When benign leiomyomas metastasize to the lungs - a case report

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Abstract

Benign metastasizing leiomyoma is a rare disease that primarily affects premenopausal women who have a history of uterine leiomyoma, which is characterized by pulmonary metastases. The pathogenesis of this condition is unknown. Patients are usually asymptomatic or have vague symptoms. Pathological examination in conjunction with immunohistochemistry is required for diagnosis. Treatment is determined by the patient's age, hormonal status, symptoms, and the extent of the lesions (number, size, and location of nodules), with surgical resection being the most effective. We present the case of a 72-year-old woman who had a total hysterectomy 30 years earlier due to myomas and developed a persistent dry cough. Her computed tomography of the chest revealed several small nodules in the pulmonary parenchyma. Because of the nodules' small size and difficult accessibility, a surgical biopsy was performed for histopathological examination and immunohistochemical staining, which revealed metastasizing leiomyoma. Letrozole treatment was started and was well tolerated.

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Introduction

Benign metastasizing leiomyoma (BML) is a rare disease that typically affects premenopausal women with a personal history of uterine leiomyoma and can manifest as solitary or multiple lesions. The lungs, lymph nodes, heart, skeletal muscle, and pelvic cavity are the most common sites [1].

The presence of multiple and bilateral nodules of varying sizes characterizes pulmonary benign metastasizing leiomyoma (PBML), which mimics metastatic cancer. The majority of patients are asymptomatic or have non-specific symptoms such as chest pain, dyspnea, or cough [2], and the location and number of metastases are unrelated to the time interval between the patient's surgery and the occurrence of metastases [3].

Case Report

We present the case of a 72-year-old nonsmoker who is now retired (previously worked in pottery). She had a personal history of arterial hypertension, dyslipidemia, a pulmonary nodule several years ago (that vanished), and a total hysterectomy 30 years earlier in France due to abnormal uterine bleeding caused by myomas. The patient's sisters had a history of breast, gastric, and lung cancer.

She was referred to a pulmonology appointment due to persistent dry cough in the last month. There were no other lung-related symptoms relevant for this case and physical examination was unremarkable. The chest computed tomography (CT) revealed multiple (at least 50) small (between 1 and 10mm) nodules in the pulmonary parenchyma affecting all lobes, well defined and with regular edges, and mosaic attenuation (Figure 1). Laboratory work, upper endoscopy, colonoscopy, thyroid ultrasound, mammography, and flexible bronchoscopy showed no relevant changes. Positron emis-

sion tomography and CT (PET/CT) presented no uptake of 18F-fluorodeoxyglucose (Figure 2).

A transthoracic biopsy was attempted but revealed normal lung parenchyma and was considered not representative of the alterations presented by the patient. The chest CT was repeated 8 months later, and the nodules were found to be stable with no further changes. Given the patient's family history, a wedge resection of the right inferior and middle lobes by uniportal video-assisted thoracoscopic surgery using mechanical staplers was performed and revealed multiple well-differentiated smooth muscle tumors, and immunohistochemistry study revealed strong and diffuse expression of actin, desmin, caldesmon, and estrogen and progesterone receptors, consistent with metastasizing leiomyoma (Figure 3). The uterus sample could not be compared because it was taken 30 years earlier in another country. Palliative hormone therapy with letrozole was started after a multidisciplinary team discussion and was well tolerated.

Discussion

Hysteromyomas are common gynecologic tumors that affect 50% of women over the age of 30. The majority of them are benign, with malignant cases accounting for 0.13-6% [4]. Lung lesions are typically discovered several years (from one month to more than 20 years) after hysterectomy or myomectomy, and their growth rate is slow [5,6]. The patient in this study had symptoms and pulmonary nodules were discovered 30 years after hysterectomy.

