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Case Report .

Histopathologically Confirmed Endobronchial Metastasis of Uterine Leiomyosarcoma: A Case Report and Literature Review

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ABSTRACT

Uterine leiomyosarcoma is a very rare malignant version of uterine leiomyoma, or fibroid, the most common benign smooth muscle tumor of the uterus in women. Uterine leiomyosarcoma has been known for its aggressive and distant metastatic behavior. Common sites of distant metastases are liver, lung, and bone. However, endobronchial metastasis is rare. We present a 52-year-old woman with uterine leiomyosarcoma. She presented with a cough and decreased air entry on one side. Imaging showed a lung collapse due to obstruction by an endobronchial tumor. Histopathological examination of the endobronchial tumor revealed pattern characteristic of leiomyosarcoma.

Keywords: Leiomyosarcoma, Endobronchial, Metastasis.

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INTRODUCTION

Fibroids are benign spindle cell neoplasm arising from the smooth muscle fibers of the uterine myometrium named uterine leiomyoma; they are considered the most common pelvic neoplasm in women. Their malignant counterparts are the uterine leiomyosarcomas (ULMS). The latter is a member of a group of uterine sarcomas that includes; endometrial stromal sarcomas, adenosarcoma, and carcinosarcoma. It has been found that the incidence of uterine sarcomas to be 0.36 per 100,000 women per year. The mean age of uterine leiomyosarcoma diagnosis is 50 years.[1] In our case report, we are presenting a case of ULMS with endobronchial metastasis (EBM) causing right lower and middle lobe collapse.

CASE REPORT

A 52-year-old woman known to have metastatic leiomyosarcoma of the uterus, with the involvement of the liver and lungs. The diagnosis confirmed by tissue biopsies from the pelvis and liver. Imaging studies revealed lung metastasis. Her medical history started in June 2013 when she presented with lower abdominal pain and mild to moderate vaginal hemorrhage. The first line therapy was based on Ifosfamide and Doxorubicin. She received 3 cycles of chemotherapy, and the tolerance of her chemotherapy was globally smooth from both clinical and biological point of view, with no significant response and without significant complications. Her abdominal pains clearly improved. She had been maintained on hormonal therapy (Tamoxifen, Letrozole, and Leuprolide), but her tumor has continued to progress.

Three years after initial diagnosis, she started to have an increasing cough associated with sputum and central chest pain. Physical examination showed decreased air entry on the right lung. A computed tomography (CT) scan of the chest with contrast showed an interval increase of the bilateral metastatic lung nodules with a new collapse in the right lower lobe due to obstruction by a metastatic lung nodule (Figure 1). Bronchoscopic examination confirmed a large endobronchial mass obstructing right bronchus intermedius, and the bronchoscope could not be passed behind it (Figure 2). She underwent flexible and rigid bronchoscopy with debulking of the bronchus intermedius. During the procedure, multiple endobronchial biopsies were taken from this lesion.

Microscopic examination of hematoxylin and eosin sections of the endobronchial mass revealed a proliferative formation of spindle-shaped cells with nuclear pleomorphism, mitosis, necrosis and eosinophilic cytoplasm. On immunohistochemical staining, the cells are positive for estrogen receptor, progesterone receptor in nuclear distribution. Desmin and smooth muscle actin are positive in the cytoplasm. Ki-67, which is a proliferative marker, was high, indicating an active proliferation of the tumor cells (Figure 3).

