

Case Report

Case Report: Pulmonary Benign Metastasizing Leiomyoma Appears 26 Years after Resection of Uterine Leiomyoma

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Benign metastasizing leiomyoma (BML) is a rare disease which usually presents as multiple pulmonary nodules several years (average 15 years) after the resection of uterine leiomyoma(s). Only about 100 cases of BML have been reported in English literature. Here we report an unusual case of BML identified 26 years after resection of uterine leiomyoma. The patient was a 44-year-old woman who was found to have an incidental lung nodule in the left lower lobe of lung during workup for a brain lesion that was biopsy-proven astrocytoma. A lung wedge resection was performed and a solid, well demarcated, 2.5 x 1.5 x 1.5 cm nodule was resected. The lesion was composed of bland appearing spindle cells without mitotic activity that were positive for smooth muscle actin, estrogen receptor and vimentin. CD117, S100, Synaptophysin, HMB-45, CD99, calretinin, pancytokeratin and CD10 were negative. MIB-1(Ki-67) staining showed very low proliferative index. In conclusion, the overall morphological and immunohistochemical features, and patient's remote history of primary uterine leiomyoma supported the diagnosis of pulmonary BML.

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Key Words: *benign metastasizing leiomyoma, primary uterine leiomyoma, pulmonary neoplasm*

INTRODUCTION

Uterine leiomyomas are common gynecological tumors in women of reproductive age. They are benign tumors of smooth muscle origin and are believed to result from a clonal proliferation of uterine smooth muscle tissue. In rare occasion, extrauterine benign metastasizing leiomyoma (BML) develops years after the diagnosis and/or resection of uterine leiomyoma. Most cases in the literatures were presented as pulmonary nodules,¹ other less common sites such as lymph nodes, heart, spine, skull base, and retroperitoneum have also been reported.²⁻⁵ Here we report a case with unusual long delay between the diagnoses of primary uterine leiomyoma and current pulmonary BML. Histology examination, immunohistochemistry studies and clinical history correlation support the diagnosis. The differential diagnosis of low grade leiomyosarcoma and its possible etiology are discussed.

CASE REPORT

A 44-year-old female was evaluated with a history of headache, dizziness and frequent fall. MRI revealed homogeneously enhancing brain lesion, which was later diagnosed as pilomyxoid astrocytoma. Patient's pertinent medical history was significant for multiple uterine leiomyoma diagnosed 26 years ago. Her past surgical history included appendectomy and exploratory laparoscopy, cesarean section, partial hysterectomy, right total hip replacement, and recent ventriculostomy. During workup for

Brain lesion, two potential pulmonary nodules at the left lower lobe and hilar area were noted by CT and subsequent PET scan. The primary nodule was 2.5 cm in maximum dimension, located at the left lower lobe. The second nodule was a 0.8 cm left hilar nodule and was considered as a possible satellite nodule or a lymph node. She was then scheduled for a left thoracoscopy and left lower lobe lobectomy. When the primary nodule was excised during the procedure, it was grossly discrete and the surgical impression was benign. Thus, the surgical team decided not to disturb the second nodule.

Grossly, the lung wedge biopsy specimen weighed 13 g and measures 14.2 x 12.5 x 5.2 cm. The pleural surface was smooth. A firm 2.5 x 1.5 cm. bulging nodule could be palpated in the parenchyma with the overlying pleura appearing hyperemic but intact. On sectioning, the well demarcated red, fleshy oval lesion was 2.5 x 1.5 x 1.5 cm. and was located 0.8 cm. away from stapled edge. The lesion extends to both pleural surfaces. Intra-operative frozen section examination revealed that the lung nodule was composed of bland appearing spindle cells without necrosis.

Histological specimen showed well circumscribed tumor of uniform spindle cells (**Figure 1**). MIB-1(Ki-67) stain of the tumor cells showed no mitosis, compatible with a benign neoplasm (**Figure 2D**). Immunohistochemical studies revealed that these cells were positive for smooth muscle actin, vimentin and estrogen receptor (ER), consistent with benign metastasizing leiomyoma from patient's known primary uterine leiomyoma (**Figures 2A-2C**). The tumor

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cells were negative for CD117, S100, Synaptophysin, HMB-45, CD99 and CD10. These findings did not support the differential diagnoses of gastrointestinal stromal tumor (GIST), tumor of neural origin, carcinoid tumor, PEComa, and metastatic endometrial stromal tumor (data not shown). Furthermore, negative staining results of calretinin and

pancytokeratin were not compatible with a diagnosis of either spindle cell mesothelioma or spindle cell carcinoma (data not shown). In summary, the morphological features, immunohistochemical studies and patient's history of remote primary uterine leiomyoma support the diagnosis of pulmonary BML.

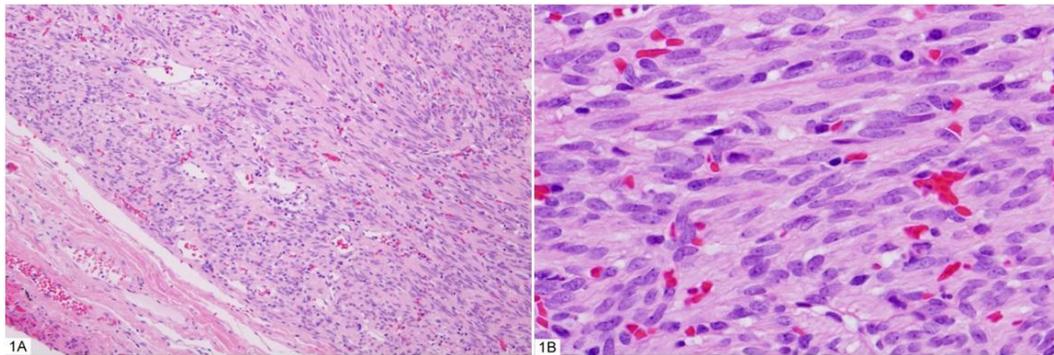


Figure 1. Low- (1A, x100) and high- (1B, x400) power views of hematoxylin-eosin-stained sections of the pulmonary tumor show a well circumscribed tumor which is composed of benign appearing spindle cells.