The pathogenesis of this disease remains poorly understood, but it seems that cells of the pulmonary nodules are derived from uterine cells dislodged from the uterus during surgery for treatment of leiomyoma, spreading by vascular or lymphatic channels [7]. However, there are some reported cases of patients that did not undergo prior surgery, suggesting a different histogenesis. Another possibility is the origin of these nodules from lung or other sites containing smooth muscle cells [2,8].

Typical radiologic features include several noncalcified multiple or solitary shadows of different sizes with smooth edges or round lobular or round soft tissues, either well-circumscribed or cavitary [9]. The imaging findings of PBML should be distinguished from malignant metastasis to the lungs, primary lung cancer, pneumoconiosis, sarcoidosis, tuberculosis, and lymphangioleiomyomatosis. Because the radiologic features of PBML are nonspecific, it is difficult to diagnose and differentiate. 18F-fluorodeoxyglucose-PET/CT imaging plays a role in the differential diagnosis of PBML and malignant diseases [10], presenting no uptake in the majority of patients with PBML, particularly if postmenopausal [11].

The diagnosis requires medical history, imaging studies and pathologic examination (combined with immunohistochemistry). The choice between transthoracic biopsy or surgical resection depends on the size and location of pulmonary nodules. PBML

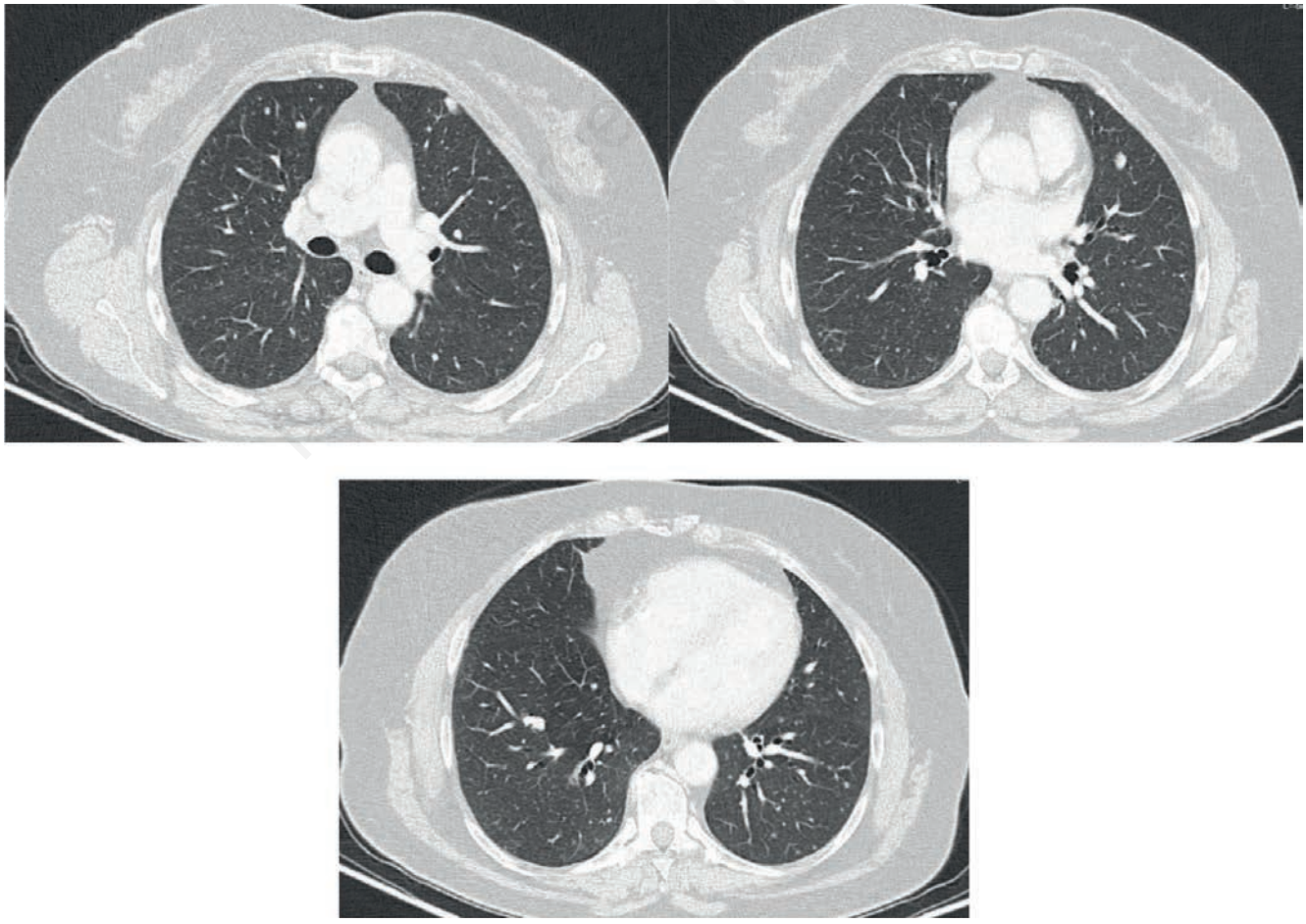

Figure 1. Chest computed tomography showed multiple small nodules in the pulmonary parenchyma.

shows the same histological findings as uterine leiomyoma under microscope, and positivity for actin, desmin, and estrogen/progesterone receptors is presented (providing therapeutic strategies), with a low mitotic index [6].

Since it is a disease with extremely low incidence, there is no standard treatment, and thus it should be individualized for each patient with close monitoring. Treatment depends on age, symptoms and extent of lesion. Surgical resection is the most effective treatment and is pursued when in presence of single or multiple pulmonary lesions [1]. Hormone therapy is the second option, aiming to regulate estrogen and progesterone levels, and includes adnexectomy and oral treatment. Adnexectomy can control tumor growth and can be used for treating premenopausal women [12]. Drug treatment reduces the size of the tumor and improves pulmonary function of patients unfit for surgery [13]. Close observation is the preferred choice for young and asymptomatic patients [2,14]. Progression is indolent, but significant morbidity may occur, which determines the need of long-term surveillance [8,15].

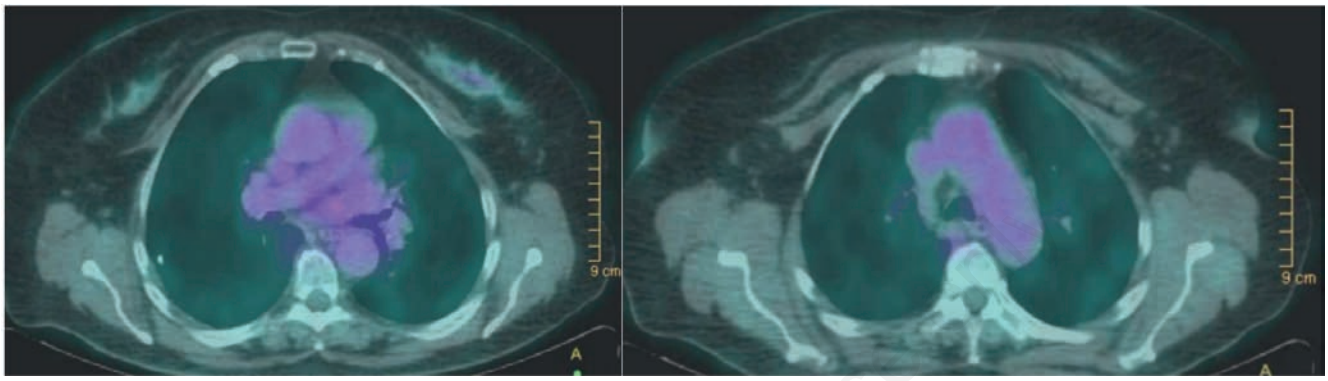

Figure 2. Positron emission tomography and computed tomography revealed no uptake of 18F-fluorodeoxyglucose.

