

# Pulmonary benign leiomyomas mimicking malignant pulmonary metastases: case report and literature review

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## ABSTRACT

**Background and aim:** Pulmonary leiomyomatosis (PBML) is the most common type of metastasizing leiomyomas. It is routinely found by a chest X-ray in women with a medical record of myomectomy related to uterine leiomyoma. These findings in young women are frequently misinterpreted as metastasized lung cancer due to the similarity of radiological findings. This article aims to describe a clinical case, define the diagnostic value of radiological imaging findings and to differentiate the distant leiomyoma metastases from malignant ones.

**Material and methods:** We present a new case of PBML post hysterectomy mimicking malignant pulmonary metastases. Additionally, a literature review was conducted for case reports and previous literature reviews describing PBML, its etiology, pathogenesis, and diagnostic features. Medline (PubMed), ScienceDirect, Hindawi, EPOSTM databases were used.

**Results:** PBML nodules pose a diagnostic ambiguity by mimicking malignant pulmonary metastases especially on routine chest X-rays and CT scans. Our presented case is similar to previously reported cases, and MRI played a crucial role in the differential diagnosis. In 10 of 13 investigated cases, nodules were multiple and bilateral, oval in shape and well-circumscribed. The average age of patients described in the reviewed case reports was 47,2 years. 77 % of them have had a history of leiomyoma and hysterectomy or myomectomy.

**Conclusion:** Although PBML is a rare condition it should be considered for patients with a history of leiomyoma or hysterectomy or myomectomy due to leiomyomatosis. It is essential seeing as these findings are often misdiagnosed as malignancy because of ambiguous radiological findings, such as bilateral and multifocal well-circumscribed rounded lesions that vary in size. MRI is a suitable tool for evaluating these nodules and ADC value can be useful to differentiate benign nodules from malignant metastasis.

**Keywords:** pulmonary leiomyomatosis, benign metastasizing leiomyoma, computed tomography.

## INTRODUCTION

Benign metastasizing leiomyoma (BML) is a rare condition that may affect females in all age groups and is frequent in those with a medical history of uterine leiomyoma and myomectomy or rarely without this procedure [1]. However, BML mostly occurs in women during their late reproductive years [2]. The BML generally metastasizes to lungs, although it can be associated with metastases in the abdominal or paraaortic lymph nodes, liver, heart, breasts, muscular tissue or even the central nervous system. Consequently, the diagnosis of pulmonary benign metastasizing leiomyoma (PBML) is complicated. It can be misdiagnosed as bronchitis, pneumonia, pulmonary tuberculosis or metastasizing lung cancer because of non-specific clinical symptoms such as chest pain, cough or shortness of

breath, although usually, BML is asymptomatic. Frequently the diagnosis is based on imaging findings which are even more deceptive [3, 4]. Most cases of PBML may be discovered incidentally by chest X-ray or CT scans during routine examinations and may resemble malignant pulmonary metastases.

## AIM

This article aims to describe a clinical case, define the diagnostic value of radiological imaging findings and to differentiate the distant leiomyoma metastases from malignant ones.

## CASE REPORT MATERIAL

We present a clinical case of a 50-year-old woman with multiple pulmonary nodules after hysterectomy due to uterine leiomyomatosis and

selective literature review for case reports and literature reviews describing the pulmonary leiomyomatosis, its etiology, pathogenesis and diagnostic features published in the last five years. Medline (PubMed), ScienceDirect, Hindawi, EPOSTM databases were used to search for publications.

A 50-year-old woman was referred to a pulmonologist for consultation at the Hospital of LUHS (Lithuanian University of Health Sciences) Kaunas Clinics after multiple lung nodules varying in size were observed on a routine chest X-ray. Nodules were differentiated between granuloma and metastatic malignancy (Figure 1). The patient denied any symptoms and laboratory results were normal. According to medical history, seven years ago the patient had undergone a hysterectomy due to uterine leiomyomatosis. Lung CT (using Toshiba Aquilion One multislice CT equipment with and without contrast agent) was performed because of the suspected malignancy. CT showed multiple nodules varying in size, with attenuation values changing from 59HU to 100 HU after the injection of contrast agent (Figure 2). The following week a bronchoscopy and transbronchial biopsy were performed, but according to the pathological report, no malignant changes were observed.

