Benign Metastasizing Leiomyomas to the Lungs: An Institutional Case Series and a Review of the Recent Literature

Jordan Miller, DO, Melina Shoni, MD, Charles Siegert, MD, Abraham Lebenthal, MD, MHA, John Godleski, MD, and Ciaran McNamee, MD, MS

Division of Thoracic Surgery, and Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, and Division of Thoracic Surgery, West Roxbury Veterans Affairs Medical Center, West Roxbury, Massachusetts

Background. **Benign metastasizing leiomyomas (BMLs) represent the extrauterine spread of a benign uterine process. Pulmonary BMLs are the most common example of distant spread of uterine leiomyomas and are usually found incidentally in premenopausal women. The rarity of BMLs accounts for the limited literature that currently exists regarding their underlying pathophysiology, disease course, and management.**

Methods. **A retrospective analysis was performed of all BML cases diagnosed and managed at Brigham and Women's Hospital during a 22-year period. The demographic and clinical characteristics of these patients were compared with a PubMed-derived cohort of BML cases reported since 2006.**

Results. **Benign metastasizing leiomyoma tumors were identified in 10 Brigham and Women's Hospital patients, whereas 57 cases were reported in the literature. The average age at diagnosis was 54.1 and 46.7 years, respectively. Mean interval time from a pertinent gynecologic procedure to BML diagnosis was 23 years at Brigham and Women's Hospital. All patients demonstrated positivity for actin, desmin, and estrogen/progesterone receptors, confirming the diagnosis of uterine leiomyomas. Management primarily consisted of diagnostic resection with subsequent observation with or without hormonal suppression for residual pulmonary nodules. Progression of residual BMLs was noticed in 30% and 8.3% of Brigham and Women's Hospital and literature patients, respectively, when follow-up was reported. One patient in our series required further surgical management.**

Conclusions. **Benign metastasizing leiomyomas are a rare cause of pulmonary nodules. They likely represent a clonal spread of uterine leiomyomas to the lungs. Management includes pathologic diagnosis with long-term surveillance with or without hormonal manipulation.**

(Ann Thorac Surg 2015;■:■–■)

Uterine leiomyomas are the most common gynecologic tumors in women of reproductive age, affecting 20% to 30% of those older than 35 years [1]. They consist of uterine cells (40% with structural chromosomal abnormalities) with smooth muscle differentiation and spindlelike features [2]. They are considered of benign histopathology, exhibiting low mitotic activity, lack of anaplasia and necrosis, and limited vascularization [1]. Despite these benign features, leiomyomas rarely metastasize to extrauterine sites, predominantly to the lungs [3]. Other sites of less frequent metastasis include bone, spine, lymph nodes, retroperitoneum, and intravascular spread. Recently there has been a report of metastasis to the heart [4]. This clinical entity is recognized by the term benign metastasizing leiomyomas (BMLs). The majority of women diagnosed with BMLs are premenopausal (by 2009, there were only six reported cases of BMLs in postmenopausal women [5]). An antecedent history of uterine leiomyomas resected in the very distant past is encountered in most of the cases [3, 6, 7]. Benign metastasizing leiomyoma tumors are bilateral in 70% of cases, with a mean number of nodules of approximately 6 and a mean nodular size of 1.8 cm [8]. A diffuse miliary pattern has also been reported at the time of initial presentation [9]. Solitary BML tumors are reported in only 13% of cases. These tumors appear to retain the benign features of uterine leiomyomas. They demonstrate growth rates that are dependent on hormonal stimulation. This is supported by the BML size reduction that has been observed and reported in menopause, after termination of pregnancy, and in cases of surgical or chemical castration [3, 10, 11].

At the time of diagnosis, solitary pulmonary BMLs are treated for curative intent with surgical excision. Multiple pulmonary BMLs are diagnosed with surgical or radiographic biopsy, and as they are usually too numerous for surgical cure are thus followed with surveillance scans or hormonal manipulation [12]. Despite the high percentage of women with uterine leiomyomas, from the time Steiner first described BML until 2013, there were only 120 cases reported in the medical literature [13]. Currently, no guidelines exist for the optimal management and

Accepted for publication May 18, 2015.

Address correspondence to Dr McNamee, 75 Francis St, CA/359, Boston, MA 02115; e-mail: ciaran_mcnamee@dfci.harvard.edu.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2015.05.107

treatment of BMLs. To further describe the clinical aspects of BMLs and to develop treatment recommendations for this rare entity, we report our institutional experience in conjunction with a systematic review of the literature of all the recently published cases since 2006.