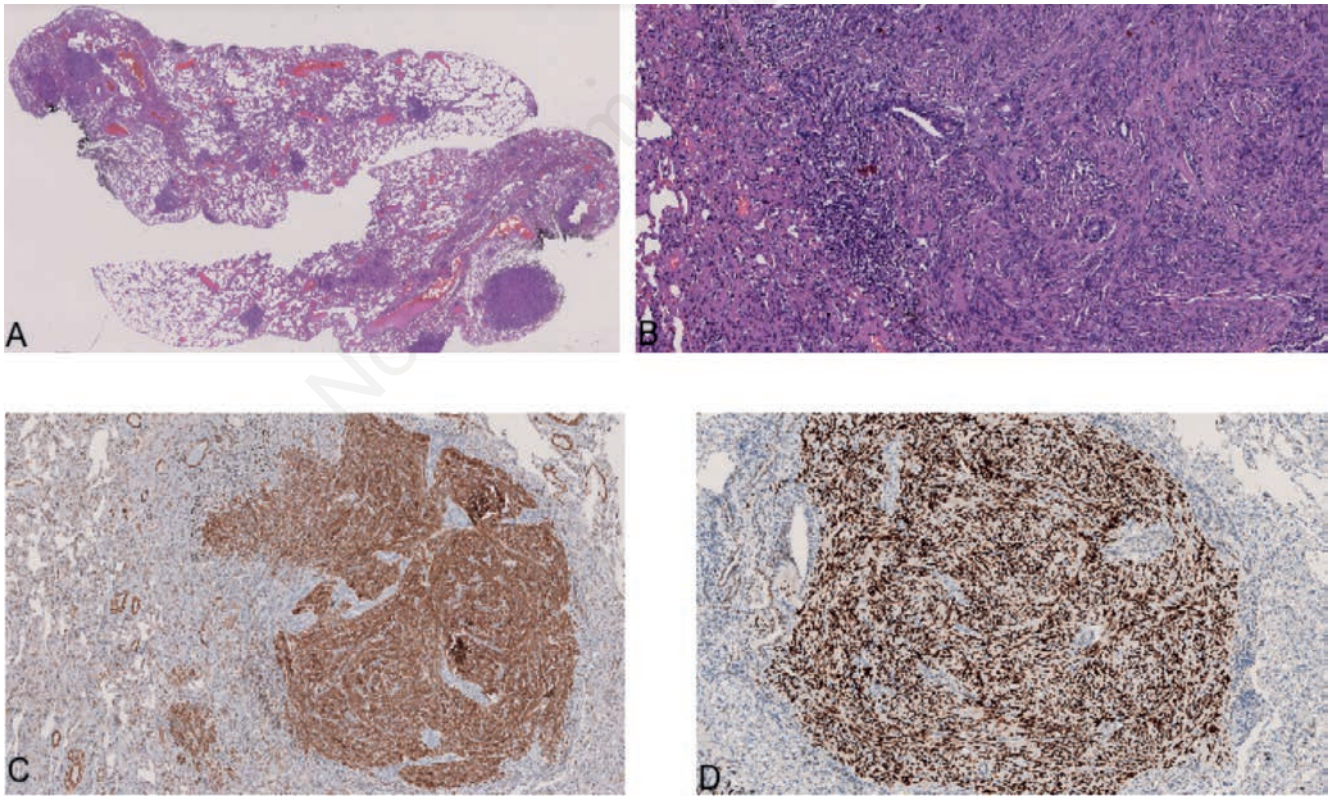

Figure 3. Pathological and immunohistochemical results. A) H&E staining. Lung parenchyma with multiple well-delimited nodules, either subpleural, parenchymal or pericentrilobular in location. B) H&E staining. Cells in the nodules are fusiform, with cigar-shaped nuclei, resembling smooth muscle cells, have little or no nuclear atypia and almost no mitosis. C) (HHF35), D) (ER) tumor cells were positive for smooth muscle markers (HHF35, desmin and h-caldesmon) and for estrogen and progesterone receptors (ER and PR), and they did not express HMB45, melan-A, CK8/18 or neuroendocrine markers.

