



Case Report

Lymphangioliomyomatosis in a Post-Menopausal Women

Cristina Soler-Ferrer,* Albert Gómez-Lozano, Carles Clemente-Andrés, Eulàlia De Cendra-Morera, Montserrat Custal-Teixidor, and Joan Colomer-Pairés

Departamento de Medicina Interna. Hospital de Santa Caterina, IAS, Salt, Girona, Spain

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ABSTRACT

Lymphangioliomyomatosis is a rare disease characterised by pulmonary cysts with abnormal proliferation in the lymphatic system. It occurs almost exclusively in women of fertile age due to a hormonal influence, for this reason it is extremely rare in post-menopausal patients. In these cases it is usually associated with hormone replacement therapies. It is known that this disease is strongly associated with other conditions, such as tuberous sclerosis and renal angiomyolipomas.

The case of a post-menopausal patient suffering from lymphangioliomyomatosis, with no history of hormone therapy is presented. Renal angiomyolipomas and clinical signs indicative of a probable tuberous sclerosis were also detected.

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Linfangioliomiomatosis en mujer posmenopáusica

RESUMEN

La linfangioliomiomatosis es una enfermedad rara caracterizada por quistes pulmonares con proliferación anómala del sistema linfático. Se presenta casi en exclusiva en mujeres en edad fértil debido a una influencia hormonal, por lo que resulta sumamente infrecuente en pacientes posmenopáusicas. En estos casos suele tener relación con tratamientos hormonales sustitutivos. Es conocido que esta enfermedad tiene un alto grado de asociación con otras afecciones, como la esclerosis tuberosa y los angiomiolipomas renales. Presentamos el caso de una paciente posmenopáusica afectada de linfangioliomiomatosis, sin ningún antecedente de tratamientos hormonales, en la que se detectaron, además, angiomiolipomas renales y criterios clínicos indicativos de esclerosis tuberosa en grado de probable.

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Palabras clave:

Linfangioliomiomatosis

Angiomiolipoma renal

Esclerosis tuberosa

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Introduction

Lymphangioliomyomatosis (LAM) is an infrequent entity of unknown aetiology that affects, almost exclusively, women of child-bearing age. A series in 2000 in our country estimated a prevalence of 1 case per 1,000,000 inhabitants.¹ It appears as an isolated disease or in association with tuberous sclerosis, in which 2%-3% of patients may present LAM.² However, specific screening in women with tuberous sclerosis reveals up to 40% LAM indicating that many of these patients do not develop clinical lung disease.³ LAM is characterised by the cystic destruction of lung parenchyma, associated with an uncontrolled

proliferation of atypical smooth muscle cells, called LAM cells.³ LAM is predominantly pulmonary although it is not uncommon to find extrathoracic involvement. Moreover, it is known that renal angiomyolipomas are detected in 40-80% of patients with tuberous sclerosis;^{4,5} nevertheless, there is also an important association (15%-30%) in LAM patients, which points to the existence of similarities between the two diseases.^{4,6}

We present a case of LAM in a post menopausal woman with probable tuberous sclerosis, according to the criteria of the Tuberous Sclerosis Alliance⁷ and renal angiomyolipomas.

Clinical Observation

The patient is a female of 70 years of age, non-smoker, who consulted the Internal Medicine Service for dyspnoea on exertion.

* Corresponding author.

E-mail address: cristina.soler@ias.scs.es, csoler@comg.cat (C. Soler-Ferrer).

Notable in her pathological history was an episode of pneumonia 20 years ago and a cerebral tumour intervened and treated with radiotherapy 3 years earlier in another hospital, of which the histology is unknown and which resulted in left-facial paralysis. Physical exploration was normal, with oxygen saturation of 98%. Discrete cutaneous lesions indicative of angiofibromas were detected in the periorbital region only; lesions were not detected in any other body region. The chest x-ray (Figure 1) showed an interstitial pattern and the computerised tomography (Figure 2) evidenced multiple cystic images throughout the pulmonary field of both hemithorax, morphology round and thin-walled, without vascular structures or septum thickening. Respiratory function exploration showed the forced vital capacity (FVC) was 1,970ml (68% of the theoretical value), the forced expiratory volume (FEV₁) in the first second was 1,260ml (61% of the theoretical value) with FEV₁/FVC of 63.65%. A fibrobronchoscopy was performed with bronchoalveolar lavage and transbronchial biopsies.



Figure 1. Chest x-ray showing an interstitial pattern.

