General Medicine: Open Access
ISSN: 2327-5146

Gironés, General Med 2015, 3:1
DOI: 10.4172/2327-5146.1000167

Case Report Open Access

Pulmonary Lymphangioleiomyomatosis (LAMP) and Adenocarcinoma of the Lung: A Case Report and Literature Review

Regina Gironés*

Medical Oncology Unit, Hospital Lluís Alcanyís, Xàtiva, Valencia, Spain

***Corresponding author:** Regina Gironés, Oncologist, Physician, Medical Oncology Unit, Hospital Lluís Alcanyís, Xàtiva, Valencia, Spain, E-mail: girones_reg@gva.es

Rec date: Jul 09, 2014 **Acc date:** Feb 19, 2015 **Pub date:** Feb 25, 2015

Abstract

Pulmonary lymphangiomyomatosis (LAMP) is a rare, progressive and fatal interstitial lung disease that affects women of childbearing age. Its association with neoplasms, mostly renal angiomyolipomas, has previously been reported. Association with lung cancer has also been documented; however there are very few reported cases.

We reported a case of a 42-year-old woman who presented with hemoptysis. Chest x-ray and computed tomography findings suggested LAMP. A lung biopsy was done, and pathological examination diagnosed LAMP and synchronous lung adenocarcinoma. Positron emission tomography with (18)F-fluorodesoxyglucose (PET-TAC FDG) after surgery did not identify pathologic uptake. At follow up, another suspicious lung nodule was found. Removal showed another lung adenocarcinoma. No more nodules have been found.

This is the first case of synchronous adenocarcinoma resected twice in combination with LAMP.

Introduction

Lymphangioleiomyomatosis (LAMP) is a progressive cystic lung disease that predominantly affects young women [1]. The most common clinical features of LAMP are dyspnea upon exertion, recurrent pneumothoraces and chylous effusions. LAMP is histologically characterized by diffuse infiltration of the lung parenchyma with benign smooth muscle-like cells and formation of cysts that vary in size from a few millimeters to several centimeters. Although LAMP occurs sporadically in patients without evidence of systemic genetic disease (sporadic LAMP), it also occurs in up to forty percent of women with tuberous sclerosis complex (TSC-LAM) [2]. The majority of studies have reported LAMP as a benign neoplasm. Its malignant nature is uncertain. Its association with tumors has been limited almost exclusively to the kidney.

Herein, we describe a patient who developed lung adenocarcinoma twice in addition to LAMP. We have found only one previous case of malignant lung nodules detected by PET in a patient with LAMP, described by Young et al. [2].

Case Report

A 42-year-old woman presented with hemoptysis in July 2007. She was a smoker (40 packs/year) and has three children. No other diseases were reported.

The patient's physician obtained a chest radiograph. Based on this, a chest high-resolution CT scan (HRCT) was performed, and the patient was referred to the pulmonary clinic for further evaluation. She reported no chest pain, cough or dyspnea. On physical examination, there were no signs that were compatible with the diagnosis of tuberous sclerosis.

Radiologic Findings

Multiple thin-walled cysts of small size (less than 1 cm) and at upper part of the lung predominance suggested LAMP. In addition, HRCT described a peripheral nodule in the right superior lung lobe that was 10x12 mm in size with pathologic contrast uptake. A radiologist suggested arteriovenous malformation.

Based on these findings, an angiographic study was obtained. This study showed an alteration of normal bronchial vasculature; therefore, embolization was performed.

After the embolization, the patient was sent to a thoracic surgeon for diagnosis. A pulmonary biopsy was done in September 2007. Two pulmonary parenchyma fragments were resected. In one of them, a subpleural nodule of 1 cm was detected. Pathologic analyses showed poorly differentiated adenocarcinoma with a diameter of 1 cm and LAMP at the surrounding parenchyma.

Analysis for epidermal growth factor receptor mutations (EGFR) at exons 18, 19 and 21 were negative.

After resection, the patient recovered at our outpatient oncology department. The patient was diagnosed with LAMP and stage I lung adenocarcinoma. She was not considered a candidate for adjuvant treatment. PET-TAC was performed, which showed no pathologic uptake. Patient attended routine follow-up visits.

In November 2008, one year after resection, another nodule was detected on a fllow-up HRCT. Because of its subcentimeter size, a PET was not done. A thoracic surgeon admitted the patient to the hospital again. In February 2009, another lung nodule, 2 cm in size, was removed. A pathological review showed adenocarcinoma and a margin free of tumor.

We again considered the patient for follow-up visits.

Since February 2009, patient is attended our outpatient clinic for follow-up. She also is been revised by neumologist to be included at pulmonary transplant program. Last visit (April 2014) HRCT found no more nodules and stabilization of LAMP.

Discussion

LAMP is a rare, progressive and fatal interstitial lung disease that affects women of childbearing age. It is characterized by non-neoplastic proliferation of atypical smooth muscle cells around lymphatics, venules and bronchioles [1].

