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Benign Metastasizing Uterine Leiomyoma: Case Report with Review of the Literature

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Case Report

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Abstract

Benign metastasizing leiomyoma is a rare disorder involving distant metastases secondary to a smooth muscle tumor of the myometrium. Oftentimes, it is easy to be misdiagnosed as a malignant tumor when nodules are found in multiple tissues. In most cases, there is a previous history of total abdominal hysterectomy for uterine leiomyoma. However, the pathogenesis of this disease has not yet been elucidated. In order to raise clinicians' awareness of BML, we present a short review of the literature in combination with an unusual case.

Keywords: Uterine leiomyoma; CT scan; Gynecologic; Peritoneal carcinomatosis; Gynecologic and uterine neoplasms

Abbreviations: IVC: Inferior Vena Cava.

Introduction

Benign metastasizing uterine leiomyoma is defined as a histologically benign uterine smooth muscle tumor that acts in a somewhat malignant fashion and produces benign metastases. The lung is the most commonly reported site of metastasis and solitary as well as multiple pulmonary nodules or masses have been reported. Familiarity with potential extrauterine sites and with the complete spectrum of imaging features characteristic of these tumors, including their more unusual manifestations, facilitates their timely diagnosis and appropriate management. This rare condition is characterized by numerous well-differentiated leiomyomas at sites distant from the uterus. The lesions are histologically identical to their uterine counterparts. Since the condition was first described by Steiner [1], 120 cases have been documented in the literature. Metastases most often affect the lungs [2], whereas the heart, brain, lymph nodes, bone, and skin are more rarely affected. The condition usually manifests as multiple incidentally detected pulmonary nodules in middle-aged women. A history of hysterectomy for uterine leiomyoma may be indicative, with the mean reported interval between hysterectomy and the appearance of pulmonary nodules ranging from 3 months to 20 years. A previous diagnosis of uterine leiomyoma may point to the diagnosis in many cases.

Case Report

A 39-year-old woman whose history started when she underwent a routine chest x-ray after she had a positive PPD, and found to have multiple bilateral pulmonary nodules though did not have any respiratory symptoms. These findings led to a CT scan of the chest, that demonstrated multiple lung nodules, three in the right upper lobe, and two in the left upper lobe. Additionally there was evidence of a uterine mass. She then went on to have a PET-CT scan in which these lung lesions were not hypermetabolic. This was followed by a lung FNA, that was nondiagnostic. One month later, she underwent a total abdominal hysterectomy, at which time pathology showed the presence of leiomyomas. She eventually was referred to our hospital and had a follow-up CT scan that identified increased size of the previously noted pulmonary nodules. She had a right-sided core lung biopsy that revealed metastasizing leiomyoma. At the time of her initial consultation treatment options were discussed and

ultimately it was decided to attempt hormone manipulation with leuprolide injections. She overall has been doing relatively well with no new complaints of ongoing cough, shortness of breath, hemoptysis nor persistent cough. Denies any abdominal discomfort, distention, nausea, vomiting, and change in neither bowel habits nor new musculoskeletal symptoms. She is eating well with no notable fatigue nor unintentional weight loss.

Pathologic Findings

From the outside pathology report, grossly multiple serosal, myometrial and endometrial nodules identified. Multiple nodules from parametrium, paraaortic and peritoneum were identified and biopsied.

Microscopic examinations of the tumor present in the parametrial, para aortic region and uterus have the histology of benign leiomyomata. The tumor cells have spindle, cigar-shaped nuclei and spindle eosinophilic poorly defined cytoplasm. Limited degenerative changes and focal cellular areas without evidence of necrosis, nuclear atypia and/or increased mitotic activity present. The lesions are best fitting a benign metastasizing leiomyomata into pelvic and abdominal cavities from the uterus (Figure 1).

Microscopic examination of the core biopsy from the lung nodule, shows benign looking smooth muscle cells showing moderate cellularity, minimal atypia, inconspicuous mitosis, and no evidence of necrosis. Based on histopathologic criteria, it was considered as benign leiomyomata with hyaline degeneration.

Slides of the retroperitoneal mass revealed a spindle cell tumor that was histopathologically similar to the uterine myomas removed three years before (Figures 1 & 2). For definite diagnosis, a panel of immunohistochemical staining was requested for both the current masses, which revealed identical immunoreactivities including positive results for SMA, desmin, vimentin, ER, BCL2 and negative results for S100, CD 34, AE1/AE3, Calretinin with less than 1% (Figure 2).

