

## Benign Metastasizing Leiomyomas of the Lungs: A Case Report

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### Abstract

**Background:** Benign metastasizing leiomyoma (BML) is a very rare condition, which is paradoxically called benign metastases and occurs among patients with previous history of leiomyomas.

**Case presentation:** We report a case of a 46-year-old woman diagnosed with benign metastasizing leiomyomas of the lungs, 16 years after uterine leiomyoma removal. The patient presented with the exertion dyspnea and dry cough lasting for several weeks. CT scan was indicative of metastatic lesions in the lung and no pathological findings within the lesser pelvis and abdominal cavity.

The patient underwent right video thoracoscopy followed by thoracotomy with wedge and marginal resections of the right lung tissue containing tumors. The histopathological diagnosis was: benign metastasizing leiomyomas.

The patient received a single dose of Triptorelinum (Diphereline SR 3.75)-GnRH analog.

Control CT performed 4, 12, 36 months later showed stabilization. The patient has been symptom-free for 5 years.

1. BML is very rare disease-no more than 100 cases have been described. Our treatment methods include: surgical resection, hormonal manipulation and observation.
2. An individual treatment strategy or observation should be consider for each patient with BML

**Keywords:** Benign metastasizing leiomyoma; BML; Leyomyoma

**Abbreviations:** BML: Benign Metastasizing Leiomyoma; CT: Computed Tomography; GnRH: Gonadotropin-Releasing Hormone; HPF: High-Power Field; Ki-67: Monoclonal Antibody; ER: Estrogen Receptor; PR: Progesterone Receptor; FSH: Follicular Stimulating Hormone; NLV: Normal Limit Values; LHRH: Luteinizing Hormone Releasing Hormone; TTF-1: Thyroid-Specific Transcription Factor-1.

### Background

The term “metastasizing fibroleiomyoma” was first used by Steiner in 1939. The author employed this term to describe well delineated, uni- or, more frequently, multifocal nodules consisting of proliferating smooth muscle cells, located in the lungs of female patients, who had undergone hysterectomy due to uterine leiomyomas [1]. BML occur extremely rarely. No more than 100 cases have been described in literature [2,3]. Currently, the term “benign metastasizing leiomyoma” indicates leiomyomas, which are paradoxically called benign metastases and occur among patients with previous history of leiomyomas. We report a case of 46-year-old patient diagnosed with benign metastasizing leiomyomas of the lungs, 16 years after uterine leiomyoma removal.

### Case Presentation

The 46-year-old patient (gravid 3, para 3) presented with the exertion dyspnea and dry cough lasting for several weeks. She had undergone a uterine subserosal leiomyoma removal (enucleation) 16 years earlier. That tumor had measured 9 cm in diameter. Microscopic examination showed a cellular leiomyoma with the mitotic index of 3/10 HPF, proliferative index-Ki-67 ca. 1%, ER +, PR +++. During the following 13 years, the patient received oral contraceptives (0.250 mg Norgestimatum + 0,035 mg Ethinyloestradiolum-Cilest Jansen-Cilag International NV). The patient discontinued contraceptive agents 3 years before admission to the hospital and has not been menstruating ever since.

Computed Tomography imaging revealed homogenous, hyperdense, round, well-delineated lesions of 5-20 mm in diameter, distributed in the middle lobe of the right lung, on the border of 5<sup>th</sup> and 7<sup>th</sup> segment. A dominant lesion was present with mediastinal pleura. It measured 40 x 26mm, was continuous and presented with mixed density of 9-80 HU. There was an enhancement in the solid part of the lesion following the IV contrast agent administration. Pleural laminae were segmentally thickened, at the locations of the subpleural metastatic changes, mostly in the peripheral paravertebral regions of the lungs. Mediastinal lymph nodes were not enlarged. Tracheal and bronchial lumina, pleural cavities and organs of mediastinum were unremarkable. Computed Tomography Imaging was indicative of metastatic lesions.

Gynecologic examination did not reveal any abnormalities. The transvaginal ultrasound examination revealed: the uterine corpus was of variable echogenicity and measured: 45 × 40 × 41 mm. The uterine cavity was empty. The endometrium was linear and thin (2 mm). Both ovaries were not palpable; they were both normal. CT scan showed no pathological findings within the lesser pelvis and abdominal cavity. Hormonal tests indicated that the patient was in the postmenopausal period:

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Estradiol: 14.6 pg/ml, for postmenopausal women NLV: <54.7

Progesterone: 0.159 ng/mL, NLV: <0.8

FSH 64.81 mIU/mL, NLV: 25.8-134.8

The patient underwent right video thoracoscopy followed by thoracotomy with wedge and marginal resections of the right lung tissue containing tumors. The histopathological diagnosis was: benign metastasizing leiomyomas containing entrapped structures of the bronchial epithelium (Figure 1). The leiomyoma showed strong expression of estrogen (Figure 2) and progesterone receptors, present in 100% of cells. The Ki-67 proliferation index was below 1%. The entrapped epithelial structures were positive for TTF-1, a marker of bronchial epithelium (Figure 3).