In the reported case, age and hormonal status of the patient and time at which metastasizing leiomyoma presented in the lung after a myomectomy were not typical, and neither were the imaging findings, with numerous diffuse and small nodules complicating and delaying diagnosis. Thus, since it was a postmenopausal 72-year-old woman and given the extent of the lesions, hormonal therapy was initiated.

Conclusions

Despite the fact that PBML is a rare disease, it should be considered in women (mostly premenopausal) who have a history of uterine myoma and present with pulmonary nodules, even 30 years after the hysterectomy. Treatment should be tailored to the patient's age, symptoms, and the size, location, and extent of the lesion. This disease progresses slowly, and patients should have long-term radiologic monitoring.

References

1. Pacheco-Rodriguez G, Taveira-DaSilva AM, Moss J. Benign metastasizing leiomyoma. Clin Chest Med 2016;37:589-95.
2. 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 2020;20:1-7.
3. Barnas E, Ksiazek M, Ras R, et al. Benign metastasizing leiomyoma: A review of current literature in respect to the time and type of previous gynecological surgery. PLoS One 2017;12:e0175875.
4. Robboy SJ, Bentley RC, Butnor K, Anderson MC. Pathology and pathophysiology of uterine smooth-muscle tumors. Environ Health Perspect 2000;108:S779-84.
5. Mahmoud MS, Desai K, Nezhat FR. Leiomyomas beyond the uterus; benign metastasizing leiomyomatosis with paraaortic metastasizing endometriosis and intravenous leiomyomatosis: a case series and review of the literature. Arch Gynecol Obstet 2014;291:223-30.
6. Kayser K, Zink S, Schneider T, et al. Benign metastasizing leiomyoma of the uterus: documentation of clinical, immunohistochemical and lectin-histochemical data of ten cases. Virchows Arch 2000;437:284-92.
7. Abramson S, Gilkeson RC, Goldstein JD, et al. Benign metastasizing leiomyoma: clinical, imaging, and pathologic correlation. AJR Am J Roentgenol 2001;176:1409-13.
8. Awonuga AO, Shavell VI, Imudia AN, et al. Pathogenesis of benign metastasizing leiomyoma: a review. Obstet Gynecol Surv 2010;65:189-95.
9. Ahmad SZ, Anupama R, Vijaykumar DK. Benign metastasizing leiomyoma - case report and review of literature. Eur J Obstet Gynecol Reprod Biol 2011;159:240-1.
10. Abu Saadeh F, Riain CO, Cormack CM, Gleeson N. Lung metastases from benign uterine leiomyoma: does 18-FDG-PET/CT have a role to play? Ir J Med Sci 2019;188:619-24.
11. di Scioscio V di, Feraco P, Miglio L, et al. Benign metastasizing leiomyoma of the lung: PET findings. J Thorac Imaging 2009; 24:41-4.
12. Chen S, Zhang Y, Zhang J, et al. Pulmonary benign metastasizing leiomyoma from uterine leiomyoma. World J Surg Oncol 2013;11:163.
13. Rivera JA, Christopoulos S, Small D, Trifiro M. Hormonal manipulation of benign metastasizing leiomyomas: report of two cases and review of the literature. J Clin Endocrinol Metab 2004;89:3183-8.
14. Ottlakan A, Borda B, Lazar G, et al. Treatment decision based on the biological behavior of pulmonary benign metastasizing leiomyoma. J Thorac Dis 2016;8:E672-6.
15. Vaquero ME, Magrina JF, Leslie KO. Uterine smooth-muscle tumors with unusual growth patterns. J Minim Invasive Gynecol 2009;16:263-8.