Material and Methods

An institutional review board–approved retrospective case series of all patients diagnosed with and managed for pulmonary BML tumors at Brigham and Women's Hospital since 1992 was performed. Eligible patients were identified using a pathology database, and data points were obtained from their longitudinal medical records. The cases were analyzed based on the patient's age at diagnosis and time from the pertinent gynecologic procedures. Radiographic as well as pathologic features of the tumors were also analyzed. The patients' treatment course was also evaluated with respect to follow-up and subsequent surgical and medical treatments.

A PubMed search was performed for the previous 8 years, using the terms pulmonary benign metastasizing leiomyoma to identify commonalities between our cases and those reported in the literature. Fifty-seven cases were identified. These cases were analyzed using the same criteria as the Brigham and Women's Hospital cohort. Literature cases before 2006 have been previously reported [14].

Results

At Brigham and Women's Hospital, we identified 10 patients with pulmonary BMLs; 5 of the patients have been previously reported by Nucci and colleagues [15] (Table 1). This single institutional case series along with a series from Germany are the largest in the current literature [16]. Our current series is the first to address long-term follow-up in patients with pulmonary BML. Eighty percent of patients had undergone gynecologic procedures for uterine leiomyomas. The mean age at diagnosis was 54.1 years. All of the patients with adequate pertinent records (50% of our series) were identified as postmenopausal, with a median age of 46 years. Two patients became aware of their uterine leiomyomas after the identification of pulmonary BML tumors. The gynecologic history of 2 patients was not available. The remaining 6 patients (60%) had a mean time to diagnosis from the index gynecologic procedure of 23 years, ranging from 16 to 36 years. The majority of patients were identified serendipitously with pulmonary BML tumors; only 30% of the patients presented with symptoms. At the time of diagnosis, preoperative radiographic imaging demonstrated a single pulmonary nodule in 3 patients (Fig 1). The remaining 7 patients had multiple pulmonary nodules (Fig 2). Bilateral nodules were found in 4 patients and unilateral nodules in 3 patients.

All lesions were identified by computed tomography of the thorax. In all cases a surgical procedure was performed with diagnostic intent, and 3 of the patients underwent surgery with curative intent. Nine patients underwent wedge resection (8 by video-assisted thoracoscopic surgery and 1 by mini-thoracotomy). One patient underwent a video-assisted thoracoscopic lobectomy owing to a centrally placed tumor. Pathologic examination in all cases demonstrated benign-appearing spindle cells lacking mitosis and necrosis. All cases were also positive for actin and desmin as well as estrogen and progesterone receptors. After surgical resection, 7 patients received no additional therapy with a median follow-up of 12 years. On radiographic surveillance, 6 of the patients had stable residual disease. One had an asymptomatic slight increase in the remaining pulmonary nodules, which did not warrant surgical excision. Further surgical treatment was not pursued in this patient because of a lack of symptoms. The 3 remaining patients underwent adjuvant hormonal suppression, with a median follow-up of 8.3 years. Two of these patients demonstrated an asymptomatic minimal increase in their pulmonary nodules. One patient required subsequent ipsilateral wedge resection of an enlarging central BML nodule to prevent hilar compression.

Fifty-seven case reports were identified in the medical literature since 2006 with nodule location identifiable in only 50 patients. The mean age at diagnosis was 46.7 years. Multiple pulmonary nodules were identified in 45 patients, of whom 42 patients had bilateral disease, 1 consisting of a diffuse miliary pattern. There were only 5 patients with solitary BML nodules. Pleural involvement was unusual as effusions were reported in only 2 patients. All invasive procedures that were reported were executed with diagnostic intent. Computed tomography–guided biopsy was performed in 6 patients, of which 2 were not diagnostic. A wedge resection was performed in 38 patients, a lobectomy in 4 patients, and a pleural biopsy in 1 patient. Surgery for curative intent was performed in only 11 patients. After pathologic diagnosis of pulmonary BML, 19 patients underwent hormonal therapy. Of these 19 patients, 17 cases reported follow-up. Only 4 demonstrated disease regression, stability was achieved in 11 patients, and disease progression occurred in 2 patients.

Overall, follow-up was reported in 35 of the 57 cases. Stable disease occurred in 28 patients, with disease progression in 3 and disease regression in 4 patients. All patients who demonstrated disease regression underwent adjuvant hormonal therapy. Of the patients in whom follow-up was reported, a follow-up period of 2 years or greater was reported in only 18 patients. The majority of these patients had stable disease; 72.2% (13 of 18) of the patients with long-term follow-up of 2 years or greater showed stable disease. Patients with disease progression required surgery; 16.6% (3 of 18) of patients had disease progression in the long term. Disease progression manifested at a mean of 11.6 years in these patients. Progression manifested as hemoptysis and compressive symptoms secondary to cyst formation. Disease regression occurred in 5.5% (1 of 18) of patients, and follow-up imaging was not reported in 1 patient.

Comment

Pulmonary BMLs are unusual in that they represent a metastatic or cellular embolization process from a benign