Due to the significant obesity of the patient and high probability of the peripheral conversion to estrone, the patient received a single dose of Triptorelinum (Diphereline SR 3.75)-GnRH analog (Figure 4).

Control CT performed 4, 6, 12, 36 months later showed stabilization in numerous and size of other changes. Patient with no complaints has been under follow-up for 5 years (Figure 5).



Figure 3: Metastasizing leiomyoma TTF 140x. TTF1 expression in the bronchioli. Epithelium, and negativity of the surrounding smooth muscle cells.

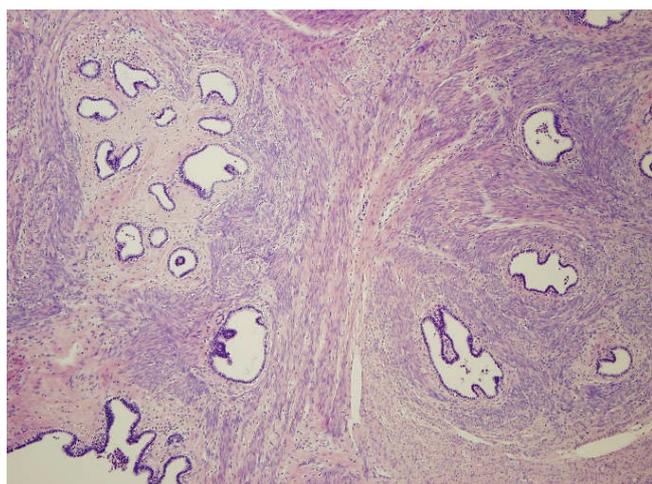


Figure 1: BML of the lungs-smooth muscle cells surrounding bronchiole (40x).

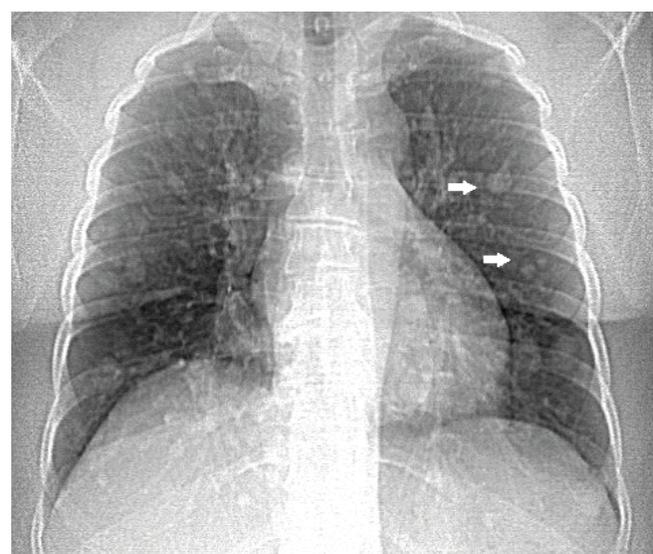


Figure 4: Multiple round nodular opacities in chest roentgenogram. Biopsy disclosed BML.

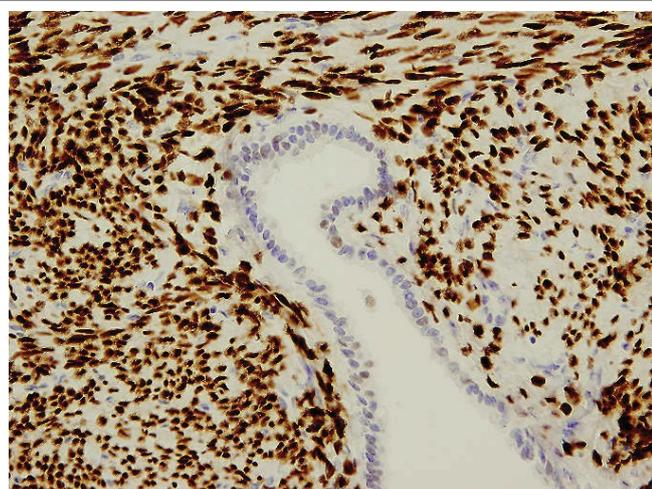


Figure 2: Metastasizing leiomyoma (ER 200x). Strong ER expression in the smooth muscle cells and negativity of the bronchioli.

## Discussion

BML is most frequently diagnosed in women aged 30-74 years [2,4]. There are only 3 cases described concerning patients older than 70 yrs. The majority of women with BML report a hysterectomy in the past. The surgery had been performed due to leiomyomas, on average ca. 10 years earlier (1-20 years) [2,5,6]. However, the changes in lungs may also occur before hysterectomy [7]. BML is most frequently diagnosed by accident, during radiologic imaging performed due to other indications. The disease is characterized by a mild course. Cough, dyspnea and chest pain are rarely present. However, there has been a report of this disease associated with poor prognosis [2]. The average size of the tumors in lungs ranges 0.5-10 cm. Most frequently, in 70% of the patients the lesions in the lungs occur bilaterally and multiple unilateral lesions are seen in 17% of cases. Solitary changes have been described in few cases only [8].