A lung MRI was performed to analyze the enhancement, contrast agent wash-out significance and apparent diffusion coefficient (ADC) value of nodules, and exclude any malignant processes. MRI was performed using 1T Siemens Mag-

netom Aera in T1\_VIBE, T2\_HASTE, TIRM, DW sequences in the axial and coronal plane. MRI showed well defined, heterogeneous nodules with solid and cystic parts, and higher signal intensities (SI) in T2\_HASTE and TIRM sequences. (Figure 3)

In the post-processing stage, SI in diffusion-weighted images was evaluated using different b values of 50,400 and 800, after this ADC was calculated to estimate restriction in nodules (Figure 4)

In precontrast T1\_VIBE nodules were isointense, in CE T1\_VIBE sequence after 5 min. of contrast agent injection SI was 40-77 and after 15 min it was approximately- 56 and wash-out was not significant (Figure 5 ) Because CE T1\_VIBE delayed scans wash-out was not significant it did not allow to exclude malignant pulmonary metastases, but ADC was high, and features of restriction in nodules indicated benign nodules. The multidisciplinary team decided to perform a typical lung resection of one nodule from the right lower lobe for histological verification. Pathology identified a smooth muscle tumor. Immunohistochemical staining showed smooth-muscle desmin and actin, but was negative for CD117. Estrogen and progesterone receptors were strongly positive. These findings suggested pulmonary leiomyomatosis.

The patient was started on tamoxifen, an aromatase inhibitor, and GnRH analog. Further follow up was suggested using CT/MRI.

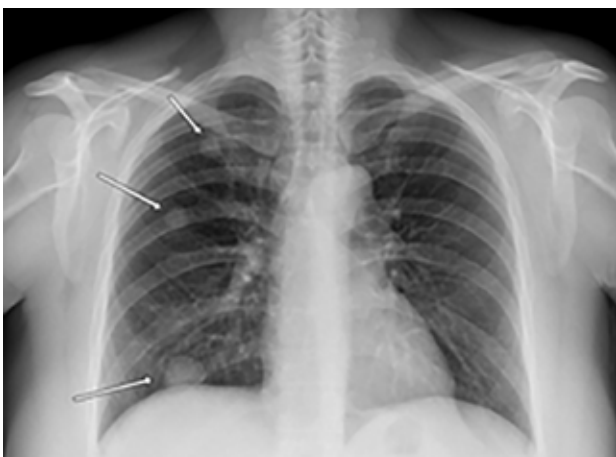


Figure 1. LUHS Radiology clinic archive  
A, B Plain films of 50-year-old women demonstrate 1,0 - 3,5 cm well-defined oval nodules in the right lung upper and lower lobes (white arrows).



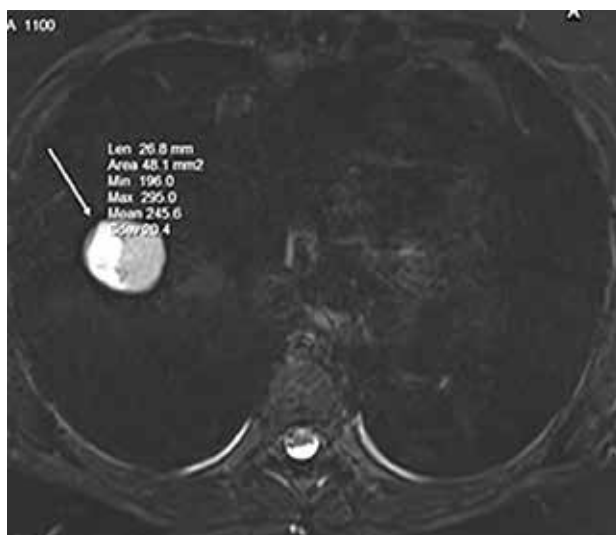
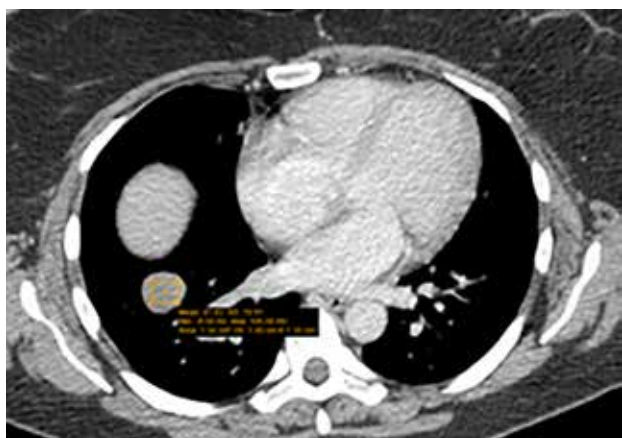
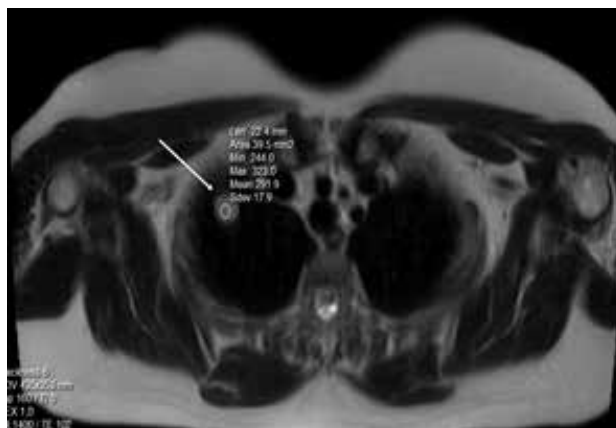
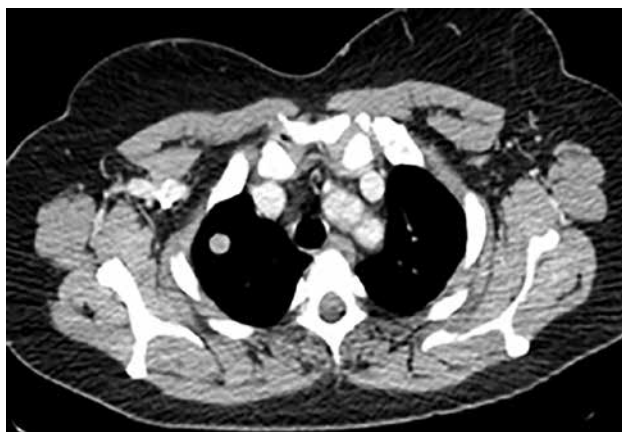


