Pulmonary lymphangioleiomyomatosis (LAM) is a rare lung disease that almost exclusively affects young women of childbearing age. The true incidence and prevalence of LAM are unknown. This study was conducted to evaluate the characteristics of lymphangioleiomyomatosis in Spain. Methods: Over a 2-year period, a questionnaire designed for this study was collected. This questionnaire included sociodemographic, clinical, radiological and functional data. Information about the study and this questionnaire were both sent by e-mail to all the participants of the interstitial disease registry of 2004. Results: Seventy-two patients, all of whom were women, were included in the registry, with a mean age of 44.56 ± 11.1 yr. Sixty-three patients (87.5%) presented the sporadic LAM and 9 (12.5%) presented LAM associated with tuberous sclerosis (LAM-TS). LAM diagnosis was confirmed with an open lung biopsy in 57 patients (79.2%) and was performed with thoracic HRCT compatible with LAM diagnosis in the other 15 cases. The most frequent symptom was dyspnoea (90%) followed by cough (44.4%). Almost 40% of patients presented renal angiomyolipomas in the study and the most frequent spirometric pattern was obstructive in more than half of the patients. Most patients with LAM-TS (88.8%) had renal angiomyolipomas compared with 31.7% in the sporadic LAM group. Conclusion: The characteristics of the Spanish population affected with LAM are similar to those of other countries. Most patients were symptomatic, had a history of previous pneumothorax and presented abnormal radiological findings and pulmonary function tests. (Sarcoidosis Vasc Diffuse Lung Dis 2009; 26: 85-91)

Key words: lymphangioleiomyomatosis, tuberous sclerosis complex, pneumothorax, HMB-45

Editorial:}
young women of childbearing age. It is characterized by the proliferation of atypical smooth muscle cells (LAM cells) in the pulmonary interstitium and around the bronchovascular structures and by the formation of parenchymal cysts, which leads to the progressive loss of pulmonary function (1, 2). Most cases appear between menarche and menopause; there is less prevalence in post-menopausal women, especially during substitutive hormonal treatment.

There are two different types of LAM: 1) without evidence of other disease (sporadic LAM); and 2) associated with tuberous sclerosis complex (TSC), an autosomal dominant syndrome characterized by the formation of hamartomas in various organs, including the central nervous system, skin, eyes, heart, kidney and lungs. Sporadic LAM, in addition to the lung disorder, can also present extrapulmonary manifestations, angiomyolipomas and lymphangioleiomyomas (3).

The outcome of patients with LAM varies widely. Older series estimated a mean survival of 10 years from the time of diagnosis. However, recent studies have reported better prognosis, with survival of around 80 to 90% at 10 years after the onset of symptoms (4).

The low prevalence of LAM means that it is a relatively unknown disease. It is frequently misdiagnosed as asthma, chronic bronchitis or other respiratory diseases, on account of the diverse initial clinical and radiological features of the disease. In fact, symptoms usually appear before the disease becomes detectable on chest X-ray (5). The differential diagnosis includes emphysema and Langerhans cell Histiocytosis, which may have a similar clinical presentation (6). The smoking history and the morphology of the cysts can be helpful in differentiating these disorders.

The current incidence and prevalence of LAM are unknown. According to previous studies, LAM affects approximately one-third of women with tuberous sclerosis and the prevalence of sporadic LAM is estimated to be 2.6 per one million women (7, 8). The prevalence of LAM is probably underestimated based on its clinical latency and the absence of specific laboratory tests. The LAM registries increase our knowledge of the disease and its clinical presentation, as well as increasing the awareness of LAM, which could lead to the development of new therapeutic strategies and reduce the number of mistakenly diagnosed patients.

The aim of the present study was to investigate the mean features of the LAM in Spain in order to identify demographic, clinical, physiological or radiological data that could be associated with the outcome of LAM patients.

**Material and methods**

This retrospective, transversal multicentre study was undertaken through the Spanish LAM Registry, which was performed by a network of chest physicians distributed nationwide, members of the Diffuse Interstitial Pulmonary Disease Workgroup (Grupo de Trabajo de Enfermedades Pulmonares Intersticiales Difusas- EPID) in the Spanish Society of Pulmonology and Thoracic Surgery (Sociedad Española de Neumología y Cirugía Torácica- SEP-AR) (9). The Spanish Registry of LAM was initiated in 2005 under the auspices of this group. Cases of pulmonary LAM were recruited from January 2005 by the participating physicians, including all the known cases of pulmonary LAM that they had followed up, previously diagnosed and newly diagnosed cases, whether dead or alive. The reported data were collected by a co-ordination centre based in Madrid, Spain. Reports to the Spanish LAM Registry were anonymous for all patients. Information about the objective and methodology of the study was conveyed at various meetings and the preliminary data were presented at the 4th International Symposium on Interstitial Pulmonary Diseases (Madrid, 2006).