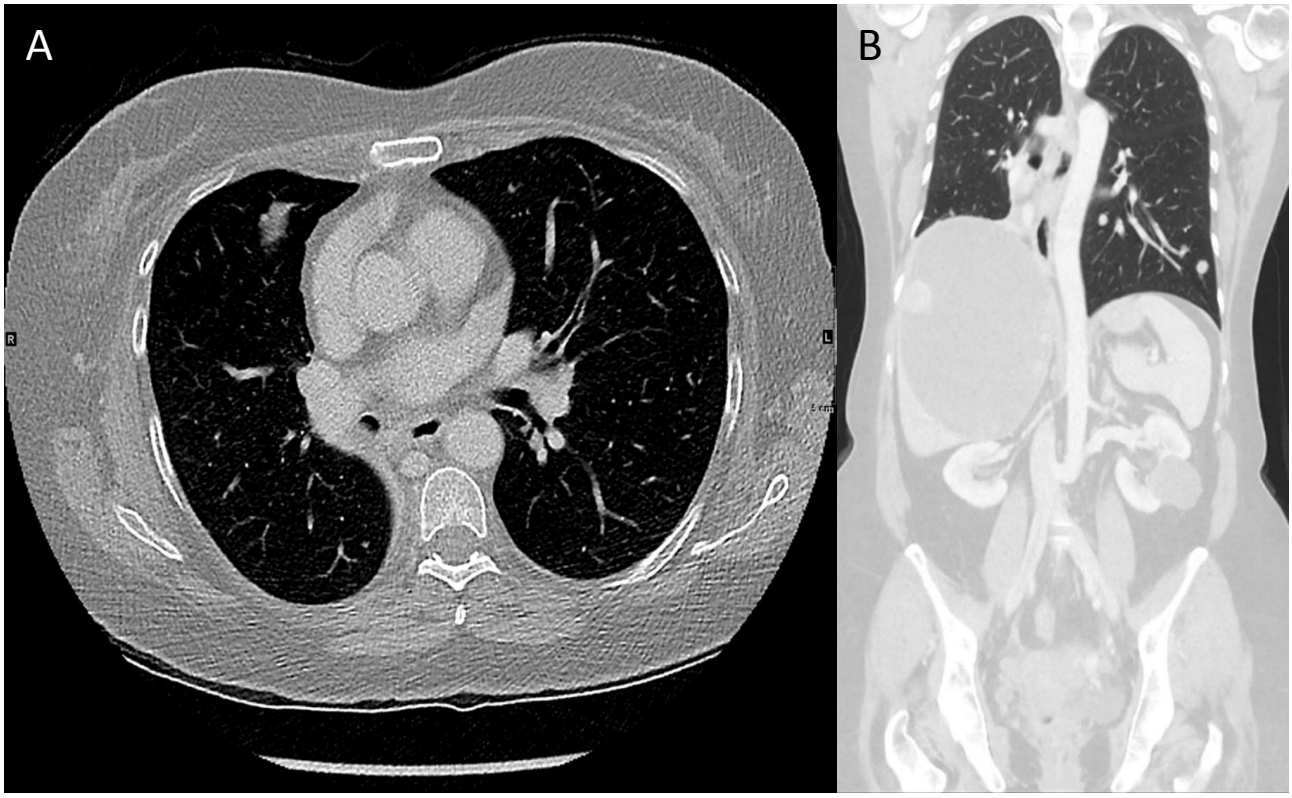

Figure 1: Enhanced computed tomography scan. A, (axial) demonstrating obstruction on the right lower lobe bronchus and right lower lobe collapse. B, (coronal) showing bronchus intermedius obstruction, huge hepatic cystic necrotic metastatic mass with multiple mural nodules, left renal metastasis, and heterogeneous solid uterine mass.

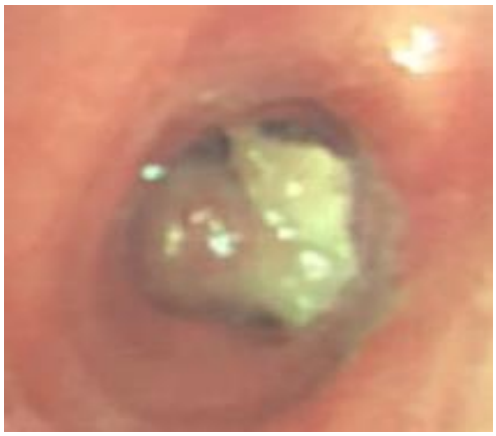

Figure 2: Bronchoscopic image showing large endobronchial mass with necrotic tissues obstructing right bronchus intermedius.

The morphology and immunohistochemical profile were compatible with leiomyosarcoma of uterine origin. It has the same morphology of both, the liver metastasis and the original tumor in the pelvis.

