Case Report

An Unusual Cause of Pulmonary Nodules in the Emergency Department

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We report a 51-year-old woman who presented to the emergency department with left-sided pleuritic chest pain 2 weeks after subtotal hysterectomy and bilateral salpingo-oophorectomy for a leiomyomatous uterus. Computed tomography scan of the chest revealed bilateral pulmonary nodules. Biopsy showed cytologically bland spindle cells without overt malignant features. Immunohistochemistry confirmed smooth muscle phenotype, in keeping with a clinicopathologic diagnosis of benign metastasizing leiomyoma (BML). BML does not frequently come to the attention of the emergency physician because it is rare and usually asymptomatic. When symptomatic, its clinical presentation depends on the site(s) of metastasis, number, and size of the smooth muscle tumors. Emergent presentations of BML are reviewed.

1. Introduction

Benign metastasizing leiomyoma (BML) is an entity in which benign-appearing uterine smooth muscle tumors are associated with similar-appearing tumors at distant sites [1]. The lung is the most common site of involvement and usually shows multiple, occasionally solitary, well-circumscribed nodules, ranging in diameter from a few millimeters to several centimeters [2]. The finding of multiple pulmonary nodules raises a broad differential diagnosis, including primary or secondary neoplasms, vasculitis, collagen vascular disease, and granulomatous diseases. BML does not frequently come to the attention of the emergency physician because it is rare and usually asymptomatic. However, BML may exhibit a range of clinical presentations, some emergent, depending on the site of involvement, number, and size of the smooth muscle tumors (leiomyomas). We report a patient with benign metastasizing leiomyoma who presented in the emergency department with pleuritic chest pain.

2. Case Report

A 51-year-old woman, gravida 2 para 2, presented to the emergency department with a 2-day history of left-sided pleuritic chest pain. Two weeks prior, she underwent subtotal hysterectomy and bilateral salpingo-oophorectomy for a leiomyomatous uterus which was approximately the size of a 12-week gravid uterus. Ten years prior, she underwent a hysteroscopic myomectomy for a submucous leiomyoma. Her medical history was further remarkable for endometriosis, primary biliary cirrhosis, chronic cholecystitis, hypertension, hypercholesterolemia, and transient ischemic attack. On physical examination in the emergency department, she was afebrile with a blood pressure of 150/87, heart rate 60/min, respiratory rate 18/min, and oxygen saturation 99% on room air. She had a BMI of 33, normal heart sounds, and clear chest on auscultation. ECG was normal. ABG showed pH 7.41 and pCO₂ 39 mmHg. She had a normal complete blood count, basic metabolic panel, and troponin. D-dimer was 1.2 μg/mL FEU (reference: less than 0.5 μg/mL FEU). Chest radiograph showed a 1.3 cm nodule in the left lower lobe (Figure 1) compared with a chest radiograph performed 4 years earlier which was clear. CT pulmonary angiogram (CTPA) showed bilateral, well-circumscribed, noncalcified, and noncavitated pulmonary nodules (Figures 2(a) and 2(b)) concerning for metastatic deposits. The nodules were not present on a chest CT performed 8 years earlier for the same indication. She was referred for thoracic surgery consultation.
BML may also be found concurrently at diagnosis of uterine leiomyomas in patients who present with leiomyoma symptoms (i.e., vaginal bleeding and abdominal or pelvic pain) [5] or in the perioperative period [6]. Uncommonly, BML involving the lung presents with a nonproductive cough or mild chest/back pain. Shortness of breath is also uncommon and tends to present late in patients when the number or size of the nodules begins to compromise lung function. Respiratory failure secondary to a large leiomyoma of the left lower lung that extended and obstructed the right mainstem bronchus has been reported [7]. Rarely, BML presents with hemoptysis [8], pneumothorax associated with lung cysts [5], hemothorax [9], or empyema [10]. Further, BML may have extrapulmonary manifestations including a systolic murmur by right ventricular metastasis [11]; abdominal pain by pelvic metastasis [12]; jaundice by metastasis to the pancreatic head [13]; arm and shoulder pain by metastatic compression of the infrachlavicular brachial plexus [14]; severe low back pain and saddle anesthesia by metastasis to the S2 vertebral body with expansion into the spinal canal [15]; and abducens and hypoglossal nerve palsy by metastasis to the posterior cranial fossa [15].

BML lung nodules typically do not calcify or enhance after intravenous contrast administration [5]. They may cavitate [16] and raise additional diagnostic considerations on imaging. Pathologic examination of a BML nodule is necessary to establish the diagnosis, because it allows confirmation of a smooth muscle phenotype by immunohistochemistry (SMA-positive tumor cells). In the clinical context of a concurrent or previously diagnosed uterine smooth muscle tumor(s), a presumptive diagnosis of BML may be rendered. In the absence of history or evidence of a uterine smooth muscle tumor(s), the presumptive diagnosis is multiple fibromiomyomatous hamartoma, which is histologically indistinguishable from BML. Definitive diagnosis requires molecular analysis of the uterine and pulmonary tumors [17], which is not performed in most cases.

