Pulmonary benign metastasizing leiomyoma: a case report

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Abstract

Benign metastasizing leiomyoma is a metastasizing form of leiomyoma, which is a benign uterine tumor that typically affects women of reproductive age. A hysterectomy is typically performed 10-15 years before the disease's metastatic progression. We present a case of a postmenopausal woman who presented to the emergency department with worsening dyspnea and a history of hysterectomy due to leiomyoma. A computed tomography scan of the chest revealed diffuse bilateral lesions. An open-lung biopsy was performed, and the lung lesions were found to have leiomyoma cells. The patient began letrozole treatment and showed clinical improvement without any serious adverse events.

Introduction

Pulmonary benign metastasizing leiomyoma (PBML) refers to usually incidental, benign, metastasizing lung nodules in women of reproductive age [1], with a history of leiomyoma with or without hysterectomy [2]. PBMLs rarely appear in postmenopausal women [1]. The lung nodules seem to appear about 15 years after the hysterectomy [3]; the synchronous appearance of the metastatic nodules and the uterine leiomyoma is quite rare, though reported [4]. We report a rare case of a 62-year-old woman diagnosed with pulmonary benign metastasizing leiomyoma 12 years after hysterectomy and treated with letrozole, an aromatase inhibitor.

Case Report

A 62-year-old non-smoker female presented with dyspnea and shortness of breath during exercise. The patient had given natural birth to two children and underwent a hysterectomy for leiomyoma of the uterus 12 years prior. The chest computed tomography (CT) scan revealed multiple bilateral lung nodules, with a maximum size of 3.5 cm, without any lymph nodes or pleural or pericardial effusion.

Routine blood tests, including ESR and CRP, and urine test results were normal. Laboratory examinations for serum anti-tuberculosis antibodies were also negative. Furthermore, serum concentrations of carcinoembryonic antigen and cancer markers, such as CA-125, CA 19-9, and CA 15-3 were all within normal limits.

An abdominal CT scan was performed without any notable findings, apart from fatty liver disease and a hemangioma. No local relapse occurred after the distant metastases. A staging positron emission tomography (PET)-CT scan revealed no fluorodeoxyglucose activity in multiple bilateral diffuse lung lesions. A repeat chest CT scan after 6 months showed no differ-

ences. Magnetic resonance imaging (MRI) of the brain was negative for lesions. The patient also underwent breast MRI and digital mammography without any significant findings. However, after 10 months, she continued to suffer from dyspnea in exercise and fatigue, and in the follow-up CT scan, there seemed to be a small increase in the size of the nodules. Subsequently, an open lung biopsy was performed, and a nodule from the left bottom lobe of the lung was removed for biopsy.

Histopathological examination demonstrated that the tumor consisted of well-differentiated uterine mesenchymal tissue (ER+, PR+), enclosing lung origin epithelial clefts, positive for thyroid transcription factor 1 (TTF-1 +) (Figure 1).

The Ki-67 positivity rate was low, at about 5% of tumor cells, indicating a low tumor proliferation index. The strong positivity of estrogen and progesterone receptors suggested the tumor cells originated from the uterus. Based on the patient's history as well as the histopathological and immunohistochemical results, she was diagnosed with PBML.

The patient started treatment with letrozole, an aromatase inhibitor, and remains on follow-up. At the first follow-up visit, 3 months after medical therapy initiation, the patient showed clinical improvement. No serious adverse effects were reported since treatment initiation, apart from mild bone pain that did not require treatment discontinuation.

Discussion

The origin of PBML remains unclear, being derived either from low-grade leiomyosarcoma, benign metastasizing hysteromyoma, or multi-focal growing leiomyomatosis [5]. The lung is not the only metastatic site of benign metastasizing leiomyoma, although it is the most frequent. Distant metastases to the heart, liver, breasts, trachea, skin, and central nervous system have been reported [6]. Approximately half of PBML patients present with respiratory symptoms, with cough, dyspnea, chest pain, and hemoptysis being the most common [7]. However, as PBML is characterized by slow progression, many patients are asymptomatic at diagnosis, and PBML is discovered incidentally during routine clinical examination or chest imaging [8].