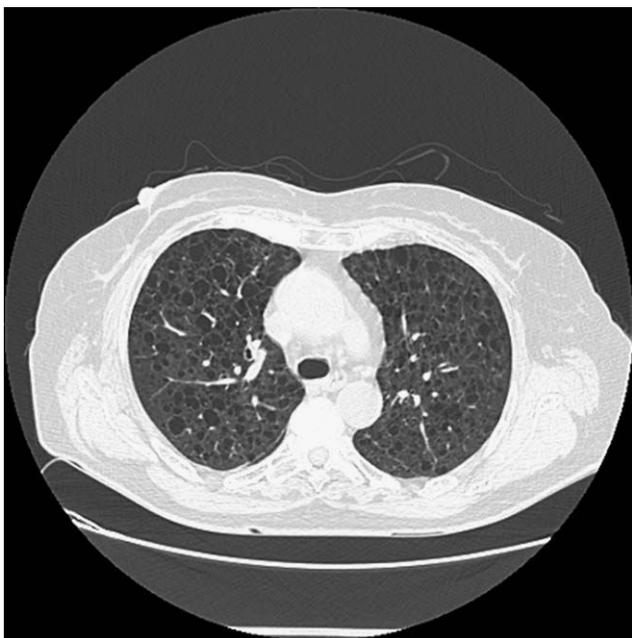


Figure 2. Computerised tomography evidencing multiple cystic images throughout the pulmonary field of both hemithorax.

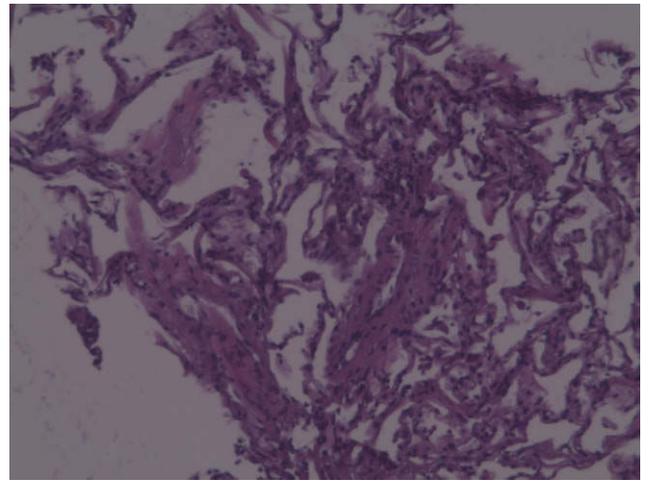


Figure 3. The anatomopathological study of the biopsies allowed diagnosis to be established as pulmonary lymphangioleiomyomatosis.

The anatomopathological study (Figure 3) of the biopsies established the diagnosis of pulmonary lymphangioleiomyomatosis. A study of the hormone receptors was performed which showed slight progesterone receptor positivity in numerous cells around the vascular structures. Computerised abdominal tomography and ultrasound were performed to rule out associated tumourations which allowed the discovery of a fat-density lesion at the lower pole of the right kidney, of 20mm, indicative of angiomyolipoma, and 2 lesions with similar characteristics but smaller size in the lower pole (7mm) and middle third (7.8mm) of the left kidney.

Discussion

LAM is a rare pulmonary disease of still unknown aetiology and pathogenesis. We know that the disease progresses slowly until death in 8 to 10 years⁸ and that it manifests in the fertile stages of a woman's life, with exacerbations during menstruation and pregnancy, which indicates a probable hormonal influence. Diverse studies indicate that the progress of LAM may be accelerated by oestrogen and slowed by progesterone.⁹⁻¹¹ It is documented that steroid, oestrogen and progesterone receptors can be found in pulmonary biopsies.¹¹ The disease is extremely rare in post menopausal women, and in these case almost exclusively with oestrogen replacement treatment.^{12,13} However, the finding of LAM in preadolescents, post menopausal women and even males indicates that oestrogens are not the only aetiological factor.

In the case in question, the patient is post menopausal with no history of hormone replacement treatment, who may have tuberous sclerosis (probable diagnosis)⁷ as the only predisposing factor. The majority of authors suggest that the association of angiomyolipomas with pulmonary LAM is a "forme fruste" of tuberous sclerosis and theorise that LAM and tuberous sclerosis represent a range of the same disease.^{4,14} The overlap between these 3 diseases (LAM, tuberous sclerosis and renal angiomyolipoma) is known as tuberous sclerosis complex.¹⁵

In older women the disease presents with similar symptoms to those in young women, with the exception that the clinical course is longer and more benign after menopause.

Current treatments for LAM are based mainly on the antagonism of oestrogen action,^{9-11,13} progestins, tamoxifen or surgical castration by oophorectomy being the most commonly employed treatments. Rapamycin is an immunosuppressant agent indicated in the treatment of tuberous sclerosis: a slight reduction in the size of renal angiomyolipomas has been confirmed although in some cases there

is a tendency for them to increase in size again when the drug is withdrawn. In contrast, LAM patients who used rapamycin showed a sustained improvement in spirometry after interruption of the treatment.¹⁶ As a last resort, in serious cases with progressive involvement of the respiratory function, a pulmonary transplant must be considered.

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