CASE REPORTS

Diffuse Thoracic Lymphangiomatosis: Diagnosis and Treatment

E.J. Bermejo Casero, R. Mongil Poce, R. Arrabal Sánchez, A. Fernández de Rota Avecilla, A. Benítez Doménech, and J.L. Fernández Bermúdez

Servicio de Cirugía Torácica, Hospital Regional Universitario Carlos Haya, Málaga, Spain.

Histologically, lymphangiomatosis is a rare type of benign neoplasm caused by abnormal development and proliferation of the lymphatic system. Thoracic lymphangiomatosis can present in a localized (lymphangioma) or diffuse form (lymphangiomatosis). In most cases the disease progresses to serious morbidity or even death.

The treatment of choice for localized disease is usually surgery or, less frequently, local injection of sclerosing agents (streptococcus antigen OK-432). However, in diffuse forms there is a gelatinous infiltrate without defined limits. In these cases the main treatment option is radiotherapy.

We report 2 cases of diffuse thoracic lymphangiomatosis with pulmonary infiltrate. In both cases radiotherapy in appropriate doses successfully eliminated pulmonary infiltrates, pleural effusion, dyspnea, and general discomfort. Surgery was needed to resolve complications of the disease and for diagnosis.

Key words: *Thoracic lymphangiomatosis. Thoracic lymphangioma. Bronchovascular infiltrates.*

Linfangiomatosis torácica difusa: diagnóstico y tratamiento

La linfangiomatosis constituye una rara clase de tumoración benigna, desde el punto de vista histológico, resultado de un anormal desarrollo y proliferación del sistema linfático. La afectación torácica puede presentarse localizada (linfangioma) o difusa (linfangiomatosis). En la mayoría de los casos el curso evolutivo de la enfermedad es progresivo con aparición de clara morbilidad e incluso mortalidad.

En las formas localizadas la cirugía, principalmente, o la instilación local de sustancias esclerosantes (antígeno estreptocócico OK-432) son el tratamiento elegido. Ahora bien, en las formas difusas existe un material gelatinoso, infiltrante, sin límites definidos. Aquí la radioterapia constituye la principal opción terapéutica.

Se presentan 2 casos de linfangiomatosis torácica difusa con infiltración pulmonar. Se comprueba que la radioterapia a dosis adecuadas consigue la desaparición de los infiltrados pulmonares y del derrame pleural, así como de la disnea y mal estado general. La cirugía es necesaria en la resolución de las complicaciones paralelas a la enfermedad y como técnica diagnóstica.

Palabras clave: *Linfangiomatosis torácica. Linfangioma torácico. Infiltrados broncovasculares.*

Introduction

Lymphangiomas are neoplasms resulting from abnormal development of the lymphatic system. They mostly affect children and are found in the neck and face (cystic hygroma).[1] In the thorax they take a localized form (lymphangiomas) or appear as diffuse proliferations (lymphangiomatosis). Symptoms—arising from compression caused by mediastinal or pulmonary masses and from pleural/pericardial effusions, or from rib or vertebral fractures—include chronic bone pain or dyspnea caused by interstitial infiltration.

Correspondence: Dr. E.J. Bermejo Casero.
Servicio de Cirugía Torácica. Hospital Regional Universitario Carlos Haya.
Avda. Carlos Haya, s/n. 29010 Málaga. España.

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We report 2 cases of diffuse thoracic lymphangiomatosis with pulmonary infiltrates. The patients, a 23-year-old woman and a 15-year-old boy, were both from Morocco. The report describes the diagnostic process for each patient and the results after specific treatment.

Case Descriptions

Case 1

A 23-year-old woman with no relevant medical history presented with a clinical picture of asthenia and general discomfort in her country of origin a year before admission to our department. Radiographic examination carried out in Morocco detected a mediastinal mass. A biopsy sample of the lesion taken by anterior left mediastinotomy led to a diagnosis of angiolipoma at that time.

The patient later went to the emergency department of a hospital near her home in Melilla with a clinical picture of

