lymphangiomyoma and chylous ascites [5]. Renal angiomyolipomas have been observed on abdominal CT scans in 20–54% of patients with LAM. These tumours are characterised by CT evidence of soft tissue, fat and enhancing vessels in variable proportions within a renal mass. Lymphangioleiomyomas result from the proliferation of smooth muscle cells in the lymph vessels, which causes dilatation and obstruction in the lymph vessels and results in cystic collections of chylous material. This process is similar to the observed obstruction and dilatation of the thoracic duct in patients with LAM. At CT, the dilated retroperitoneal lymph vessels may have either thin or thick walls and may contain material low in attenuation

(3–25 HU). These features may be explained as a mechanical complication of lymphatic obstruction and of the disruption of lymphatic flow. Lymphangioleiomyomas may lie between and displace vascular structures in the retroperitoneum and, along with abdominal adenopathy, may be misdiagnosed as a neoplastic process such as lymphoma. Overdistention of lymph cysts may result in rupture and chylous ascites [5]. Cysts may also be related to other acute presentations such as abdominal or pelvic pain [6, 7]. Cyst-related complication (rupture) was related to the venous thrombosis in our case as there was no other evident cause of venous thrombosis, which was restricted around the location of cyst and distally upstream in the neck and upper limb.

Other non-thoracic imaging findings in patients with LAM (renal AML, enlarged lymph nodes and lymphangiomyoma) in conjunction with the classic thin-section CT finding of pulmonary cysts, help to support the radiological diagnosis of this disease [7]. CT findings of multiple, bilateral thin-walled pulmonary cysts with retroperitoneal lymphadenopathy and cervical lymphangioleiomyoma were compatible with the diagnosis of LAM in our case.

Disease severity and progression are variable, and are evaluated with pulmonary function and gas exchange testing, complemented by radiological evaluation [8].

Treatment of pneumothorax in LAM includes simple aspiration or intercostal drainage and surgical interventions such as pleural abrasion, pleurodesis, pleurectomy, thoracoscopic pleurodesis with long-term drainage or bullectomy with pleurodesis. Chylous effusions may be managed by thoracentesis, chemical pleurodesis or parietal pleurectomy (with or without thoracic duct ligation). The efficacy of hormone therapy including anti-oestrogen interventions and progesterone administration for LAM remains controversial. Single- or double-lung transplantation (or, in rare cases, combined heart-lung transplantation) may be performed in end-stage disease [9].

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