After rigid bronchoscopy and debulking, cough disappeared. She was given a trial of antibiotic (Augmentin) to reduce the risk of obstructive pneumonia. The plan was to receive local radiotherapy to the right lower lobe of the lung to prevent recurrence of the endobronchial lesion and further collapse, and to start her on Pazopanib for disease progression. CT scan after 6 weeks demonstrated interval resolution of right lower lobe collapse. Molecular profiling is going to guide further therapy, since this is a rare tumor which has not responded to heavy chemotherapy.

DISCUSSION

Uterine sarcoma is an uncommon tumor, accounting for 1% to 3% of all uterine malignancies. Its clinical behavior is characterized by the predilection toward local recurrence as well as a high incidence of metastatic disease.[2,3] In the case of distant metastasis, endometrial cancer spreads commonly through pelvic and para-aortic lymph nodes or pelvic viscera including adnexae. Endometrial cancer showed low Incidence of hematogenous metastasis. EBM can be unsuspected because of the long interval between initial diagnosis and clinical presentation of its metastasis (up to 18 years). EBM is defined as a non-pulmonary tumor, involving the sub-segmental or proximal central bronchus, with lesions histologically identical to the primary tumor.[4]

EBM originates from different extrapulmonary primary tumors, usually cancer of the breast, colon, melanoma and renal neoplasms. Other rare primary tumors include sarcoma, thyroid gland, uterine cervix.[5] Primary tumors usually manifest locally before clinically apparent EBM. EBM of ULMS is an extremely rare complication. We found few cases reported in our literature review. The first case of EBM of ULMS was described by Flynn et al. in 1978.[6] In Sorensen's study of 204 EBM patients, he only found five patients' primary tumors were from endometrial origins.[5] Salud et al. reviewed EBM cases for 9 years and found that only one patient had endometrial carcinoma as a primary tumor.[4] Nishida et al. reported two cases of metastatic ULMS to lung, age 59 & 58 yr, with metastasis to right lower lobe and left lower lobe, respectively.[7] None of them had endobronchial metastasis. Miglietta et al. reported two cases of osteoblastic metastatic lesions from ULMS. Those patients did not have lung metastasis which is unusual behavior in this tumor type.[8]

