

Benign metastasizing leiomyoma – a case of benign metastasis

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Abstract

Leiomyomas are benign tumours of smooth muscle cells that most often affect the female genital tract, but their metastasis to extra-uterine locations represent rare, yet misunderstood phenomena. The authors present a clinical case of a 42-year-old woman, who underwent a hysterectomy 15 years ago due to myomas, admitted with multiple pulmonary nodules and abdominal mass, diagnosed by imaging tests, in the context of haemoptysis. The anatomicopathological exams of the pulmonary and abdominal lesions were compatible with the diagnosis of benign metastatic leiomyoma. Benign metastatic leiomyoma is a rare condition that particularly affects women of childbearing age, with a history of hysterectomy for uterine fibroids. Hence, this entity must be considered in the differential diagnosis of women with pulmonary nodules of uncertain aetiology.

Keywords

metastatic benign leiomyoma, smooth muscle uterine neoplasia, pulmonary nodules, haemoptysis

Key message

Benign metastatic leiomyoma (BML) it's a diagnosis that should be considered in premenopausal women with multiple pulmonary nodules.

Introduction

Uterine fibroids (leiomyomas) are benign tumours that exhibit various forms of smooth muscle differentiation. There is a spectrum of leiomyoma variants, therefore microscopy is essential for proper classification since benign and malignant tumours may have similar macroscopic features. Extra-uterine manifestations, such as disseminated peritoneal leiomyomatosis and metastatic leiomyomatosis, represent growth patterns that should not be considered as pathognomonic of malignancy.¹

Benign metastatic leiomyoma (BML), first reported in 1939 by Steiner, is a rare disease characterized by well-differentiated smooth muscle tumours that affect extra-

uterine sites, namely lungs (79.5%), abdominal cavity, retroperitoneum, muscle tissue, lymph nodes, blood vessels or even the heart.^{2,3} Pulmonary BML is characterized by the presence of multiple bilateral pulmonary nodules of different sizes that can be confused with metastatic cancer.³ Studies suggest that metastatic leiomyoma derives from uterine leiomyomas.¹ The most accepted hypothesis is that the cells of the pulmonary nodules of the BML derive from uterine cells that migrated by the moment of myomectomy or hysterectomy, due to uterine leiomyomas. However, there are cases of women diagnosed with BML without a history of previous surgery, suggesting different histopathology.³ Also, BML may result from smooth muscle cells originating from the lung or from a smooth muscle tumour of uncertain malignant potential, which has migrated through venous access.^{3,4}

The median age at diagnosis of BML is 46 to 47 years and it is frequently diagnosed in pre-menopausal women.³ Lesions are discovered accidentally in about half of asymptomatic patients. However, some may have nonspecific symptoms such as cough, chest pain and dyspnoea. Typical radiographic findings include well-circumscribed solitary or multiple pulmonary nodules, as well as miliary pattern, cavitary pulmonary nodules and interstitial lung disease. There is little correlation between the extent of the disease and respiratory symptoms.⁵

The distinction between uterine leiomyoma and leiomyosarcoma is made by morphology, degree of cytological atypia, mitotic index and presence of tumour cell necrosis.^{1,2} BML can also be confused with Pulmonary Lymphangioleiomyomatosis (LAM), which constitutes a progressive proliferation of perivascular epithelioid cells along the bronchial interstitium, instead of inert nodular aggregates of smooth muscle cells that involve the alveolar parenchyma.^{1,2}

The diagnosis of BML is based on the histological diagnosis of extra-uterine lesions with microscopic features of leiomyoma.¹

Expectant conduct is an option for asymptomatic disease.¹ Surgical resection, namely oophorectomy, can be a measure to be adopted as a primary treatment. However, hormonal treatment constitute a valid alternative to unresectable tumours.² Hysterectomy may be necessary to exclude sarcoma if the patient has a mass or several uterine masses.¹

Case description

The referring case describes a 42-year-old caucasian woman who was admitted to the emergency department due to haemoptysis without other complaints. She had a hysterectomy about 15 years ago, due to benign uterine leiomyoma. Objectively, no alterations were found, however, in imaging exams whether in chest radiography or computed tomography, multiple nodules were documented in both lungs (Figure 1), as well as an abdominal mass. Routine laboratory investigations and tumour markers, namely alpha-fetoprotein, CA 19-9 and CA-125, were within normal parameters. Percutaneous lung biopsy guided by computed tomography was performed with a histological result of smooth muscle proliferation (desmin+, actin+, S100-, CAM5.2-, CD10-, DC117-, CD34-, inhibin-, KI67 < 1%, high positivity for oestrogen and progesterone receptors) without atypical necrosis or mitosis. Based on clinical and histological findings, a diagnosis of benign metastatic leiomyoma was established. The abdominal mass biopsy, performed by abdominal laparoscopy, showed the same histological findings. The patient underwent bilateral oophorectomy. After completing 9 months of follow-up, the patient remained asymptomatic, without requiring hormonal

therapy, with partial remission of the pulmonary nodules and with no signs of recurrence.