Figure 2. LUHS Radiology clinic archive CT scans of the same 50-year old female with a history of uterine myomectomy. (A, B) native and C after i/v contrast agent administration. Scans demonstrate multiple well defined pulmonary nodules in variable size 2-32 mm in the right lung field, i/v contrast-enhanced from 59 HU in the native scan (C) to 100 HU in CE scan (B).

Figure 3. LUHS Radiology clinic archive MRI scans of the same patient: A, B T2\_HASTE axial images- white arrows show SI in the solid part of nodule – 373; C- TIRM axial slice – arrow show cystic part of nodule, SI -245.

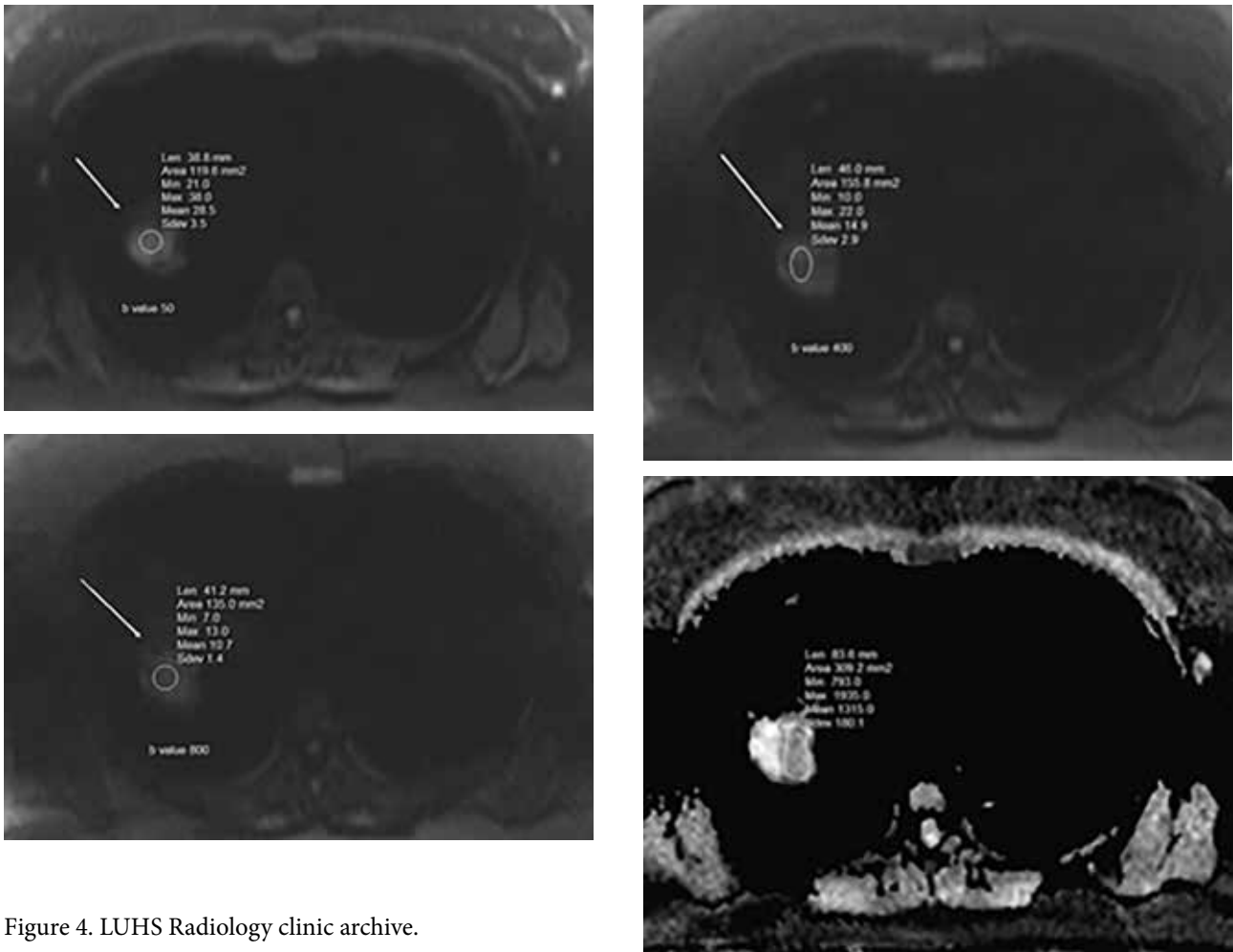


Figure 4. LUHS Radiology clinic archive.

A, B and C demonstrate the patient's MRI scans of DW sequences with different b values they show no restriction in nodule and D - ADC map with ADC value of solid part of nodule calculated  $1,3 \times 10^{-3}$ .

