



## Case report

## Benign metastasizing leiomyoma, a rare imposter of metastatic cervical cancer

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## ABSTRACT

Benign metastasizing leiomyoma (BML) is a rare variant of common benign smooth muscle neoplasm. We report a case of BML in a 45-year-old premenopausal woman with a significant smoking history and no previous history of cervical cancer screening. The patient presented with vaginal bleeding, abdominal pain, a necrotic mass in the vagina, and an incidental finding of diffuse pulmonary nodules on chest imaging. A total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO) was performed for symptomatic management and adequate tissue sampling followed by fine needle biopsy of a pulmonary lesion. The pedunculated uterine mass and the pulmonary nodule were both consistent with smooth muscle neoplasm suggestive of myoma. Six-months following surgery, the patient is asymptomatic with partial regression of her lung nodules and no evidence of new or enlarging lesions while on treatment with Megestrol.

## 1. Introduction

Leiomyoma is the most common gynecological tumor in women. Although it is a benign entity that is commonly asymptomatic, its potential to reach a remarkable size can result in bleeding, mass effect, pain, dyspareunia and/or infertility. Leiomyomas are usually an uncomplicated presumed diagnosis, recognized by pelvic imaging modalities with a characteristic whorled appearance on ultrasonography and superior detection with magnetic resonance imaging with sensitivity and specificity both near 90% (Khan et al., 2014). However, leiomyomas can demonstrate unique qualities that can distort normal pelvic tissue architecture, mimic clinical features of carcinoma, and challenge the diagnosis (Fasih et al., 2008). Concerning features for malignancy warrant pathologic evaluation, as it is the only reliable method to differentiate between benign and malignant etiology for uterine tumors.

Benign metastasizing leiomyoma (BML) is a rare manifestation that presents with extra-uterine proliferation of smooth muscle cells, most commonly in the lung. Reported in more than 200 cases, BML should be considered in a premenopausal patient with pulmonary nodules and a history of leiomyoma or hysterectomy (Fasih et al., 2008). We present a case of BML in a patient with risk factors for a gynecologic malignancy leading to a diagnostic conundrum.

## 2. Case report

We report a case of a previously healthy 45-year-old G7P4 Micronesian woman who initially presented to the emergency department for one week history of heavy intermenstrual vaginal bleeding and symptomatic anemia. Her past medical history was notable for a 32-pack year smoking history and absent cervical cancer screening. Her surgical history was limited to two Cesarean deliveries in 2015 and 2016, which also marked the last time the patient had accessed medical services. A limited pelvic exam by an emergency room provider revealed moderate amounts of blood in the vaginal vault, a foul-smelling discharge, and a necrotic upper vaginal mass. A computerized tomography (CT) of the abdomen and pelvis showed a diffusely enlarged cervix and a distended uterus with enhancing nodular endometrial masses and fluid (See Fig. 1). Also notable was bladder distension with mild bilateral hydro-ureteronephrosis without evidence of obstructing stone or mass and an incidental finding of numerous nodules at the lung bases. Chest CT was subsequently acquired which showed greater than 30 round, discrete pulmonary nodules scattered bilaterally with reported suspicion for metastatic involvement (See Fig. 2). Given the patient's symptoms and history, this presentation was highly concerning for cervical or endometrial cancer metastatic to the lung. With ongoing moderate blood loss

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and a hemoglobin of 7, the patient was given two units of packed red blood cells and urgently scheduled to follow-up with a gynecologic oncologist as an outpatient.

During the brief interim, the patient's clinical course was complicated by new urinary retention prompting repeated emergency department visits and requiring placement of a foley catheter. When the patient was seen in our clinic that same day, she endorsed severe abdominal pain, ongoing vaginal bleeding, and a malodorous discharge. A pelvic exam revealed the "presumed" cervix and upper vagina replaced by an exophytic, friable, foul smelling necrotic mass and copious amounts of blood. The immobile pelvic mass demonstrated mimicked bilateral parametrial involvement to the pelvic sidewalls. A portion of the mass was digitally removed and sent for pathology. Radiology Oncology was recruited in this patient's care with the anticipation for urgent palliative radiation to control the patient's bleeding, which would then be followed with systemic chemotherapy for presumed metastatic cervical cancer. However, pathology was discordant, reporting histological features consistent with infarcted smooth muscle and without evidence of atypia or malignancy. Palliative radiation for her worsening symptoms could not be pursued without pathologic confirmation of a suspected gynecologic malignancy. Therefore, given the severity of the patient's symptoms of ongoing bleeding and pain, a diagnostic versus palliative surgery was urgently scheduled.

The patient returned to the emergency department the night prior to her scheduled surgery with worsening abdominal pain meeting sepsis criteria with fever and leukocytosis. She was admitted for occult malignancy versus necrotic pelvic mass with concomitant bacterial superinfection. Blood cultures were obtained and empiric treatment with ceftioxin and doxycycline was initiated. Given the presence of pulmonary nodules and unknown etiology of the pelvic mass, the differential diagnosis of her lung lesions was expanded to include tuberculosis (TB) considering the patient's pertinent history of having recently immigrated from a TB-endemic area (Micronesia). However given the peripheral distribution and radiographic appearance of the pulmonary nodules, infectious disease consult and radiology considered TB less likely. Out of an abundance of caution, suitable precautions were enabled and TB workup was initiated. Surgery was pursued as scheduled



**Fig. 2.** Chest CT at the time of initial diagnosis showing multiple pulmonary nodules, the largest located in the anterior segment of the right upper lobe measuring 1.2 cm (arrow).

prior to definitive exclusion of TB as it was our clinical judgement that metastatic disease was most likely and further delay would be detrimental to the patient's health. The differential diagnosis entering the operating room included locally advanced cervical cancer with lung metastasis, metastatic leiomyosarcoma, or leiomyosarcoma with concurrent pulmonary pathology.