Discussion

Leiomyomas are benign tumours of smooth muscle cells that most often affect the female genital system.⁴ Its metastasis to other extra-uterine structures, mainly the lung, is a rare situation.⁵

The pathophysiology of this entity remains unknown. Despite being a benign neoplasm, it is admitted that its metastatic behaviour results from lymphatic or haematogenous dissemination of a benign leiomyoma or a well-differentiated low-grade leiomyosarcoma.⁴

The identification of oestrogen and progesterone receptors in lung lesions enabled the development of therapeutic options based on hormonal manipulation, either surgically or medically.⁵

Given the limited understanding of this entity, no standard management guidelines have been postulated regarding to the treatment of BML. Management of BML, case by case, varies with the pattern of presentation and the extent of symptoms. Regarding isolated lesions, surgical resection may be the treatment of choice. In case of diffuse disease, a systemic approach might be more beneficial. An expectant attitude, surgical resection, hysterectomy, bilateral oophorectomy, administration of progestins and aromatase inhibitors, and luteinizing hormone-releasing hormone analogs have all been reported as potential treatment options. In most reported cases, BML express estrogen and progesterone receptors. Evidence of a hormonal influence includes the fact that the pulmonary nodules wither following menopause, during pregnancy, and after the withdrawal of hormonal contraception, and by bilateral oophorectomy. Although ulipristal acetate (a selective progesterone receptor modulator) is frequently used as an effective treatment for uterine broids, its effect on BML is uncertain.⁶

All patients must be submitted to a long-term follow-up regimen, with imaging reassessment by computed tomography.³

The authors with this clinical case aim to illustrate an example of a benign histological tumour with a clinical presentation that resembles malignant diseases. BLM, despite tending to be asymptomatic, some are accompanied by symptoms. Therefore, the diagnosis of BML in women with multiple pulmonary nodules must be taken into consideration, particularly in women with a history of hysterectomy due to uterine fibroids.

Declarations

Contribution statement: Mónica Caldeira conceived the original idea. Diogo André took the lead in writing manuscript and contributed to the interpretation of the data gathered. Mónica Caldeira encouraged to investigate and supervised the findings of this work. All authors contributed to the final version of the manuscript.

Figure 1. Chest radiograph of female patient in child-bearing age with haemoptysis showing multiple lung nodules.



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References

1. Elizabeth AS, Laughlin-Tommaso SK and Schoolmeester JK. Uterine fibroids (leiomyomas): variants and smooth muscle tumors of uncertain malignant potential - UpToDate. *Uterine Fibroids* 2018; 24.
2. Aoki K, Yamamoto T, Terauchi R, Mori T, Shirai T and Kitawaki J. Benign metastasizing leiomyoma in femur and thigh with a history of uterine leiomyoma: a case report and literature review. *J Obstet Gynaecol Res* 2020; 8 de Novembro de 2020:jog.14545.
3. Fan R, Feng F, Yang H, et al. Pulmonary benign metastasizing leiomyomas: a case series of 23 patients at a single facility. *BMC Pulm Med* Dezembro de 2020; 20(1): 292.
4. Cardoso AR and Pereira E. Benign metastasizing leiomyoma: a clinical case report. *Revista da Sociedade Portuguesa de Medicina Interna* 2005; 12(4): 230–233.
5. Abramson S, Gilkeson RC, Goldstein JD, Woodard PK, Eisenberg R and Abramson N. Benign metastasizing leiomyoma: clinical, imaging, and pathologic correlation. *Am J Roentgenol* Junho de 2001; 176(6): 1409–1413.
6. Wojtyś ME, Kacalska-Janssen O, Ptaszyński K, et al. Benign metastasizing leiomyoma of the lung: diagnostic process and treatment based on three case reports and a review of the literature [Internet]. In Review; 2021 Jan [citado 1 de Novembro de 2021]. Disponível em: <https://www.researchsquare.com/article/rs-143780/v1>.