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Successful pregnancy in a woman with lymphangioleiomyomatosis: a case report

Gravidez numa mulher com linfangioleiomiomatose: um caso clínico

Margarida Pavão[1], Luísa Pinto[2]
Centro Hospitalar Universitário Lisboa Norte

Abstract

Lymphangioleiomyomatosis (LAM) is a rare disease that mainly affects women of childbearing age. Literature on pregnancy outcomes in women with LAM is limited. This paper reports a successful pregnancy in a woman previously diagnosed with LAM. Despite experiencing a spontaneous hemorrhage from a pelvic lymphangioleiomyoma, which required emergent embolization at 20 weeks' gestation, a cesarean was performed at 39 weeks, resulting in a healthy newborn.

Keywords: Lymphangioleiomyomatosis; Pregnancy; Tuberous sclerosis.

Resumo

A Linfangioleiomiomatose (LAM) é uma doença rara que afeta principalmente mulheres em idade fértil. A literatura sobre desfechos da gravidez em mulheres com LAM é escassa. Este artigo relata uma gravidez bem-sucedida numa mulher previamente diagnosticada com LAM. Apesar da ocorrência, às 20 semanas, de hemorragia espontânea por rotura de linfangioleiomioma pélvico, com necessidade de embolização emergente, foi realizada uma cesariana às 39 semanas, da qual resultou um recém-nascido saudável.

Palavras-chave: Linfangioleiomiomatose; Gravidez; Esclerose tuberosa.

INTRODUCTION

Lymphangioleiomyomatosis is a rare and progressive disease characterized by abnormal smooth muscle proliferation within the lungs, leading to multiple cystic lung disease and progressive parenchymal destruction. Additionally, this condition affects the lymph nodes, lymphatics, mediastinum, and abdomen. On computed tomography (CT) scans, the pathognomonic features include numerous thin-walled cysts throughout the lungs[1].

Primary extrapulmonary lymphangioleiomyomatosis, with no pathological changes in the respiratory system, is uncommon. Extra-pulmonary lymphadenopathy and cystic masses of the axial lymphatics, termed lymphangioleiomyomas, can lead to abdominal and pelvic lymphatic obstruction[1,2]. LAM is often associated with angiomyolipomas (AML) in the kidneys (20-54%) and meningiomas[1,2].

LAM can occur sporadically or as a part of tuberous sclerosis complex (TSC). In both scenarios, mutations in the TSC1 or TSC2 genes are implicated. Sporadic

1. Centro Hospitalar de Setubal EPE.
2. Faculdade de Medicina da Universidade de Lisboa.

LAM affects 1 in 400.000 adult females. In TSC, LAM occurs in 30-40% of adult females and exceptionally in males and children[3]. The average age of manifestation is 34 years, often with a delay in diagnosis of 3-5 years[2].

Treatment relies on supportive care, including bronchodilators and supplemental oxygen. Other interventions include lung transplantation if appropriate, thoracostomy or chemical pleurodesis for chylous effusions, paracentesis or peritoneovenous shunting for chylous ascites, and surgical resection of retroperitoneal masses[3].

The most common symptoms of LAM include a non-productive cough, progressive dyspnea on exertion, recurrent pneumothoraxes, hemoptysis and chylous effusions, potentially leading to severe respiratory impairment. LAM is characterized by chronic airway obstruction, increased lung volume, and decreased CO2 diffusion, requiring differential diagnosis from conditions like emphysema and sarcoidosis[2].

Disease progression varies but is generally slow. The 10-year survival rate from the onset of symptoms is approximately 71-90%[1]. Since LAM predominantly affects women of childbearing age, pregnancy becomes a concern for patients and healthcare providers[4].

We present the case of a successful pregnancy in a woman previously diagnosed with LAM. The objective of this case report is to enhance the understanding of maternal and perinatal outcomes in patients with LAM, thereby contributing to better counseling for women/couples planning a pregnancy under these circumstances.

Patient written consent was obtained.

CASE REPORT

A 39-year-old primigravida woman, diagnosed with LAM two years' prior, was referred to our maternal-fetal outpatient clinic at 9 weeks' gestation.