The most typical findings of PBML in plain chest X-ray, CT scan, or PET-CT scan are multiple or solitary diffuse lesions of different shapes and sizes, usually well-circumscribed and non-calcified, and sometimes accompanied by a small pleural effusion [9]. These nodules are usually scattered within normal lung tissue, as in our case, and can be accompanied by lymph node metastases. As mentioned, the main imaging findings of PBML are non-specific. The differential diagnosis includes other benign or malignant lesions, tuberculosis, sarcoidosis, pneumoconiosis, and lung metastases. Therefore, thoracoscopic or open lung biopsy is crucial and the gold-standard diagnosis for PBML, as in our case.

Histopathologically, PBML is characterized by well-defined nodules with a solid surface and no necrosis or hemorrhage [10]. The cells found in PBML have a histologic smooth muscle appearance entrapped in normal lung bronchoalveolar epithelium [10]. Apart from the absence of tumor cell necrosis and cytological atypia, a low mitotic range, as well as low Ki-67 activity, suggest the benign nature of the tumor [10]. The mesenchymal origin of these tumors is confirmed by the strong presence of immunohistochemical markers, such as desmin and actin (Desmin+, α-SMA+), as well as the positivity of estrogen and progesterone receptors (ER+, PR+), which not only suggests uterine origin but also demonstrates the hormone-dependent nature of the disease [11].

There is no evidence-based treatment for PBML, although treatment practice is being reported in the literature. Surgical removal of the pulmonary nodules is an option, depending on the number and size of the pulmonary lesions [12]. As mentioned, there is a vast presence of progesterone receptor/estrogen receptors receptors in leiomyomas. Surgical castration, including hysterectomy and/or bilateral adnexectomy, has been reported [12]. Nevertheless, medical castration using hormone-blockade therapy might be a superior option, as it is reversible and avoids the adverse effects of surgical intervention. Several agents have been used, such as estrogen blockade with tamoxifen or raloxifene and GnRH agonism [13]. In this case, monotherapy with letrozole produced clinical improvement with limited adverse events.

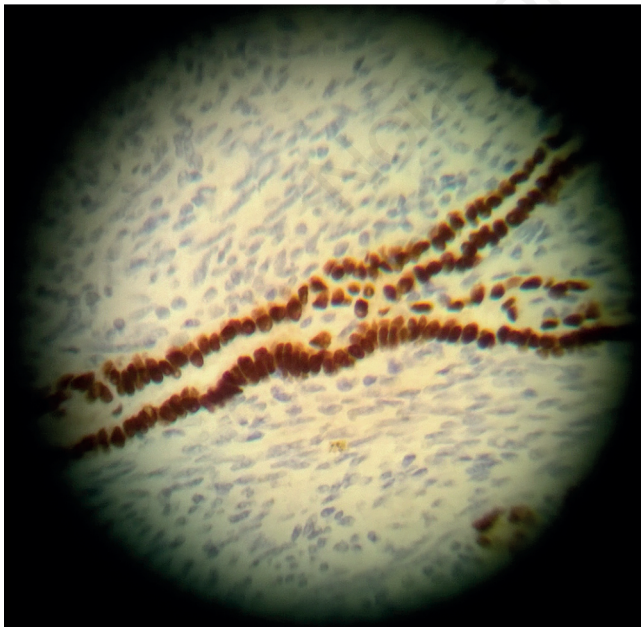

Figure 1. Bland-looking fascicles of smooth muscle are entrapping bronchiolar structures. Thyroid transcription factor 1 was positive.

Conclusions

PBML is a rare disease affecting women with a history of leiomyoma that presents unique challenges in diagnosis and management. Shortness of breath in postmenopausal women should be evaluated with caution, especially when there is a history of leiomyoma, hysterectomy due to leiomyoma, or hysterectomy without any reported cause. A chest CT scan should be performed on postmenopausal women with dyspnea and a history of hysterectomy. A lung biopsy should be performed in the presence of bilateral diffuse lesions or nodules, which is the gold-standard method to diagnose pulmonary benign metastasizing leiomyoma. Treatment options include surgical tumor resection, hormone therapy, and surgical castration. Physicians treating patients with suspected or diagnosed PBML should address and contact oncology centers with more experience in the treatment of this dangerous, if not diagnosed and treated optimally, condition.

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