Findings at the time of surgery: 12-week size uterus (729 g) with an expanded lower uterine segment, normal appearing tubes and ovaries, smooth peritoneum, and no gross adenopathy. At the time of the hysterectomy, a circumferential incision was made at the level of the



**Fig. 1.** CT abdomen and pelvis at the time of initial diagnosis. Well demarcated large enhancing endometrial mass with diffuse enlargement of the cervix (dashed outline) seen in coronal and sagittal planes.

dilated, attenuated uterine isthmus. The vaginal mass was delivered abdominally through the incision quite easily and the pedunculated nature of the vaginal mass was appreciated. Intraoperative pathology consult identified the mass as benign submucosal leiomyoma with degeneration and hemorrhagic necrosis. Following negative TB workup, a CT guided fine needle aspiration of the lung lesions was performed which revealed spindle cells with low grade cytologic features, low proliferative index, and positive staining for desmin. Staining was negative for pancytokeratin, S100, TTF-1 and CD34. Both uterine and lung specimens displayed morphologic and immunophenotypic impression suggestive of low-grade smooth muscle neoplasm, most consistent with benign metastasizing leiomyoma.

Following recovery, the patient was started on Megestrol therapy at a dose of 160 mg daily. The patient remains asymptomatic and has tolerated the medication with no adverse side effects. Three- and six-month follow-up have shown partial regression of several of the pulmonary nodules with no evidence of any new lesions.

### 3. Discussion

Much of the knowledge on benign metastasizing leiomyomas has been collected through case reports and case series. Typically, clinical detection occurs following one of two ways: 1) Incidental pulmonary nodules in an asymptomatic patient or 2) Predominant respiratory symptoms leading to detection of pulmonary nodules (Barnas et al., 2017; Miller et al., 2016; Fan et al., 2020). Very rarely are benign metastasizing leiomyomas diagnosed due to a workup for typical complications of leiomyoma such as vaginal bleeding or pelvic pressure (Jo and Baek, 2018; Ki et al., 2013). This may be due to the fact that most of the diagnoses of BML frequently occur years following a major gynecological surgical procedures such as hysterectomy or myomectomy (Barnas et al., 2017). No such pattern has been recognized following surgical history limited only to cesarean sections.

The pathogenesis of BML is undetermined. The prevailing hypothesis describes hematogenous or lymphatic spread of uterine tissue to distant sites, commonly following surgical manipulation of leiomyomas (Barnas et al., 2017; Awonuga et al., 2010). Ectopic tissue sharing characteristic features of uterine tissue, such as estrogen and progesterone receptor positivity and hormone responsive growth, support the hypothesis. Alternative theories include metaplastic transformation of coelomic tissue, independent non-uterine smooth muscle proliferation, and low-grade leiomyosarcoma (Awonuga et al., 2010).

Our patient's case is a very unusual presentation of rare variant of uterine leiomyomas. The patient's acute presentation of vaginal bleeding, abdominal pain, and necrosis was due to a prolapsed leiomyoma. Imaging studies were equivocal and unable to aid the diagnosis. Although the CT abdomen and pelvis identified an enlarged and distended uterus, due to extensive hemorrhagic necrosis, it was unable to distinguish tissue borders necessary to clearly identify the prolapse. In conjunction with extensive necrosis of the upper vagina/cervix, incidental pulmonary nodules, and high-risk factors, this clinical picture increased our suspicion of cervical cancer. Therefore, we proceeded to obtain confirmatory pathological diagnosis before initiating treatment for presumed metastatic cervical cancer. The final diagnosis of BML offers this patient a more favorable prognosis.

There are no established guidelines on the treatment of BML. Treatment options include TAH and BSO and/or surgical resection of large symptomatic lesions in the lung. Surgery is followed by close surveillance with or without adjuvant antiestrogen therapies such as gonadotropin-releasing hormone analogs, aromatase inhibitors, estrogen receptor modulators, or progesterone (Lewis et al., 2013). Surgical interventions alone without hormonal therapy have shown adequate stabilization likely by estrogen depletion and in some, even lead to regression of disease (Fan et al., 2020; Jo and Baek, 2018). However, there is also favorable evidence in the efficacy of antiestrogen therapy in treating BML. In premenopausal women who opted for surveillance

alone and were later found to have enlarging nodules on follow-up, the initiation of antiestrogen therapy demonstrated a halt in growth (Bakken et al., 2018). Another case reported a woman with stable disease on letrozole who was later found with enlarging nodules after stopping therapy (Fan et al., 2020). However, postmenopausal women appear less responsive to antiestrogen therapies at suppressing disease progression, representing the complexity in the pathogenesis of BML (Miller et al., 2016).

In conclusion, this case highlights important clinical considerations in the diagnosis and management of BML. The diverse and unique manifestations of leiomyomas reiterate the importance of including leiomyomas in the working differential diagnosis of cervical and vaginal masses.

### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

### Author Contributions

SGW reviewed literature and prepared the original draft. MG provided revisions. RSR prepared the manuscript. All authors read, revised, and approved the final manuscript.

### Disclosure

The authors have no conflict of interest to disclose.

### CRediT authorship contribution statement

**S.G. Whang:** Investigation, Writing – original draft, Writing – review & editing. **M. Gholson:** Writing – review & editing. **R.S. Rushing:** Writing – review & editing, Supervision.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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