The patient reported a history of dyspnea when walking up hills and stairs since childhood, progressively worsening over the years. She had no prior history of respiratory infections, asthma, or pneumothoraxes. In 2020, during a gynecology evaluation, a pelvic ultrasound incidentally revealed a large abdominal mass. Subsequent MRI confirmed a posterior pararenal and lumbar aortic lymphangioleiomyoma measuring 11 cm x 23 cm. Aspiration cytology of the mass revealed a lymphangioma.

Further investigation, including a thoracic CT scan, revealed multiple lung cysts that suggested the diagnosis of LAM. Genetic studies for TSC were negative. At that time, the fraction of expiratory volume (FEV) was 1.75 liters, vital capacity was 2.55, and gas transfer 4.27. She could walk approximately 660 meters without significant desaturation. Upon the diagnosis of LAM, the patient discontinued oral contraceptives and cigarette use.

The patient wished to become pregnant, so she underwent preconception counseling. Since her LAM was stable, she was advised that it was safe to proceed with pregnancy. In June 2021, conceived through in-vitro fertilization (IVF) after being diagnosed with idiopathic infertility. The pregnancy was monitored in a muldisciplinary team between the pulmonologists and maternal-fetal medicine specialist. She performed 4 fetal ultrasounds during her pregnancy and had Obstetric appointments every two to three weeks. Her pulmonary function was normal, with no episodes of pneumothorax and a good quality of life during pregnancy. At 20 weeks' gestation, she presented to the emergency department with acute abdominal pain, hypotension, and tachycardia, accompanied by metabolic acidosis, anemia (Hb-7.2 g/dl), and thrombocytopenia (platelet count: 70 000). An angiographic CT revealed an arterial hemorrhage from the pelvic lymphangioleiomyoma. Emergent embolization of the hypogastric vessels through the femoral artery was performed. During the procedure, one unit of red blood cells and 1 g of tranexamic acid were administered. The patient was transferred to the intermediate care unit, breathing spontaneously, with normal urinary output, and a post--transfusion hemoglobin of 8.3 g/dl. The postoperative period was uneventful, and she was discharged one week after the procedure.

From this point on, the patient had weekly obstetric visits and an additional fetal ultrasound at 35 weeks to assess fetal growth. She also had a follow-up appointment with vascular surgery after the embolization. After a multidisciplinary discussion on the route of delivery involving the Obstetrics and Pulmonology teams, induction of labor at 39 weeks' gestation was

attempted but proved unsuccessful. Consequently, a cesarean was performed, resulting in a healthy newborn weighing 3260 g, Apgar score 8/9/10 at 1, 5, and 10 minutes. The postpartum period was uneventful, and the patient was discharged 72 hours after delivery.

DISCUSSION

We present a case of a successful pregnancy in a woman previously diagnosed with LAM.

LAM is a rare multisystem disease primarily diagnosed in women of childbearing age. It is characterized by cystic lung destruction, benign abdominal tumors, and lymphatic involvement. The exact pathogenesis of LAM is unknown, but smooth muscle proliferation is believed to be estrogen dependent. This is supported by the fact that LAM almost exclusively affects women, progresses more rapidly during reproductive years, and its cells are estrogen receptor positive[5].

Definite diagnosis is made by biopsy (lungs, lymph nodes or lymphangioleiomyomas) or a combination of history and high-resolution computed tomography (HRCT). HRCT is being increasingly used to diagnose LAM without resorting to lung biopsy[5].

Numerous conditions characterized by multiple pulmonary cysts may resemble lymphangioleiomyomatosis (LAM). These include chronic obstructive pulmonary disease or emphysema, smoking-related interstitial lung diseases (such as Langerhans cell lung disease and diffuse interstitial pneumonia), respiratory bronchiolitis, idiopathic pulmonary fibrosis, eosinophilic hypersensitivity pneumonia, and sarcoidosis. Infectious agents like *Pneumocystis jirovecii, Staphylococcus species, Coccidioides species,* and parasitic infections induced by the lung *fluke Paragonimus westermani* can also induce widespread cystic alterations in the lungs[4].

Since LAM occurs mainly in women and is possibly accelerated by estrogens, oophorectomy, tamoxifen, progesterone and gonadotropin-releasing hormone (GnRH) analogues have been empirically used[2]. However, our patient did not receive any of these treatments.

