Lymphangioleiomyomatosis (LAM) is a disease mainly affecting women, most often between the ages of 20 and 40, often associated with tuberous sclerosis complex (TSC). We report the case of a 31-year-old patient, treated for schizophrenia, who presented with acute respiratory failure. Chest imaging revealed the presence of multiple thin-walled cystic formations with well-defined contours, of diffuse distribution, extended to both pulmonary fields. The diagnosis of definite LAM was made based on the diagnostic criteria for LAM according to the ERS 2010 international guidelines associated with definite TSC was made based on the presence of two major criteria also according to the consensus conference on the diagnosis of TSC from 2012. The development was marked by the death of the patient the day following her hospitalization. Through this observation, we wish to shed light on a relatively rare disease whose diagnosis remains well codified and easy.

**Keywords:** Tuberous sclerosis complex, women, Lymphangioleiomyomatosis, pulmonary.

## INTRODUCTION

Lymphangioleiomyomatosis (LAM) is a rare disease occurring almost exclusively in women of childbearing age, either sporadically or associated with tuberous sclerosis.

Tuberous sclerosis complex (TSC) is an autosomal dominant genetics disease characterized by benign tumors in various organs, including the skin, brain, retina, kidneys, heart, and lungs [1, 2]. The prevalence of TSC is approximately 1/15,000. Although inheritance is autosomal dominant, most patients have de novo germline mutations and have no family history of TSC. It is usually present from birth, but symptoms can be subtle or develop slowly, making the disorder difficult to identify early. The diagnosis of this rare pathology is based on the criteria of the consensus conference on the diagnosis of TSC from 2012 [3]. The prognosis depends on the severity of the symptoms. Management is based on sirolimus in addition to symptomatic treatment.

Through a case of TSC as part of a LAM of late discovery, we discuss the different clinical and progressive aspects of this condition.

## OBSERVATION

This was a 31-year-old patient with a history of schizophrenia for which she had been receiving anxiolytics for 7 years, with no other specific pathological history.

The patient was hospitalized in our unit with a picture of acute respiratory failure that had been developing for 24 hours, including 75% desaturation in the open air, polypnea at 30 cycles per minute, tachycardia at 120 beats per minute with presence signs of respiratory struggle such as intercostal and suprasternal drawing and flapping of the wings of the nose. Cyanosis of the lips and extremities was observed. Clinical examination revealed bilateral crackles at the pleuropulmonary level. Skin examination revealed the presence of diffuse hamartomas on the face, mainly the nose and cheeks, and on the chest. We also noted the presence of café-au-lait spots on both forearms. These lesions had been recognized by the patient since a young age but had never been the subject of a specialist consultation.

After conditioning and faced with this respiratory emergency, a chest CT angiogram was
performed and did not reveal any signs of pulmonary embolism.

Chest imaging revealed the presence of multiple thin-walled cystic formations with well-defined contours, of diffuse distribution, extended to both lung fields, without respect to the lower lobes or bases and without nodules, micronodules or pneumothorax observed.

Figure 1: Chest CT scans: showing multiple cystic formations extended to both pulmonary fields

Faced with this scan aspect, the suggestive skin examination, the female gender and the young age, we thought of a cystic pulmonary disease, namely LAM – TSC. And so a brain scan was carried out and in turn showed calcified nodules in the subependymal area next to V3 and the lateral ventricles associated with a right cerebellar hemispheric calcified nodular lesion related to a cortical tuber. Retrospective questioning revealed the notion of unmonitored convulsive attacks since adolescence.

Figure 2: Brain CT scans: showing calcified nodules in the subependymal area

Abdominopelvic CT revealed a large mass with dual fatty and tissue components, enhanced early and heterogeneously after injection of contrast product. It developed at the expense of the lower pole of the right kidney. It was associated with other bilateral renal cortical lesions (at least 6), with the same characteristics. This appearance was suggestive of angiomyolipomas.

Figure 3: Abdominopelvic CT scans: showing a large mass with dual fatty and tissue components
A cardiac exploration in search of cardiac rhabdomyomas was normal.

The diagnosis of a certain LAM was retained based on the diagnostic criteria for LAM according to international guidelines ERS 2010; the patient presented characteristic thoracic lesions associated with the presence of angiomyolipomas. The diagnosis of definite TSC was retained in the presence of two major criteria also according to the consensus conference on the diagnosis of TSC of 2012, namely LAM and the presence of subependymal nodules.

### Table 1: Diagnostic criteria for LAM according to the international ERS 2010 guidelines [4]

<table>
<thead>
<tr>
<th>Definite LAM</th>
<th>Probable LAM</th>
<th>Possible LAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Characteristic or compatible lung HRCT, and lung biopsy fitting the pathological criteria for LAM; or</td>
<td>1. Characteristic lung HRCT and compatible clinical history; or</td>
<td>Characteristic or compatible HRCT.</td>
</tr>
<tr>
<td>2. Characteristic lung HRCT and any of the following: angiomyolipoma (kidney); thoracic or abdominal chylous effusion; lymphangioleiomyoma or lymph-node involved by LAM;</td>
<td>2. Compatible HRCT and any of following: angiomyolipoma (kidney); and thoracic or abdominal chylous effusion.</td>
<td></td>
</tr>
<tr>
<td>Definite or probable TSC.</td>
<td>Definite or probable TSC.</td>
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</tbody>
</table>