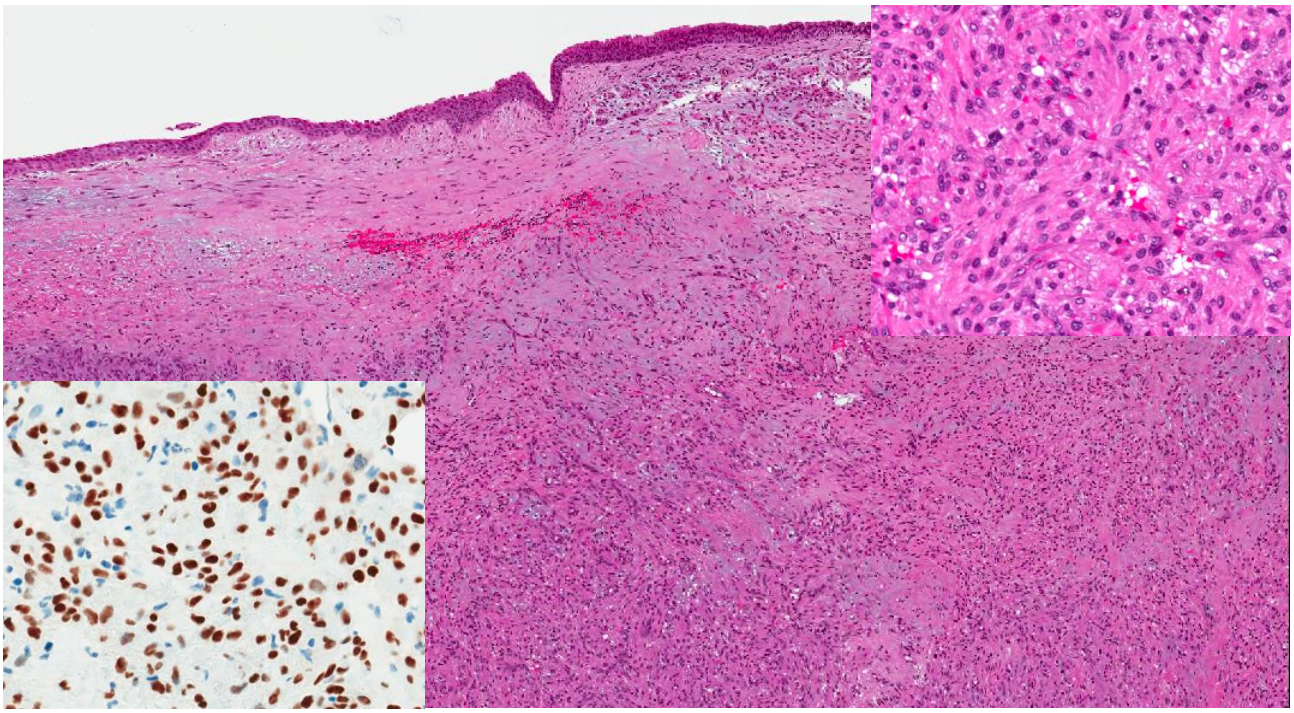

Figure 3: Low power hematoxylin eosin stain view, showing a spindle cell tumor in the bronchial submucosa (Low power X 50). High power (Inset, right upper corner) showing tumor composed of spindle cells with pleomorphism and moderate amount of eosinophilic cytoplasm. (Inset, left lower corner) the tumor cells stain for progesterone receptor immunohistochemistry antibody in nuclear distribution (power X 40).

The pattern of pulmonary metastasis from uterine malignancies which includes carcinomas and sarcomas are studied by Bouros et al., they identified 90 patients with lung metastases at the time of diagnosis of the primary uterine tumors of different types. Twenty patients (22%) are found to have lung metastasis identified by imaging. Sixty-five (72%) presented with multiple pulmonary nodules; 16 (18%) presented with a solitary lung nodule, mass lesion seen in 10 (11%), lymphangitic spread in 3, and pleural effusion in 6 (6.7%). Cavitations and tracheal metastasis were observed in one case each.[9]

Symptoms of ULMS include abnormal vaginal bleeding, pelvic mass, and pelvic pain.[10] These symptoms can be found in any pelvic tumor, particularly leiomyomas which are more common than ULMS. If a woman is menopausal and not receiving any hormonal replacement therapy, malignancy is suspected. If the tumor reaches a large size, it may rupture and cause acute abdominal pain. The criteria for a definitive diagnosis of ULMS is a high mitotic rate generally exceeding 15 mitotic figures per 10 high-power-fields. Other features seen in malignant tumors but not in benign leiomyoma are an extrauterine extension, necrosis, large size, and infiltrating border.

Leiomyosarcoma might express some immunohistochemical stains; smooth muscle markers, such as smooth muscle actin, desmin, and histone deacetylase 8, epithelial markers, such as keratin and epithelial membrane actin (EMA). ULMS also express estrogen receptors, progesterone receptors, and androgen receptors. There are higher levels of Ki67 and mutation and overexpression of p53 and P16 in ULMS compared with benign smooth muscle tumors.[11]

Treatment of ULMS is surgical. Total abdominal hysterectomy and debulking of the tumor if it is metastasized are considered to be the standard surgical treatment of leiomyosarcomas. Ovarian preservation may be performed in premenopausal patients with early stage endometrial cancer desiring fertility preservation.[12,13] The effect of adjuvant therapy on survival is not clear. Chemotherapy is usually used for advanced or recurrent diseases and radiotherapy might help in controlling local recurrences.[10,14] Many Studies of various cancers including uterine cancer have shown that surgical treatment of pulmonary metastasis may contribute to a survival benefit.[15]

When 2003 WHO criterion is used to establish the diagnosis, it confirmed a poor prognosis of these tumors even when confined to the uterus, and even if diagnosed at an early stage. Five-year overall survival of local leiomyosarcomas is known to be 51% at stage I and 25% at stage II. The recurrence rate of ULMS is 53% and median overall survival is 10 months.[16] Many studies have been found to show the correlation between survival and patient age, clinical stage, tumor size, presence or absence of necrosis, pushing versus infiltrative borders, the degree of nuclear pleomorphism, mitotic rate, and vascular invasion.[8,14,17] The most significant prognostic factor for uterine sarcomas is tumor stage.[17,18]

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