All patients diagnosed with LAM were included, sporadic cases as well as those associated with tuberous sclerosis. LAM diagnosis was considered acceptable for inclusion in the study only in diagnosed cases following diagnostic criteria: 1) histological findings on lung biopsy (8), 2) typical cystic appearance on high resolution CT scan (HRTC) and compatible symptoms or related disorders (renal angiomyolipomas, chylous ascitis).

**Data collection**

Initially, a questionnaire was sent to all physicians who participated in the LAM registry in January 2005. The report on each patient included: age at the time of the Registry, time from the onset of symptoms to diagnosis, diagnostic methods (open lung biopsy, transbronchial biopsy, bronchoalveolar lavage), per-
sonal and family past medical history, drug history, smoking habit, hormonal therapy, pregnancies or menopause, concomitant diseases, clinical presentation, physical examination, radiological findings – including chest X ray and HRCT –, pulmonary function tests and arterial blood gases, therapeutic procedures and responses to treatments and outcome. Biopsy slides were reviewed by a pathologist familiar with LAM if there was any doubt about the diagnosis. For the cases it was available, immunostaining with HMB-45, a monoclonal antibody, was carried out. This immunostaining procedure was performed on formalin-fixed paraffin-embedded sections that were stained with the monoclonal antibody. Clinical and radiological data were accurately recorded from the onset of disease and during the whole clinical course, ending data collection on December 2007.

Pulmonary function tests were performed following standardized methods in all the centres and the reference values used were the same (10). Obstructive ventilatory defect was defined as forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) < 70% and restrictive ventilatory defect as FEV1/FVC > 80% and total lung capacity (TLC) < 80% predicted. Mixed ventilatory defect was defined as TLC < 80% predicted and FEV1/FVC < 70%. DLco was considered low if < 80% predicted. FEV1, FVC, TLC, and DLco were expressed as percentages of predicted normal values.

Statistical analysis

Data from quantitative variables were expressed as mean ± standard deviation (SD) and values from qualitative variables were expressed as differences in percentages. Statistical differences were analyzed using the Student t test for the comparison between sporadic LAM and TSC-LAM, and the chi-squared test was used for other variables. Data analysis was carried out with SPSS 11.5 statistical software (SPSS Inc, Chicago, IL, US). Statistical significant was defined as p≤0.05.

Results

Demographic data

Seventy-two patients were included in the registry, all women, with a mean age (±SD) at the time of inclusion of 44.56 ± 11.1 yr, and an age range from 18 to 73 yr. Sixty-three patients (87.5%) presented the sporadic form of LAM and 9 (12.5%) presented LAM associated with tuberous sclerosis. Thirty (41.8%) patients had been smokers (40.4% former-smokers and 1.4% current smokers). The packs/year average, in the 21 patients for whom this data was available, was 15. Only one patient had a family history of diffuse interstitial pulmonary disease. Nineteen (26.4%) patients were post-menopausal when included in the registry (Table 1).

Prior to diagnosis, no patient had received chemotherapeutic drug treatment and only one case had been treated with azathioprine. Approximately 25% of patients had taken oral contraception previously, and 20.8% had been treated with corticosteroids.

Diagnostic criteria

The pulmonary LAM diagnosis was histologically confirmed by surgical lung biopsy in 57 patients (79.2%). In the remaining 15 cases, thoracic HRCT