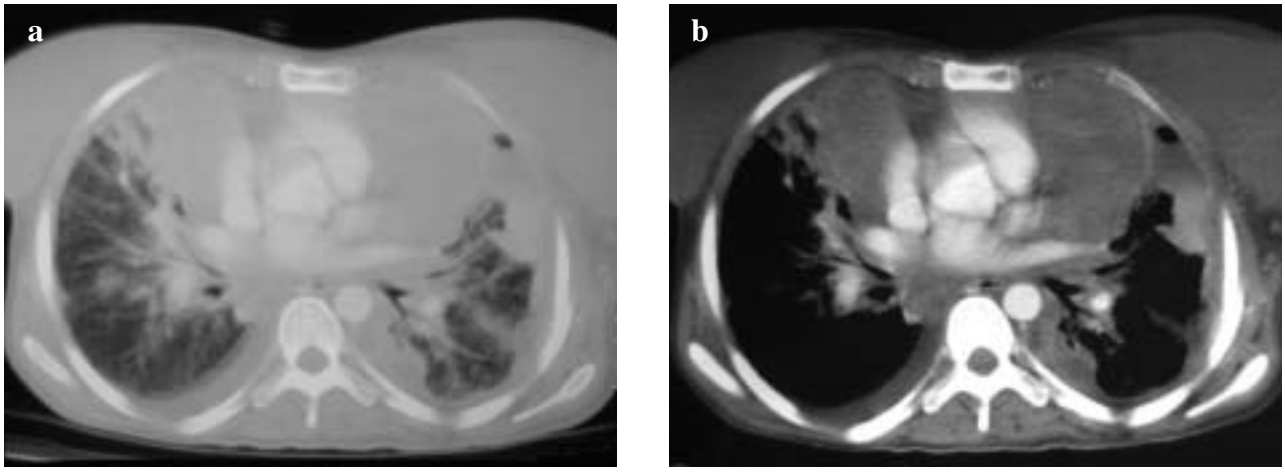

Figure 1. Mediastinal neoplasms with peribronchovascular infiltrate *(a)* and bilateral pleural effusion in the mediastinal window *(b)*.

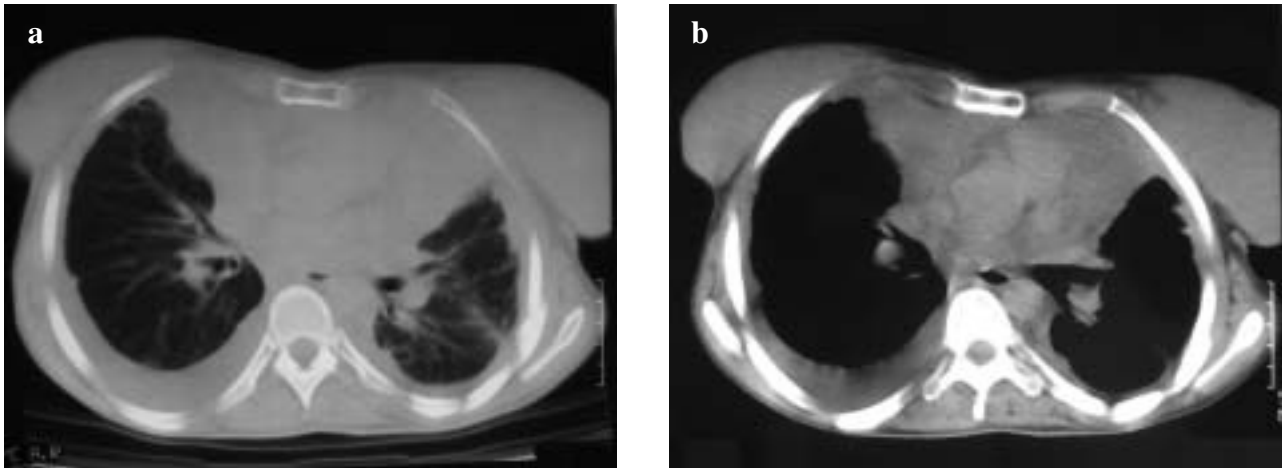

Figure 2. Disappearance of pulmonary infiltrate *(a)* and reduction of mediastinal neoplasms *(b)* after radiotherapy.

sudden dyspnea caused by a massive left pleural effusion and from there she was referred to our hospital. Physical examination revealed very poor nutritional status and pale skin and mucous membranes. Auscultation revealed hypophonesis of the left hemithorax. Blood tests showed a hemoglobin concentration of 9.1 g/dL, a platelet count of 103 000/nL, and a white cell count of 13 700/nL with a normal leukocyte formula. Coagulation and biochemical results were normal. The total protein level was low (4.9 g/dL) and the albumin level was 1.82 g/dL. Posteroanterior and lateral radiographs of the thorax showed a massive left pleural effusion. A tube inserted to drain the thoracic fluid was left in place for 6 days.

Computed tomography (CT) of the thorax revealed a large mediastinal mass surrounding the great vessels and the heart, a left pleural empyema, and a bilateral interstitial pulmonary pattern with thickening of the peribronchovascular interstitium and bilateral effusion (Figure 1). The images suggested the following diagnostic possibilities: aggressive lymphoma, embryonic mediastinal tumor, carcinoma of the thymus, or lymphangiomatosis.