On imaging, these tumors do not appear calcified and show no

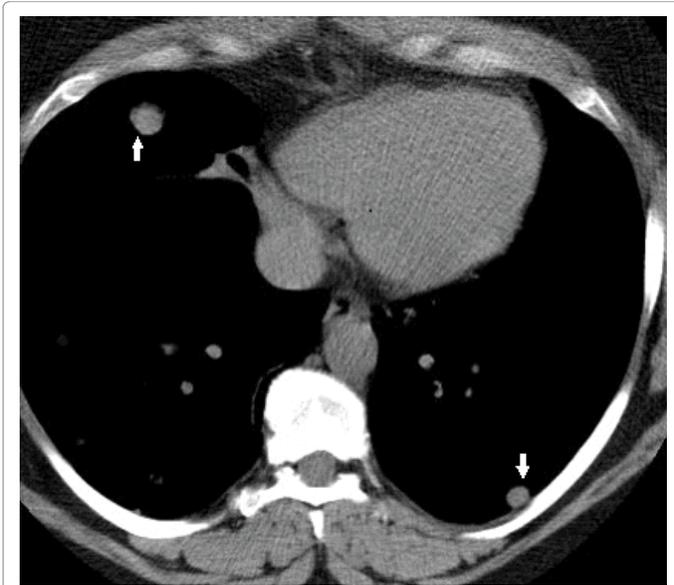


Figure 5: Multiple pulmonary nodules in CT (arrows). Biopsy disclosed BML.

contrast enhancement. Mediastinal or hilar lymphadenopathy, as well as pleural effusions, are rarely found [7,9]. The coexistence of pericardial effusion was described in one case report [7].

Even though the metastasizing leiomyomas are most commonly diagnosed in the lungs, they can also occur in the lymph nodes, peritoneal cavity, mediastinum, omentum, right atrium, right ventricle, muscular tissue, bones, spine and extraperitoneally [6,9-13].

There is also a case report on the benign leiomyomas metastasizing to the lungs, which coexisted with disseminated peritoneal leiomyomatosis [7].

The microscopic appearance of the BML is benign. They are composed of densely concentrated smooth muscle cells without encapsulation. Cell nuclei are quite homogenous in size and volume. Mitotic figures are rare. Necrosis is not observed; inflammation is minimal and is seen only sporadically. The tumors sometimes are paucicellular and collagenized [7].

Immunohistochemically, there is a strong reaction for desmin and muscle-specific actin, as well as a weak reaction for vimentin. Estrogen and progesterone receptors are also detected in the pulmonary lesions, but sometimes their expression is not so strong as in the antecedent uterine leiomyoma [7,11]. Therefore, some pathologists suggest that the pulmonary leiomyomas are rather metaplastic, not metastatic [11,14]. The hypotheses explaining histogenesis and metaplastic mechanisms are subject of discussion and controversy. In the past, they were described as multiple fibroleiomyomatous hamartomas, assuming they developed de novo in the lungs [6,7,13]. Currently, the majority of authors regard them as hematogenous metastases originating from benign leiomyomas with likely increased mitotic activity [7,9]. According to some, primary uterine tumors in these cases should be classified as low-grade leiomyosarcoma, due to their ability to metastasize. On the other hand, their benign microscopic appearance and clinical course contradicts such hypothesis [7,15]. It has also been suggested that smooth muscle proliferation occurring in various organs might result from the improper hormonal status [13]. BML should not be mistaken for lymphangioleiomyomatosis which is a disease caused by proliferation of smooth muscle cells in the lymphatic vessels

of the lungs and lymph nodes. Among young patients, spontaneous pneumothorax, progressive dyspnea and pleural effusion may occur. The characteristic microscopic features are: hyperinflation and thin-walled cystic spaces [7].

The fact of their shrinkage, postmenopausal or following contraceptive therapy withdrawal, stands as the clinical proof of hormonal dependency of BML [2]. Since BML is extraordinarily rarely diagnosed, there is no standard treatment established for this disease. In the cases described in the literature the following options were applied: LHRH-agonists, anti-estrogens, aromatase inhibitors, progesterone, oophorectomy, hysterectomy, lung tumor removal or solely patient observation [16-18]. The appropriate treatment should be introduced following precise histopathologic diagnosis and determination of the hormonal status of the patient.

If women in the postmenopausal period show no clinical symptoms, they may be followed-up since these tumors might undergo spontaneous regression or stabilization during this period. Younger patients, before the menopause, undergo surgical or hormonal treatment. There is one report in the literature about malignant transformation from BML [15].

## Conclusions

1. BML is very rare disease-no more than 100 cases have been described. Our treatment methods include: surgical resection, hormonal manipulation and observation.
2. An individual treatment strategy or observation should be considered for each patient with BML depending on the size and location of the tumor and the hormone receptors status.

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