<table>
<thead>
<tr>
<th>Table 1. LAM patient characteristics</th>
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</thead>
<tbody>
<tr>
<td>Patient characteristics</td>
</tr>
<tr>
<td>Mean age (SD)</td>
</tr>
<tr>
<td>Smoking habit nos.</td>
</tr>
<tr>
<td>Current smoker (%)</td>
</tr>
<tr>
<td>Former-smoker (%)</td>
</tr>
<tr>
<td>Never smoker (%)</td>
</tr>
<tr>
<td>DK/NA (%)</td>
</tr>
<tr>
<td>Family history of DIPD no. (%)</td>
</tr>
<tr>
<td>Tuberculous sclerosis n (%)</td>
</tr>
<tr>
<td>Menopause no. (%)</td>
</tr>
<tr>
<td>Symptoms nos.</td>
</tr>
<tr>
<td>Dyspnoea (%)</td>
</tr>
<tr>
<td>Cough (%)</td>
</tr>
<tr>
<td>Pneumothorax (%)</td>
</tr>
<tr>
<td>No. of pneumothorax/patient (%)</td>
</tr>
<tr>
<td>Haemoptysis (%)</td>
</tr>
<tr>
<td>Cyanosis no. (%)</td>
</tr>
<tr>
<td>Finger clubbing no. (%)</td>
</tr>
<tr>
<td>Crackles (%)</td>
</tr>
<tr>
<td>Renal angiomyolipoma no, (%)</td>
</tr>
<tr>
<td>Death no. (%)</td>
</tr>
<tr>
<td>DK/NA: Don’t know/No answer. DIPD: diffuse interstitial pulmonary disease</td>
</tr>
</tbody>
</table>
images were compatible with LAM and patients showed other typical findings; 11 patients presented renal angiomyolipomas (5 cases with LAM-TSC and 6 sporadic LAM), one patient with LAM-TSC presented renal angiomyolipomas and chylothorax, and another one presented chylothorax alone. Twenty-six patients (36.1%) underwent bronchoscopy with transbronchial biopsy. Three out of 11 patients diagnosed by transbronchial biopsy presented angiomyolipomas and 2 patients presented chylothorax disease. In 11 of these patients, surgical lung biopsy was not performed as the transbronchial biopsy showed findings suggestive of lymphangioleiomyomatosis. Thirteen patients had not undergone tissue biopsy, and eight of these had no TSC. All of these patients had angiomyolipomas and cystic lesions in chest CT.

The HMB45 marker could be measured in 30 subjects (42%); it was positive in 29 patients (96.6%) and negative in one case (3.3%). The study of oestrogen receptors was performed in 24 patients (33.3%) and the results were positive in 18 of them (75%). Progesterone receptors were measured in 22 cases and were positive in 18 patients (81%). The patient with a negative HMB-45 was diagnosed because of a TC compatible with LAM (multiple generalized cystics), obstructive spirometric pattern, low DLCO and an open biopsy with positive actin, miosyn and oestrogen receptors.

Clinical characteristics

The most frequent symptom was breathlessness, present in nearly 90% of patients, followed by cough in 44.4% of cases. Dyspnoea was present in all patients with an obstructive or mixed spirometric pattern, in 8 patients with restriction and in 4 patients with normal spirometry. No relationship between cough and spirometric pattern and DLco was found.

Eight patients (11.1%) had presented haemoptysis at some time after diagnosis (Table 1). Pneumothorax occurred in more than half of cases (51%). The mean number of pneumothoraces in patients who had had at least one pneumothorax was 3.22. Almost 40% of patients had renal angiomyolipomas. Respiratory crackles were found on physical examination in 22.2% of cases. Finger clubbing was only present in 2 patients. Hospitalization was required in 27.8% of cases because of acute respiratory failure.

Radiological data

Simple chest X-ray was normal at the time of diagnosis in 10 patients (13.9%). Thoracic HRCT was performed on all patients, and the most frequent radiological finding was cystic lesions (91.7%), while pleural effusion was present in 16.7% of cases. HRCT was not described as suggestive of LAM in only 5 patients, because no cystic lesions were found. In these cases diagnosis was made based on the presence of positive LAM markers in the open biopsy or transbronchial biopsy.

Pulmonary function tests

The most common spirometric pattern in pulmonary function tests was obstructive in more than half of the patients (54.2%). There were normal spirometric results in 9 patients (12.5%). The restrictive pattern was present in 12.5% of patients. Lung volume measurements were available in 81.9% of patients, single-breath diffusing capacity (DLco) results were collected in 94.4% of cases and arterial blood gases were obtained in 75% of patients. Reduced DLCO, was the most frequent finding (83.3%). A low DLco was found in 4 patients with normal spirometry, 38 patients with obstruction, all patients with restriction and 3 patients with a mixed pattern. The 6-minute walking test was performed in 62.5% of the cases. In those patients who had undergone arterial blood gases, chronic respiratory failure - defined as PaO2 <60 mmHg – was present in 26 cases at the time of enrolment (Table 2).