The exact pathogenesis of BML is unknown. Three hypotheses have been proposed [17]: (1) BML represents proliferation of smooth muscle that is native to the lungs; (2) BML gains venous access from the trauma of myomectomy or hysterectomy; (3) BML represents a very low-grade leiomyosarcoma. The first two hypotheses are problematic because BML may involve extrapulmonary sites and may occur in the absence of uterine surgery, respectively. The third hypothesis is most widely accepted and likely reflects sampling error on grossing of the uterine smooth muscle tumor(s).

Investigation and management in the emergency department must be tailored to the particular BML presentation. As mentioned, BML involving the lung is usually asymptomatic. Its presentation as pleuritic chest pain is uncommon and invokes a broad differential diagnosis [18], the most critical of which include pneumothorax, myocardial infarction, and pulmonary embolus (PE) (Figure 4). In this case, the patient’s risk of PE was low/intermediate by Wells score [19]. Without evidence of PE on CTPA, her elevated D-dimer most likely reflects the normal process of recovery after hysterectomy. In current practice, a normal D-dimer (i.e., below a cut-off value of 500 μg/L) may allow the exclusion of PE. However,
alternative D-dimer cut-offs may exclude PE more reliably in clinical settings where D-dimer may be elevated for another reason(s), such as older patients [20, 21], postsurgery, and malignancy.

Suspected lung metastases of unknown primary should be referred for biopsy. There is no standardized management approach for lung involvement by BML. Because most lesions stay constant in size for a long time, a wait-and-see strategy consisting of periodic serial imaging is usually reasonable. This strategy also allows detection of lesions suspicious for lung adenocarcinoma, which may be present concurrently among the BML nodules [22] or develop in the course

**Figure 2**: CT pulmonary angiogram performed the same day as the chest radiograph. (a) Axial image (lung windows): left lower lobe soft tissue nodule corresponding to the abnormality on the CXR (arrow) demonstrates no internal calcification or cavitation. Six other similar-appearing nodules of varied sizes were scattered throughout the lungs. (b) Coronal MIP image (soft tissue windows): two well-circumscribed left lower lobe nodules (arrows).

**Figure 3**: (a) A well-circumscribed tumor with a pushing border to the lung parenchyma (green arrow) (H&E, 40x). Note entrapped bronchiolar epithelium encircled by collagen (red arrows). (b) Bland smooth muscle cells without cytological atypia (H&E, 100x). (c) Diffuse staining (brown) for SMA (12.5x). Note negative staining (white) of collagen and bronchiolar epithelium in the tumor. (d) Diffuse staining (brown) for desmin (12.5x). There was negative tumor cell staining for p16, p53, WT-1, CD10, CD31, HMB-45, CD117/c-kit, and ALK-1 (not shown).
Patient presents with pleuritic chest pain

**History and physical examination**

- Abnormal chest radiograph
- Abnormal ECG

**Persistent clinical suspicion of PE**

- No
- Yes

**Persistent clinical suspicion of pericarditis**

- No
- Yes

**Imaging (e.g., CT-PA)**

- Diffuse concave upward ST segments
- High sensitivity D-dimer
- Age < 50
- ≥500 ng/mL
- Age ≥ 50
- <(age × 10) ng/mL
- Yes
- No

**Drug-induced pleuritis**

- Infection (e.g., tuberculous or viral pleuritis)
- Connective tissue disease

**Baseline and serial troponin**

**Consider**

- PE
- MI
- Pericarditis
- MI
- PE
- PE

**Consider pneumonia, aspiration, hemorrhage, or pulmonary edema**

*Figure 4: Diagnostic algorithm for pleuritic chest pain (modified from Kass et al. [18] and Cuker [21]).*

**Abbreviations**

- ABG: Arterial blood gas
- ALK-1: Anaplastic lymphoma kinase-1
- Bcl-2: B-cell lymphoma-2
- BMI: Body mass index
- BML: Benign metastasizing leiomyoma
- CD: Cluster of differentiation
- CT: Computed tomography
- CTPA: Computed tomography pulmonary angiogram
- CXR: Chest X-ray
- ECG: Electrocardiogram
- FEU: Fibrinogen equivalent units
- H&E: Hematoxylin and eosin
- HMB-45: Human melanoma black-45
- MI: Myocardial infarction
- MIP: Maximum intensity projection
- NSAID: Nonsteroidal anti-inflammatory drug
- PA: Posterior-anterior
- PE: Pulmonary embolus
- SMA: Smooth muscle actin
- VATS: Video-assisted thoracoscopic surgery
- WT-1: Wilms tumor-1.

**Consent**

Written consent has been obtained from the patient and is available upon request.

**Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this paper.

**References**