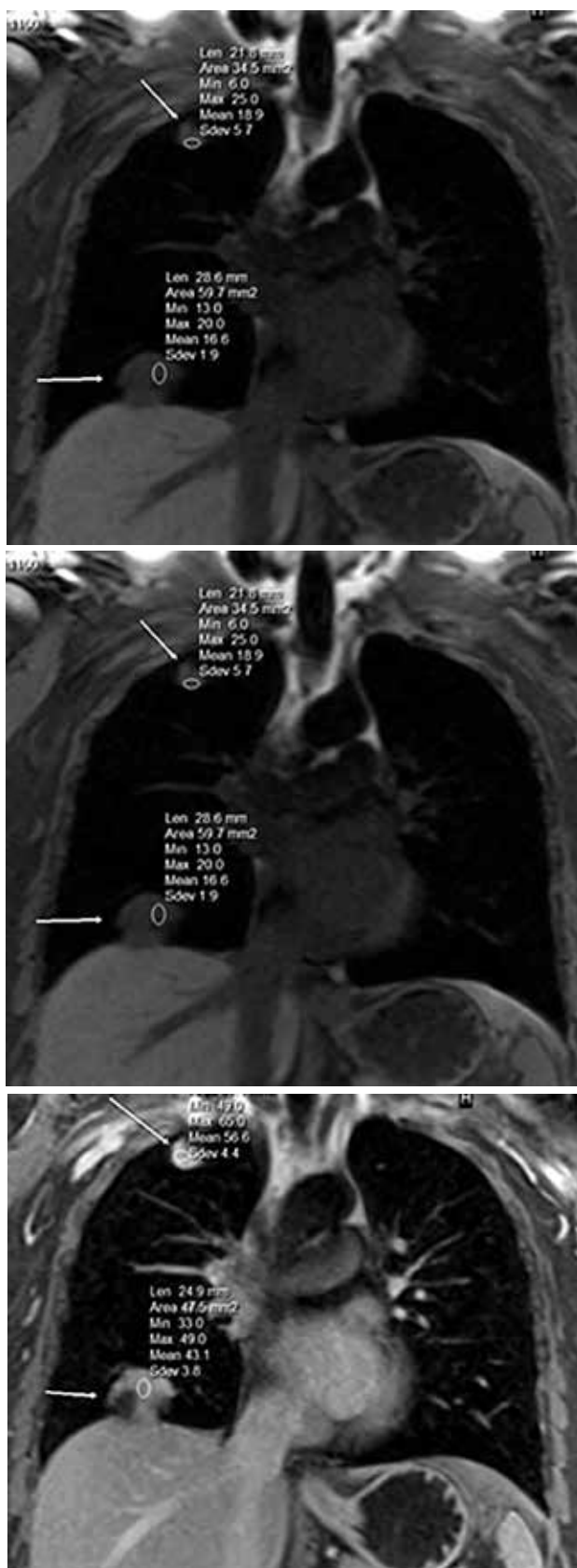


Figure 5. LUHS Radiology clinic view archive  
 A- Fat suppressed T1\_VIBE coronal image before contrast injection: white arrows show nodules with measured SI- 19- 25, B- after 5 min of contrast enhancement (CE) SI was 77 and C after 15 min SI – 56. Heterogeneous nodules with solid and cystic parts.

## DISCUSSION

The mechanism of the leiomyomas dissemination is under consideration. It is believed that the smooth muscle cells spread to distant sites after uterine extension into pelvic venous channels. However, in some cases, the uterine leiomyoma is diagnosed after metastases [4,5]. For the most part, patients diagnosed with PBML are in their fifties. The average age of a patient from analyzed case reports was 47,2 years.

The majority of the PBML patients are asymptomatic, although an investigation of 13 case reports showed that 8 of them complained of pulmonary symptoms, such as shortness of breath, cough or chest pain.

The diagnosis of PBML is usually based on findings of multiple nodules in the lungs (rarely a single node) on routine radiological examination such as chest X-ray and CT scan. These nodules can be discovered before hysterectomy or even three months – 20 years afterward. In a report of 13 analyzed case reports of PBML, this interval ranged from 1 month to 20 years with a mean of 9.3 years. 3 out of 13 patients had no history of hysterectomy or myomectomy. Most importantly, PBML nodules pose diagnostic ambiguity mimicking malignant pulmonary metastases especially on routine X-ray (Figure 1) [4].

Both CT and MRI imaging may be useful in finding pulmonary nodules in the setting of PBML (Figure 2; Figure 3). The nodules are usually 0,2 – 8 cm but can vary in size from a few millimeters to several centimeters, and the distribution of these nodules is random. It is worth mentioning that nodules can regress in size during pregnancy or after menopause [6]. The radiologic appearance is well-circumscribed round lesions; the majority of them are bilateral which can be misinterpreted incorrectly as malignant pulmonary metastases. Usually, the nodules have a homogenous appearance on a CT scan. Typically these nodules are non-calcified and do not enhance using i/v contrast agent [1]. In 10 out of 13 investigated cases, the nodules were multiple and bilateral. One of these cases was multiple and unilateral. The other two were solitary in one lung. All of the nodules in X-ray and CT scans were without calcifications and were described as round or oval and well-circumscribed.

In patients with a history of hysterectomy or myomectomy due to leiomyoma, even the ambiguous radiological findings should strongly suggest PBML.

In the setting of inconclusive imaging findings, an imaging-guided biopsy can help to confirm the diagnosis [4]. Pathologically PBML nodules consist of benign smooth cells similar to uterine leiomyoma. Usually, estrogen and progesterone receptors are positive. Pathologists investigated nodules from all 13 cases. Microscopic examinations revealed a proliferation of the differentiated spindle cells without nuclear atypia, anaplasia, necrosis, and neovascularization. The mitotic index was low. Inflammation was not observed. Estrogen and progesterone receptors from all samples were positive. All of these criteria can help to show the benign process and origin from the uterus and can be useful in differentiation from malignant processes.

Our presented case is similar to previously reported cases. Most of the PBML cases were related to previous myomectomy or hysterectomy (77 %). Indeed, a previous diagnosis of uterine leiomyoma may help to point the diagnosis.

The method of choice for the differentiation and diagnosis of these nodules remains a chest CT scan. However, taking into account the fact that this disease affects young women in their reproductive years, the onset of a new era in lung MRI and sensitivity of proton sequences for nodules provides with the opportunity to use MRI as an alternative imaging method.