Surgery was first carried out to treat the pleural empyema and obtain a diagnostic biopsy sample from the mediastinal mass. The radiographic images indicated a nonresectable tumorous growth. During surgery, left pulmonary decortication was carried out and a biopsy sample was taken from a soft diffuse trabecular mediastinal mass with cavities containing a serosanguinous effusion. The pathology report found mediastinal pleura with acute abscessed inflammation, fibrin deposits, and reactive fibrosis; the pathological diagnosis was lymphangiomatosis. After decortication the patient´s respiratory symptoms improved but she continued to suffer from intense and generalized weakness and gradually increasing dyspnea, attributable to the pulmonary infiltrate from tumor growth.

Case 2

A 15-year-old boy with no relevant medical history presented in his country of origin with a clinical picture of right pleural pain in the absence of signs of infection. A chest x-ray showed right pleural effusion and cardiomegaly. The patient was referred to this hospital, where an effusion of chylous appearance was observed. A diagnosis of chylothorax was confirmed on finding a pleural fluid triglyceride level of 802 ng/mL.

Pericardiocentesis also indicated chylopericardium. The pericardial effusion had caused a right ventricular and atrial end-diastolic collapse. The only significant result in the follow-up analysis was an eosinophil level of 6%.

A CT scan of the thorax showed pneumomediastinum and moderate pericardial effusion. Infiltrates were evident at the base of the right lung, and bilateral pleural effusion and peribronchovascular thickening were both more pronounced on the right.

A tissue sample was taken using video-assisted thoracoscopy. The lung adhered closely to the chest wall with whitish, milky parietal loculations. A fragment of pulmonary parenchyma was extracted using a 45 mm endoscopic cutter. Pleural samples were also taken. The findings were fibrinous pleuritis and severe lymphangiectasias in the visceral pleura, without significant parenchymal alterations. As none of the histological samples conclusively confirmed the diagnosis, an anterior left mediastinotomy was carried out a few days later to obtain mediastinal tissue that led to a diagnosis of lymphangiomatosis.

Both patients received radiotherapy of 18 Gy in 12 sessions over 18 days. These dosages effectively controlled the disease without causing pulmonary fibrosis. A follow-up CT scan and physical examination were carried out 1 month later in the outpatient department. In the first patient the peribronchovascular pulmonary infiltrate had disappeared (Figure 2), the mediastinal neoplasm had become smaller, and the clinical picture of dyspnea, asthenia, and general discomfort had diminished. In the second patient the pulmonary infiltrates had also disappeared, as had the pleural/pericardial effusions.

Discussion

Lymphangiomatosis is a rare entity that should always be diagnosed histologically from a biopsy sample. Although it is a benign neoplasm, it rarely undergoes spontaneous remission and often progresses to serious morbidity and even death. It can cause pleural/pericardial effusions, compressive symptoms, or dyspnea.[2] Rib and vertebrate infiltration also occurs, accompanied by pathological fractures or chronic bone pain. Surgery is the treatment of choice only in localized forms of the disease.[3]

So-called sclerosing treatments, such as streptococcus antigen OK-432 infusion, bleomycin, or radiotherapy have been used with varying results. Their effectiveness lies in causing sclerosis of the endothelium that covers the cysts or dilated vessels, thus destroying them through an inflammatory reaction.

Two sclerosing treatments—radiotherapy and local instillation of OK-432—have given encouraging results. In localized cystic forms of the disease an instillation of 0.1 mg of OK-432 can be applied after aspiration of the cystic fluid. Local instillation may be repeated up to 4 times depending on response. A prospective study over 5 years carried out at the University of Witwatersrand in Johannesburg demonstrated that it is the macrocystic form of the disease, with up to 5 cysts, that benefits from this treatment, since microcystic forms, with dozens or hundreds of small cysts, have large amounts of connective and fibrous tissue, which does not respond to the attempt at sclerosis.[4]

In diffuse lymphangiomatosis several kinds of treatment have been tried without success, including chemotherapy and interferon gamma treatment. Radiotherapy has proved to be the only effective treatment and it also leads to sclerosis of the dilated lymph vessels.

The total fractionated dose should be no more than 20 Gy to avoid causing pneumonitis and subsequent pulmonary fibrosis. Usual doses are 20 Gy in 10 fractions or 18 Gy in 12 fractions over 18 days. This treatment achieves radiation-induced lymphatic endothelial swelling and the resulting fibrosis causes obstruction of the lymph vessels.[5]

In conclusion, lymphangiomatosis is a very rare disease that requires a tissue sample for diagnosis. We found that diffuse forms of lymphangiomatosis affecting the mediastinum respond well to radiotherapy.

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