Treatment

Thirteen patients had undergone oophorectomy; 37.5% of the women had been treated at some time with medroxyprogesterone and 19.4% with tamoxifen. Thirty-two (44.4%) patients were on bronchodilator therapy. Eighteen patients were receiving supplementary oxygen therapy at the time of the registry inclusion, due to chronic respiratory failure. Sixteen patients (22.2%) had undergone lung transplantation.

Sporadic LAM versus LAM associated with tuberous sclerosis

Most patients with LAM-TS (88.8%) presented renal angiomyolipomas, compared with 31.7% in
The Spanish Registry of LAM

The Spanish Registry of LAM

Table 2. Pulmonary function tests in LAM patients

<table>
<thead>
<tr>
<th>Pulmonary function tests</th>
<th>Normal</th>
<th>Obstructive</th>
<th>Restrictive</th>
<th>Mixed</th>
<th>DK/NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spirometric pattern nos. (%)</td>
<td>9 (12.2)</td>
<td>39 (54.2)</td>
<td>9 (12.5)</td>
<td>9 (12.5)</td>
<td>6 (8.3)</td>
</tr>
<tr>
<td>DLco (%)</td>
<td>Normal</td>
<td>Low</td>
<td>DK/NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 (11.1)</td>
<td>60 (83.3)</td>
<td>4 (5.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABG nos. (%)</td>
<td>Normal</td>
<td>Chronic respiratory failure</td>
<td>Not performed</td>
<td>NS/NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>28 (38.8)</td>
<td>26 (36.1)</td>
<td>16 (22.2)</td>
<td>2 (2.8)</td>
<td></td>
</tr>
</tbody>
</table>

DK/NA: Don’t know/No answer. ABG: arterial blood gases

the sporadic LAM group (p<0.05). As for symptoms, no significant differences were observed regarding dyspnoea, which was the most frequent symptom in both groups. Cough was more frequent in sporadic LAM patients (49.2%) than in those with LAM-TS (11.1%) (p<0.05). At the time of their inclusion in the study, no patients from the LAM-TS group had received lung transplantation (Table 3).

Table 3. Sporadic LAM vs. LAM-tuberous sclerosis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sporadic LAM (No.=63)</th>
<th>LAM- tuberous sclerosis (No.= 9)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD)</td>
<td>44.8 (10.0)</td>
<td>42.7 (17.6)</td>
<td>0.611</td>
</tr>
<tr>
<td>Cough (%)</td>
<td>31 (49.2)</td>
<td>1 (11.1)</td>
<td>0.032</td>
</tr>
<tr>
<td>Dyspnoea no. (%)</td>
<td>55 (87.3)</td>
<td>9 (100)</td>
<td>0.324</td>
</tr>
<tr>
<td>Haemoptysis no. (%)</td>
<td>8 (12.6)</td>
<td>0</td>
<td>0.436</td>
</tr>
<tr>
<td>Cyanosis no. (%)</td>
<td>4 (6.3)</td>
<td>1(11.1)</td>
<td>0.498</td>
</tr>
<tr>
<td>Crackles no. (%)</td>
<td>16 (25.3)</td>
<td>0</td>
<td>0.089</td>
</tr>
<tr>
<td>Pneumothorax no. (%)</td>
<td>32 (50.7)</td>
<td>5 (55.5)</td>
<td>0.536</td>
</tr>
<tr>
<td>Mean NO. of Pneumothorax (SD)</td>
<td>1.7 (2.8)</td>
<td>1.3 (1.6)</td>
<td>0.713</td>
</tr>
<tr>
<td>Pleural effusion no. (%)</td>
<td>10 (15.8)</td>
<td>2 (22.2)</td>
<td>0.589</td>
</tr>
<tr>
<td>Renal angiomyolipomas no. (%)</td>
<td>20 (31.7)</td>
<td>8 (88.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Low DLCO no. (%)</td>
<td>55 (83.3)</td>
<td>5 (55.5)</td>
<td>0.027</td>
</tr>
<tr>
<td>Medroxyprogesterone no. (%)</td>
<td>24 (38)</td>
<td>3 (33.3)</td>
<td>0.029</td>
</tr>
<tr>
<td>Tamoxifen no. (%)</td>
<td>14 (22.2)</td>
<td>0</td>
<td>0.010</td>
</tr>
<tr>
<td>Oophorectomy no. (%)</td>
<td>10 (15.8)</td>
<td>3 (33.3)</td>
<td>0.099</td>
</tr>
<tr>
<td>Corticosteroids no. (%)</td>
<td>14 (22.2)</td>
<td>1 (11.1)</td>
<td>0.397</td>
</tr>
<tr>
<td>Bronchodilators no. (%)</td>
<td>28 (44.4)</td>
<td>4 (44.4)</td>
<td>0.929</td>
</tr>
<tr>
<td>Home oxygen therapy no. (%)</td>
<td>17 (26.9)</td>
<td>1 (11.1)</td>
<td>0.182</td>
</tr>
<tr>
<td>Chronic respiratory failure no. (%)</td>
<td>24 (38)</td>
<td>2 (22.2)</td>
<td>0.205</td>
</tr>
<tr>
<td>Previous hospital stays no. (%)</td>
<td>18 (28.5)</td>
<td>2 (22.2)</td>
<td>0.519</td>
</tr>
<tr>
<td>Lung transplantation no. (%)</td>
<td>16 (25.3)</td>
<td>0</td>
<td>0.149</td>
</tr>
<tr>
<td>Death no. (%)</td>
<td>9 (14.2)</td>
<td>0</td>
<td>0.144</td>
</tr>
<tr>
<td>Mean survival in months (SD)</td>
<td>57.1 (43.7)</td>
<td>46.6 (35.8)</td>
<td>0.686</td>
</tr>
</tbody>
</table>