The immunohistochemical studies confirmed that the tumor was a mesenchymal derivation with smooth muscle differentiation and ruled out the possibility of epithelial origin and gastrointestinal or endometrial stromal tumors. The morphologic features and pattern and intensity of immunostaining support a diagnosis of metastatic smooth muscle tumor.

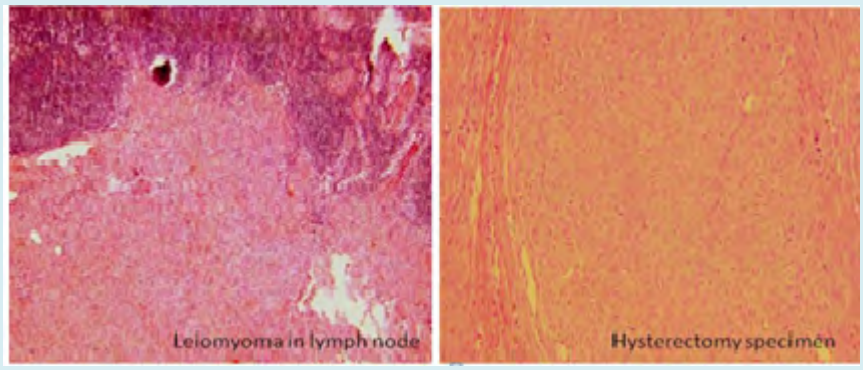

Figure 1: Microscopic examinations of the tumor present in the parametrial, para aortic region and hysterectomy specimen.

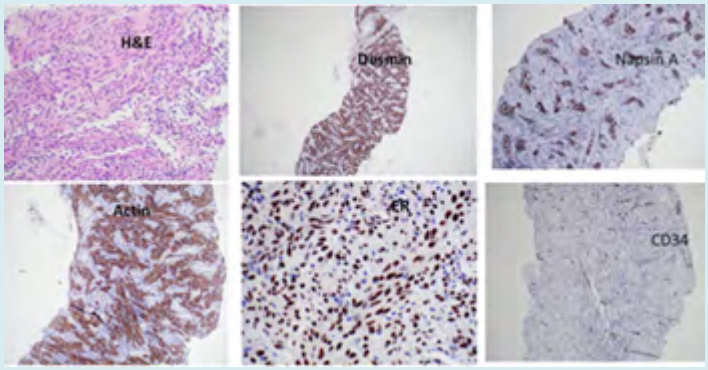

Figure 2: Microscopic examination of the core biopsy from the lung nodule.

Discussion

Leiomyomas represent the most common gynecologic and uterine neoplasms. Approximately 20%–30% of women older than 35 years have uterine leiomyomas that are manifested clinically [3,4]. The radiologic diagnosis of classic uterine leiomyomas is straightforward, given their typical imaging features and their common clinical manifestations. However, leiomyomas occasionally occur with unusual growth patterns or in unusual locations that make their identification more challenging both clinically and radiologically.

Examples of leiomyomas with an uncommon growth pattern include diffuse peritoneal leiomyomatosis, intravenous leiomyomatosis, benign metastasizing leiomyomas, retroperitoneal leiomyomas, and parasitic leiomyomas. Leiomyomas with a rare growth pattern occur most often in women of reproductive age. A history of hysterectomy or the presence of concurrent uterine leiomyomas may be suggestive of the diagnosis. Diffuse peritoneal leiomyomatosis manifests as innumerable peritoneal nodules resembling those in peritoneal carcinomatosis.

Intravenous leiomyomatosis sometimes manifests as serpentine growths within the inferior vena cava (IVC) and other systemic veins and may extend to the heart. Benign metastasizing leiomyoma may manifest as multiple nodules or masses in the lungs or other sites, mimicking metastases from malignant tumors. Parasitic leiomyoma and retroperitoneal leiomyomatosis usually manifest as single or multiple pelvic or retroperitoneal masses. Knowledge of the unusual and protean imaging manifestations of these almost always benign entities is essential to distinguish them from malignant tumors that may bear a close resemblance.

BML is a rarely described condition of the women aged 35–55 years old, occurring years after hysterectomy. The most common site of metastasis is lung [5], although cases have been reported with involvement of lymph nodes, heart, skull [6], spine [7], and retroperitoneum [8]. It appears that the tumor metastasizes to lungs and other extrauterine tissues via hematogenous spread [9]. Although some cases of benign metastatic leiomyomas have been reported, some authors still believe that they are metastasis of previously misdiagnosed low-grade uterine leiomyosarcomas [10]. Definite diagnosis of BML should only be made after careful reviewing of the numerous samples of the primary uterine leiomyoma to exclude small foci of missing sarcoma [3].