Recent discoveries of abnormalities in the TSC1/2 genes have prompted trials with mTOR inhibitors, including sirolimus, in patients with LAM and angiomyolipoma. These trials indicate a potential reduction in angiomyolipoma volume and improved pulmonary function[3]. Sirolimus, categorized as a class C drug, should be suspended 12 weeks prior to conception, during pregnancy, and breastfeeding, and its role during pregnancy requires further investigation[7,8,9]. In our case, the patient did not receive sirolimus.

Cohen et al. refer that 8% of women were unable to conceive (compared to 4% in the general population), indicating a potential association between LAM and infertility[6]. In our case, the patient had idiopathic infertility and underwent in vitro fertilization.

Pregnancy outcome in patients with LAM is generally favorable, with most patients diagnosed after pregnancy. However, there is a higher incidence of complications, such as chylous effusions and pneumothoraxes[4]. Surgical pleurectomy is the first line treatment for recurrent pneumothoraxes during pregnancy, since chemical pleurodesis may cause maternal and fetal hepatic toxicity. If possible, surgery should be undertaken in the 2nd trimester, to avoid teratogenicity and prematurity[2].

AMLs are benign mesothelial tumors. They are usually asymptomatic but may present with abdominal pain, hypotension, and shock when bleeding occurs. Pregnancy can increase the risk of rupture and bleeding[3]. According to the literature, the average gestational age upon the occurrence of hemorrhage is 27 weeks. This is likely associated with a progressive increase in the size of the tumor, an increase in renal blood flow, and an elevation in abdominal pressure throughout gestation. Embolization is the treatment of choice, as it usually allows the preservation of renal function. The radiation dose should be kept as low as possible to minimize consequences to the fetus[2]. Embolization is associated with high recurrence rates, necessitating close follow-up. At 20 weeks' gestation, our patient presented to the emergency department with acute abdominal pain and was diagnosed with an arterial hemorrhage from the pelvic lymphangioleiomyoma. Emergent embolization was performed.

Risk factors, such as the extension of LAM, baseline pulmonary function, pulmonary function decline rate, previous history of pneumothorax or chylothorax, existence and size of renal or retroperitoneal AML, and

previous history of pregnancy, should be evaluated when considering pregnancy. Surveillance by a multidisciplinary team is recommended to ensure optimal management during pregnancy. The European Respiratory Society (ERS) discourages pregnancy in patients with severe disease and recommends genetic counseling for patients with TSC. The main risk factor for our patient's pregnancy was the large retroperitoneal AML. The pregnancy was monitored by a multidisciplinary team including pulmonologists and obstetricians.

Cohen et al. surveyed 328 pregnancies with LAM, reporting on pulmonary function, subjective and psychological functioning, quality of life, dyspnea, and fatigue. Women diagnosed with LAM during pregnancy (n=15) had higher rates of pneumothorax (67%), miscarriage (7%), and preterm birth (47%). The group diagnosed before or during pregnancy (n=12) exhibited lower mean forced expiratory volume in 1s (FEV1), forced vital capacity (FVC), and carbon monoxide diffusion (DLCO) after pregnancy, compared to those diagnosed after pregnancy or who were never pregnant. No significant differences were observed in subjective or psychological functioning, quality of life, dyspnea, or fatigue between the groups. In newly diagnosed LAM patients, there was a high incidence of premature birth and pneumothorax, suggesting a more aggressive phenotype[6].

Our patient presented with a less aggressive LAM phenotype and successfully completed pregnancy despite experiencing a severe complication.

The European Respiratory Society (ERS) guidelines for LAM mention that pregnancy in patients with LAM is associated with an increased risk of pneumothorax, chylothorax, bleeding, and rupture from angiomyolipoma, with an acceleration of lung function decline.[3] Miscarriage and premature birth rates in pregnant women with LAM are comparable to those in the general population[6,7].

Pregnant women with LAM should be closely monitored in tertiary hospitals, where facilities for interventional radiology are readily available in case serious complications occur. The route and timing of delivery should be individualized to achieve the best outcomes for both mother and fetus[2,8].

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AUTHOR CONTRIBUTIONS

LP carried out the medical management. MP wrote the first draft. Both authors contributed to the intellectual content and revised the article.

CONFLICT OF INTEREST

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDENCE TO:
Margarida Pavão
E-mail: margpavao@gmail.com
https://orcid.org/0009-0001-4696-7562

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