### Table 2: Criteria of the consensus conference on the diagnosis of TSC from 2012 [2]

<table>
<thead>
<tr>
<th>MAJOR CRITERIA</th>
<th>MINOR CRITERIA</th>
</tr>
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<tbody>
<tr>
<td>Facial angiofibromas (≥3) or fibrous cephalic plaque</td>
<td>Cerebral white matter radial migration lines</td>
</tr>
<tr>
<td>Nontraumatic ungl or periungual fibroma (≥2)</td>
<td>Retinal achromatic patch</td>
</tr>
<tr>
<td>Hypomelanotic macules (&gt;3) at least 5 mm diameter</td>
<td>Intra oral fibroma</td>
</tr>
<tr>
<td>Shagreen patch</td>
<td>Confetti&quot; skin lesions</td>
</tr>
<tr>
<td>Multiple randomly distributed pits in dental enamel</td>
<td></td>
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<tr>
<td>Hamartomatous rectal polyps</td>
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</table>

The family investigation did not find an identical family case. The development was marked by the death of the patient the day following her hospitalization.

**DISCUSSION**

LAM is a rare lung disease. It almost exclusively affects women during periods of genital activity [5], but can occasionally appear after menopause. It occurs sporadically or as part of a genetic disease; notably the TSC.

During TSC, LAM is identifiable on chest CT in 30 to 40% of adult women [6, 7]. LAM is characterized by a progressive infiltration of lung tissue by atypical smooth muscle cells, leading to cystic destruction of the lung parenchyma [8].

Pulmonary symptoms during LAM are dominated by progressive exertional dyspnea, cough, the
Patients with LAM must be systematically examined for signs of associated TSC, particularly cutaneous signs, namely: hypomelanotic spots on the trunk, fibrous plaques on the forehead, shagreen plaques, dental enamel pits or even nail or gingival fibromas. Compared to sporadic LAM, LAM occurring during TSC is usually less severe and pulmonary involvement more frequently includes pulmonary micronodules suggestive of multifocal micronodular hyperplasia of pneumocytes. Renal and hepatic angiomyolipomas are more common.

On chest CT, LAM is characterized by multiple thin-walled, rounded, well-demarcated air-filled cysts without other significant pulmonary involvement. These cysts are generally small, with very thin walls, and uniformly distributed throughout the lung fields without zonal predominance. The CT presentation is considered consistent with AML when only 2 to 10 cysts are present. Exceptionally, an appearance of multiple micronodules can be observed in patients with TSC; it reflects lesions of micronodular multifocal hyperplasia of pneumocytes (HMMP) [11]. HMMP is not present in sporadic-AML.

An Abdominopelvic CT, in contiguous thin sections of 3 mm or less with and without intravenous injection of product non-ionic contrast, is recommended at the time of diagnosis of LAM, to identify angiomyolipomas and other possible abdominal lesions (lymphangiomatosis, lymphadenopathy), or chylous ascites. LAM can sometimes be discovered incidentally on a CT scan performed for another reason [10].

The assessment of the prognosis of LAM is difficult, due to the great interindividual variability, the severity and the severity of the disease, but is based, among other things, on measuring the speed of decline of the maximum expiratory volume in one second.

Due to the rarity of the disease, we do not yet have controlled therapeutic trials in pulmonary LAM. Recommendations are largely based on expert consensus [17]. Most of the treatment is symptomatic, and patient information is a crucial element of care. Non-specific therapeutic measures include inhaled bronchodilators in cases of obstructive ventilatory disorder with a significant response in 25% of patients [14]. Smoking cessation, vaccination against influenza and pneumococcus and respiratory rehabilitation. Patients with LAM should be informed of the high risk of pneumothorax, and to seek medical attention if they develop sudden dyspnea and/or chest pain [17]. Air travel is not systematically contraindicated, but patients should be cautioned not to travel if recent respiratory symptoms have not been assessed.

It is recommended to avoid estrogens, including birth control pills and hormone replacement therapy. Preferred contraceptive methods include progestin-only or drug-eluting intrauterine devices. Pregnancy is not systematically contraindicated in cases of LAM, but patients with mild LAM who desire pregnancy should be informed of the increased risk of complications [17]. But it may be appropriate to advise against pregnancy in women with severe LAM. Patients with TSC should receive genetic counseling before conception.

Pneumothorax occurs in 2/3 of patients during the disease and relapses are frequent. Pleurodesis is recommended after the first episode of pneumothorax, preferably by pleural abrasion.

Regarding the management of parenchymal lung disease, the discovery of the role of mTOR activation in the pathogenesis of LAM and the availability of mTOR inhibitor used for kidney transplantation, has enabled rapid progress from understanding pathogenesis to therapeutic advances. International recommendations suggest starting treatment if respiratory function is abnormal (FEV < 70% of predicted) or declining (a loss of FEV > 90 ml/year over 6-18 months has been proposed as a threshold) [18].
Hormonal treatments (including oophorectomy, progesterone, antiestrogens, and GHRH) have been widely used in LAM, but discordant results have been reported [19, 20], and no randomized trials are available. These treatments are no longer recommended [18].

Lung transplantation is an effective treatment for advanced LAM. HMMP of TSC generally does not require specific monitoring or treatment.

The treatment of choice for hemorrhagic renal angiomyolipomas is percutaneous endovascular embolization; renal parenchyma-preserving surgery can also be performed when interventional treatment is not possible [17].

The prognosis is uncertain, but the disease slowly progresses to chronic respiratory failure and death.

**CONCLUSION**

The Lymphangioleiomyomatosis is a condition which remains rare, can be associated with tuberous sclerosis of Bourneville and whose prognosis remains variable.

**REFERENCES**

management. *American journal of respiratory and critical care medicine*, 194(6), 748-761.