Macroscopically all of the nodules were ovoid-shape and well-circumscribed. Because of that, differentiation with malignant pulmonary metastases was necessary. Diagnoses were confirmed by histological examination. Pulmonary leiomyomas are slow growing nodules. Their histological pattern is identical to the tissue of uterine leiomyoma. During microscopic examination spindle cells appear proliferated, benign, well-differentiated with a moderate degree of vascularization, insignificant nuclear atypia, mitotic activity, anaplasia, necrosis, vascular invasion. Because the progression of this disease is closely related to sex hormone levels, it is important to find positive estrogen and progesterone receptors during an immunological examination of nodules tissue. It reveals the uterine origin [3].

Actin, desmin, vimentin are immunohistochemical markers that confirm mesenchymal derivation with smooth muscle differentiation of these tumors [7].

One of the analyzed cases was misdiagnosed as pulmonary tuberculosis because of no history of smoking, no family history of cancer and tuberculoma resembling radiological findings. Accordingly, careful collection of patient history is the primary method to suspect the right diagnosis and avoid unnecessary antibiotics.

Differential diagnosis is complicated because other types of spindle cell neoplasm such as malignant melanoma, sarcoma, nerve sheath tumor should be excluded. Immunostains to demonstrate smooth muscle is helpful [2].

Additionally, entrapped alveolar or bronchiolar epithelium can be found in the metastatic foci which can sometimes complicate diagnosis for pathologists. Cavitation and miliary pattern have been reported as well [8, 9].

Furthermore, positive estrogen and progesterone receptors aid in understanding other essential aspects of patient medical history. The doctor should pay attention and consider PBML diagnosis if a patient is in the premenopausal age group, obese or uses estrogens [10].

Although PBML is hormone-sensitive and has a good prognosis is uncommon for this disease to be related to serious complications, such as cor pulmonale, respiratory failure, or even fatal outcomes [7]. The progression of PBML differs and appears to rely on the status of estrogen in the patient. The course of the disease is slow, and patient mortality is not related to the disease in postmenopausal women, while the progress in premenopausal women may lead to death [4].

## CONCLUSION

Although PBML is a rare condition, it should be considered for the patients with a history of leiomyoma or hysterectomy or myomectomy due to leiomyomatosis. It is essential seeing as these findings are often misdiagnosed as malignancy because of ambiguous radiological findings, such as bilateral and multifocal well-circumscribed rounded lesions that vary in size. MRI is a suitable tool for evaluating these nodules and ADC value can be useful to differentiate benign nodules from malignant metastasis.

**REFERENCES**

1. Barnaś E, Książek M, Raś R, Skręt A, Skręt-Magierło J, Dmoch-Gajzlerska E. Benign metastasizing leiomyoma: A review of current literature in respect to the time and type of previous gynecological surgery. *PLoS One*. 2017;12(4):e0175875.
2. Taftaf R, Starnes S, Wang J, et al. Benign metastasizing leiomyoma: a rare type of lung metastases-two case reports and review of the literature. *Case Rep Oncol Med*. 2014;2014:842801.
3. Chen S, Liu RM, Li T. Pulmonary benign metastasizing leiomyoma: a case report and literature review. *J Thorac Dis*. 2014;6(6):E92-8.
4. Teixeira BC, Mahfouz K, Escuissato DL, Costa AF, Noronha Ld. Solitary benign metastasizing leiomyoma: imaging features and pathological findings. *J Bras Pneumol*. 2014;40(2):193-5.
5. Aka N, Iscan R, Köse G, Kaban I. Benign Pulmonary Metastasizing Leiomyoma of the Uterus. *J Clin Diagn Res*. 2016;10(9):QD01-QD03.
6. Latif MF, Sirelkhatim MS, Osman B and Azam F. Benign Pulmonary Metastasizing Leiomyoma of Uterus Presenting as Malignancy of Unknown Origin, A Diagnostic Dilemma. *Austin J Med Oncol*. 2015; 2(2): 1019.
7. Ki EY, Hwang SJ, Lee KH, Park JS, Hur SY. Benign metastasizing leiomyoma of the lung. *World J Surg Oncol*. 2013;11:279. Published 2013 Oct 17. doi:10.1186/1477-7819-11-279
8. Rajesh S, Adam M. Benign metastasizing leiomyoma: "A sheep in wolf's clothing". *Community Oncol* 2013;10:122-5
9. Sousa IR, Campos P, Tavora I. Imaging features of pulmonary leiomyomatosis. *European Congress of Radiology 2013*. <https://doi.org/10.1594/ecr2013/c-1455>.
10. Wiencek-Weiss AJ, Bruliński K. Benign metastasizing leiomyomas in the lungs: a case study. *Kardiochir Torakochirurgia Pol*. 2016;13(1):61-3.