LAMP predominantly affects women and is exacerbated by pregnancy. Additionally, LAMP is predominantly sporadic; however, it can manifest in association with TSC, an autosomal dominant inherited disorder [3,4].

At clinical presentation, dyspnea and chronic cough are commonly presented in patients with LAMP. Hemoptysis occurred less frequently [1,4]. Our patient presented only with hemoptysis.

On a chest radiograph, LAMP is characterized by an increased number of interstitial markings in the presence of normal lung volumes or hyperinflation. Although rarely seen on chest radiograph, thin-walled cysts surrounded by normal parenchyma, which are pathognomonic of LAM, are easily identified on an HRCT scan of the chest [1,4].

The diagnosis of LAMP can be made with reasonable certainty by expert radiologists using an HRCT scan. However, a lung biopsy is generally required in cases where TSC, angiomyolipoma or chylous effusions are absent (such as our patient).

The diagnosis of LAMP requires an HRCT scan demonstrating thin-walled cystic changes and either a positive tissue biopsy (including immunohistochemical reactivity with human melanoma black-45 HMB-45) or a compatible clinical context [5].

Regarding other radiographic examinations, a pilot study by Young et al. suggests that FDG-PET is negative in benign lesions; no abnormal uptake was identified in the LAMP lesions in their study. They concluded that FDG-PET is therefore not likely to be useful for estimating the burden of disease in patients with LAMP; however, it can be used to identify or exclude other neoplasms in these patients, as in our case. The knowledge that LAMP is PET-silent can be clinically useful because coincident neoplasms can develop in LAMP patients [2].

It has been previously described that malignant tumors of the kidney, which develop either as malignant angiomyolipomas (AML) or as renal cell carcinomas, occur in about 63% of sporadic LAM and in most TSC patients [3].

Until recently, LAMP and TSC tumors were considered benign. However, clinical and genetic data suggest a link between loss of TSC2 function and cell invasion and metastasis. Goncharova et al hypothesize that LAM cells are metastatic cells from AML or renal tumors, and LAMP cells represent metastasized secondary tumors [3].

Interestingly, about a third of sporadic LAMP cases are without AML; in such cases, LAM cell origin cannot be explained by metastatic or neoplastic cell dissemination [3,6].

Only a lung transplant can save the life of a patient with LAMP [3]. However, malignant history is a known transplant contraindication.

Recent evidence suggests that the proliferative and invasive nature of LAM cells may be due in part to somatic mutations in the TSC2 gene, which has been implicated in the pathogenesis of TSC [4].

Experimental therapies that would be useful for LAMP patients, such as mTOR inhibitors, are being tested in lung cancer [4,5]. If carcinogenesis of LAMP and lung cancer has common molecular pathways, an opportunity would exist for combined therapy.

There are few cases reporting lung cancer in LAMP patients. In a pilot study by Young et al., FDG-PET revealed an increased uptake in a lung nodule at the left upper lobe but not in other regions of the lung that are affected by LAMP. The nodule proved to be a lung adenocarcinoma upon biopsy [2].

Information on the treatment of non-small cell lung cancer (NSCLC) with comorbid interstitial lung disease (ILD) is extremely limited. Most clinical trials exclude patients with ILD. Usually, clinicians hesitate to treat lung cancer with ILD, because the treatment, including surgery, chemotherapy, and radiotherapy, can itself induce interstitial pneumonia (IP) or exacerbate preexisting ILD

We presented a case with double resection of lung adenocarcinoma in combination with LAMP. Currently, the patient has been excluded from lung transplantation. The patient is one year free of lung cancer. She could be included from lung transplantation program if remains five years free of cancer. We ignore the best approach for this difficult case.

References

1. Prieto VC, Zambrano CD, Del CPE, Torrado C, Macías JP (2004) Linfangioleiomiomatosis pulmonar: presentación de un caso de evolución fulminante y revisión de la literatura. Rev Esp Anestesiol Reanim 51: 595-599.
2. Young LR, Franz DN, Nagarkatte P, Fletcher CDM, Wikenheiser-Brokamp KA, et al. (2009) Utility of FDG-PET in Sporadic and Tuberous sclerosis associated lymphangioleiomyomatosis. Chest 09: 0336
3. Goncharova EA, Krymskaya VP (2008) Pulmnary lymphangioleiomyomatosis (LAM): progress and current challenges. J Cell Biochem 103: 369-382
4. Gustavo PR, Arnold SK, Linda AS, Yi Z, Dense C, et al. (2002) Genetics and Gene Expresión in Lymphangioleiomyomatosis. Chest 121: 56S-61S
5. McCormack FX (2008) Lymphangioleiomyomatosis. Chest 133: 507-516
6. Karbowniczek M, Astrinidis A, Balsara BR, Testa JR, Lium JH, et al. (2003) Recurrent lymphangiomyomatosis after transplantation: genetic analyses reveal a metastatic mechanism. Am J respir Crit Care Med 167: 976-982