Among many different pathological features, it is now recognized that the mitotic index, the degree of cytological atypia, and the presence or absence of coagulative necrosis are the most important predictors of tumor behavior [2]. Uterine leiomyomas with less than 5 mitoses per 10 HPFs, with no cellular atypia or necrosis, are considered benign. On the other hand, a mitotic index greater than 10, marked cellular atypia, and coagulative tumor cell necrosis characterizes overt leiomyosarcomas. For tumors with characteristics between these extremes, the term, "leiomyoma of uncertain malignant potential" is reserved [2,6].

The pathogenesis of BMLs has been object of controversy. Several hypotheses have been proposed, but vascular dissemination is at present the most widely accepted. The majority of women with these tumors have a prior dilatation and curettage, myomectomy, or hysterectomy. This raises the possibility of surgically induced vascular spread. However, some cases have been described in which the uterine tumor is discovered simultaneously [11] or even after the metastases [9].

A multifocal origin has been advocated in some cases with unusual distribution of metastatic lesions [11-13]. Smooth muscle neoplasm can in fact develop de novo in virtually any location (from vascular smooth muscle). However, extrauterine leiomyomas are uniformly ER negative, and only few (13%) extrauterine leiomyosarcomas show weak and focal ER immunoreaction [14,15]. In contrast, most BMLs are ER positive. Moreover, genomic hybridization and X-chromosome inactivation analysis demonstrated a balanced karyotype and identical X-chromosome inactivation pattern consistent with a monoclonal origin of pulmonary and uterine tumors in one case of BML [16].

Some investigators have suggested that the primary lesions could actually be low-grade sarcomas with metastatic potential, and that sampling error may account for their deceivingly benign appearance [13]. Still others have suggested that the tumor metastases might have undergone maturation [17]. Occasional cases of metastasizing leiomyoma also have been reported in male patients [18,19].

Symptoms of chest pain, shortness of breath, and cough have been described. Although the clinical course is usually indolent, a more rapid progression to severe respiratory symptoms also has been reported [20].

It is now largely accepted that the lesions arise as hematogenous metastases from benign tumors; however, a second school of thought still supports a hypothesis of multiple independent foci of smooth muscle proliferation. The primary uterine lesions are classified as smooth muscle tumors of unknown malignant potential because of the limitations of current histopathologic tests.

Associations with diffuse peritoneal leiomyomatosis [21], intravenous leiomyomatosis [22], and diffuse uterine

leiomyomatosis Kjerulff KH, et al. [23] have been observed and may be indicative of a common pathologic origin.

The current criteria used for distinguishing benign, malignant, smooth muscle tumors of undetermined malignant potential in the uterus is the presence of necrosis, the mitotic index, nuclear atypia, cellularity, and the tumor border [10] Various histologic patterns such as myxoid differentiation coupled with enlarged and atypical cells and epithelioid feature in more than just a few foci of uterine smooth muscle are in favor of sarcoma [24]. Necessity of histopathologic and immunohistochemical studies to exclude other neoplasms, is obvious, especially when the site of metastasis is uncommon.

These metastatic tumors reported in the literature tended to have greater mitotic index [25] than the primary sites and revealed features of benign leiomyomas to low-grade leiomyosarcomas [1] Some researchers believe that only patients in whom no mitosis and nuclear atypia was present in their histologic samples should be placed in this category. They then, question the origin of the tumors: uterine metastasizing leiomyoma, multifocal hamartomas synchronous or metachronous leiomyomas [26]. These tumors may be estrogen and progesterone receptor positive [27,28]. Therefore, hormones may be used for their treatment. Regression of the tumor after hormonal manipulation through oophorectomy or medical treatment [29,30] such as luteinizing hormone.

Although an assessment with MR imaging may help increase the physician's confidence in the preoperative diagnosis of small tumors with typical imaging characteristics, cystoscopic biopsy and histopathologic analysis are required to verify the diagnosis. The selection of a management method is based on the symptoms, since the tumors typically have a benign course. Small tumors are treated with transurethral resection; larger tumors and those with extravesical components often require partial cystectomy. As is true of urethral leiomyomas, malignant transformation of urinary bladder leiomyomas has not been reported and recurrence is uncommon [17,31-34].

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