Follow-up

Death was the final outcome in 9 patients; 6 of these deaths occurred after lung transplantation, one during the wait for transplantation, another was due to breast cancer and the other due to unknown causes.

Discussion

LAM is a rare disease, and its prevalence is unknown in most countries. The national registry was introduced to obtain consistent data about epidemiological and clinical features of these patients, while facilitating future recruitment of LAM patients for clinical trials on new therapies. Furthermore, another aim of our study was to improve information about this disease among Spanish physicians in order to obtain an earlier diagnosis. The present study includes one of the largest cohorts of patients with LAM reported to date and it provides demographic, clinical and pulmonary function data about this disease.

Some studies have been published on the prevalence of LAM in different countries; the most im-
portant being that of Ryu et al (11). The demo-
graphic, clinical and radiological characteristics of
our patients are similar to those found in other series
(12, 13). The mean age of our patients was 45±11.1,
similar to that of recent studies but older than that of
earlier series. Unlike other studies, ours registers
record the current age of the patient, not the age at
the diagnosis, and this discrepancy can explain these
differences.

In the 72 cases included, the most frequent
symptom was dyspnoea, present in 90% of patients.
According to the spirometry, most patients present-
ed dyspnoea, except those with a normal spirometric
pattern. More than half of the cases had presented at
least one pneumothorax. Patients frequently present
repeated pneumothoraces before the LAM diagno-
sis, so LAM should be suspected in any young
woman who presents recurrent pneumothorax, em-
physema or a chylous pleural effusion.

Angiomyolipomas were present in a similar
proportion to that found in other series, being sig-
ificantly more common in those patients with
tuberous sclerosis (14). TSC patients have two types
of lung disease: non-calcified nodular lesions charac-
terized by multifocal micronodular pneumocyte hy-
perplasia and cystic lung disease similar to LAM. It
has been reported that up to 40% of patients affect-
ed by tuberous sclerosis may present pulmonary
LAM, although only 2-3% present respiratory
symptoms (15-17). In a recent study it has been
shown that HRCT on 23 asymptomatic women
with TSC identified cystic or nodular changes in
52%, while cystic pulmonary parenchymal changes
consistent with LAM were found in 9 patients
(39%) (18). Due to this high prevalence of LAM in
TSC patients, and in order to identify patients at risk
developing pneumothorax and candidates for ear-
ly treatment, screening by HRCT scan would be in-
dicated in all women with TSC. Airway obstruction
and reduced diffusing capacity were the most fre-
cent pulmonary function abnormalities. Although
forced spirometry was normal in 9 patients, almost
half of these had a low DLco, which was the most
common pulmonary lung function abnormality.
These results suggest that DLco could be a more
sensitive test for diagnosis and follow-up of the dis-
ease because it can provide data sooner than FEV1 (8,
19). Apart from spirometry, other pulmonary func-
tion tests were not performed on patients, in spite of
the diagnosis of interstitial pulmonary disease. This
lack of data may be due to either the loss of infor-
mation in transferring the patient to another hospit-
al, or to recent diagnoses of cases in which it had
still not been possible to complete all the tests.