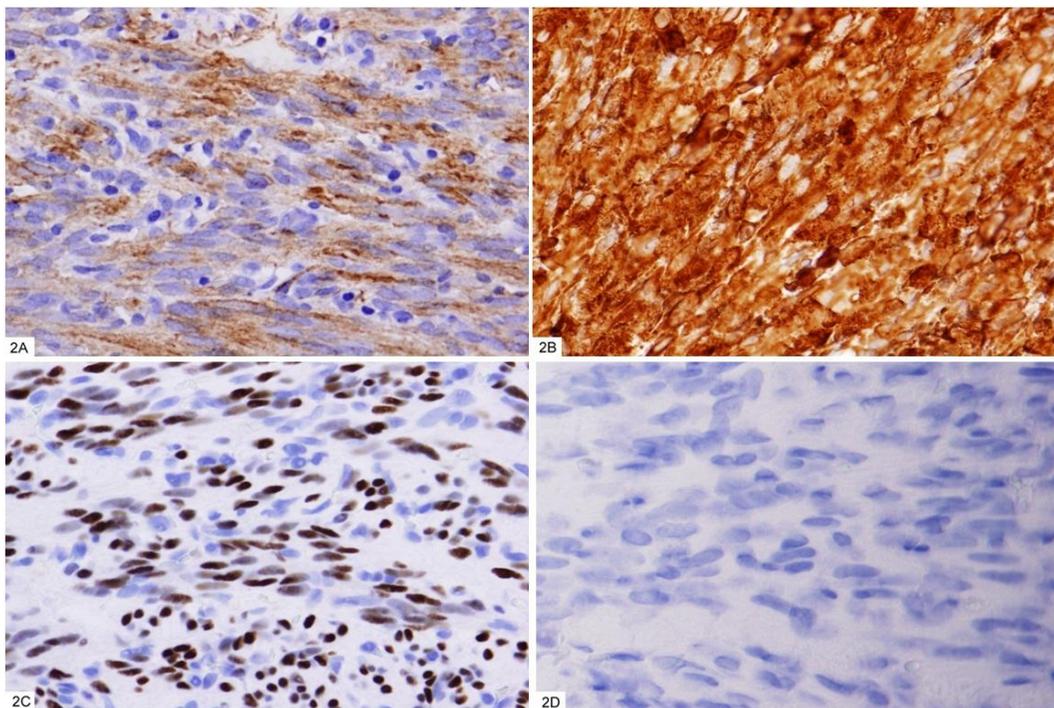


Figure 2. Immunohistochemical studies show that the tumor cells are positive for smooth muscle actin (2A, x400), vimentin (2B, x400), and estrogen receptor (2C, x400), and negative for MIB-1(ki-67) (2D, x400).

DISCUSSION

Benign metastasizing leiomyoma is a benign appearing extrauterine smooth muscle tumor. It is usually associated with current or prior diagnosis of uterine leiomyoma and occurs mainly among premenopausal and perimenopausal

women. The lung is the most common site of extrauterine involvement. The average interval between diagnosis of primary uterine leiomyoma and extrauterine metastatic tumor is 10 to 15 years.⁶⁻⁷ Here we report a case with an unusual

long delay, 26 years between the diagnoses of uterine leiomyoma and current pulmonary BML. The pathophysiology of the extrauterine metastasizing process is still controversial. Multiple factors, including the metastasizing route and individual hormone level may affect the development and growth of the extrauterine tumor. Furthermore, both primary and metastatic tumors are slow growing tumors. They could be asymptomatic for long period of time and diagnoses are often incidental. Thus clinical correlation with past history of uterine leiomyoma is important for correct diagnosis of cases with unusual long interval.

Uterine smooth muscle tumors can usually be divided histologically into leiomyoma and leiomyosarcoma. Occasionally, when histological features are indeterminate, the tumor can be classified as smooth muscle tumor of uncertain malignant potential (STUMP). The following criteria were proposed and used to evaluate the uterine smooth muscle tumors: degree of cytological atypia, presence or absence of necrosis and mitotic index (MI).⁸ MIB-1 (Ki-67) is useful in distinguishing leiomyosarcoma from STUMP and cellular leiomyomas.⁹ In the case we presented here, the tumor cells had similar histological and immunohistochemical properties of uterine smooth muscle cells. They appeared uniform with minimal atypia. In addition, no necrosis or mitotic activity was observed. Therefore, the tumor was most consistent with benign leiomyoma.

Metastasis is often associated with malignant potential and poor prognosis. However, tissues such as endometrium and chorionic villi can migrate and colonize distant organs and are considered benign processes. Benign metastasizing leiomyoma is generally considered as a benign entity, although adequate sampling is required to rule out fraction of potential malignant component. Several hypotheses have been proposed for the pathophysiology of BML, including: retrograde menstruation similar to peritoneal endometriosis, transcoelomic spread at cesarean section and other pelvic surgery, lymphatic or vascular spread, or coelomic epithelium metaplasia.¹⁰ In addition to similar histological properties to uterine leiomyoma, BML is also found to respond to hormonal regulation.¹¹⁻¹² Molecular studies further support the clonality of the metastasizing tumor and primary uterine leiomyoma.¹³⁻¹⁴ The patient's past cesarean section

and pelvic surgical history may suggest transcoelomic spread as one possible etiology for her current BML.

CONFLICT OF INTEREST

None.

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