HRCT was the most sensitive imaging test for
the diagnosis of LAM as it proved pathological in all
the cases in which data was available. Bilateral thin-
wall cysts were the more frequent HRCT finding.
In our series, they were present in 91.7% patients.
Our results agree with those of Urban et al and Chu
et al, who found that thin-walled cysts are present in
100% of patients (3, 20). Pleural effusion, present in
12 cases, is another typical sign of LAM, although
due to the characteristics of our study we do not
know their composition. Chest X-ray was less sensi-
tive for the diagnosis of the disease. As has been pre-
viously described, the chest X-ray may be normal en
9% of cases (20). In our series, 13% of patients had
no alterations in chest roentgenogram.

In most cases, diagnosis was histological,
mainly through open lung biopsy. Only in a few cases
was the presence of compatible symptoms and typical
thoracic HRCT enough for the diagnosis of LAM,
mainly due to a previous diagnosis of tuberous scler-
osis. Biopsy confirmation is not necessary in all cas-
es but is often required if the patients are to be con-
sidered for lung transplantation8. We are unaware of
the histopathological markers used in most samples,
but the available data confirm, the HMB-45 mark-
er, which was positive in 96.6% of the analyzed cases,
as a highly sensitive method for the identification
of LAM cells, and it is particularly valuable when
only small specimens of lung tissue are available.
Due to the fact that ours is a retrospective study,
some patients were diagnosed before the diagnostic
procedure of immunostaining with the anti-HMB-
45 was available. The HMB-45 staining was nega-
tive in only one case, leaving the diagnosis to be
based on a compatible HRCT, an obstructive pat-
tern and an open lung biopsy with positive actin,
myosin and oestrogen receptors.

Because ours is a transversal study, we have no
tested the effect of different treatments on our pa-
tients over time. Unless there are no proven therapies
for LAM, bronchodilators and hormonal therapy
has been traditionally used in these patients. In this
sense, Schiavina et al treated 36 patients with hor-
monal therapy during 20 years and they found that
at 10 years, the survival rate was 90%, considerably higher than previous studies, which may suggest that the hormonal therapy may reduce mortality of these patients (21). New treatments are being tested now in different clinical trials, the most important one is sirolimus, which reduces AML volume and increases lung function after 1 year treatment. When medical therapies fail and lung function declines, lung transplantation becomes a viable option to improve the quality of life and prolong survival (5, 22).

The main limitation of this study was the retrospective nature of data collected for some patients, as well as the loss of some cases through the requirement for specialized centres for evaluation. LAM registry is a transversal observational study and the cohort of individuals was not monitored over time. The fact that LAM is a disease with no effective treatment and that patients should move on to specialized health centres for transplantation during the disease progression makes data collection more difficult. Another limitation of our study is that the identification of HMB-45 was only performed in 30 cases. However, in the remaining cases, diagnosis was established through histological and radiological findings.

In conclusion, our study confirms that lymphangioleiomyomatosis is a rare disease that affects young women of childbearing age, resulting in the obstruction of small airways leading to pulmonary cyst formation and pneumothorax. The characteristics of the disease in our country are similar to those found in other series. This study is the largest to focus on LAM in Spain and we hope that it can increase our awareness and understanding of this rare disease.

Acknowledgements

We would like to acknowledge the Pulmonary and Thoracic Surgery Departments that supplied cases to the Spanish LAM Registry, these being the university hospitals of La Princesa (Madrid), Vall d’Hebron (Barcelona), Clinic (Barcelona), 12 de Octubre (Madrid), Juan Canalejo (A Coruña), Virgen de las Nieves (Granada), Ramón y Cajal (Madrid), Doctor Negrin (Las Palmas), Clínico de San Carlos (Madrid), Nuestra Sra de la Candelaria (Tenerife), Complejo Hospitalario de León (León), Móstoles (Madrid), Son Llàtzer (Mallorca), Nuestra Sra de Meritxell (Andorra), Terrasa (Barcelona), Dr. Peset (Valencia) and Sagunto (Valencia).

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