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ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Dr. Iva Brčić finished medical studies at the Medical University of Graz and received her MD degree in 2003. She received her doctoral degree in 2006 at the same institution. In 2007, she enrolled in the pathology residency program at the University Hospital Center Zagreb. In 2012, she passed her board exam and, until 2015, worked as a staff pathologist at the University Hospital Center Zagreb. From 2015, she is working as the University Assistant at the Medical University of Graz. At the end of 2017, she joined the bone and soft tissue team and spent 4-mo observership at the University of Miami, FL, USA. Her ongoing research interests include bone and soft tissue neoplasms.

AIMS AND SCOPE

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The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for *WJCC* as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Electronic Editor: Ji-Hong Liu, Production Department Director: Xiang Li, Editorial Office Director: Jin-Lai Wang.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Semimonthly

EDITORS-IN-CHIEF

Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

July 26, 2020

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INSTRUCTIONS TO AUTHORS

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PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Pulmonary benign metastasizing leiomyoma: A case report and review of the literature

Hai-Yun Dai, Shu-Liang Guo, Jian Shen, Li Yang

ORCID number: Hai-Yun Dai 0000-0001-5416-2185; Shu-Liang Guo 0000-0003-1453-1585; Jian Shen 0000-0002-6143-3964; Li Yang 0000-0001-7412-9841.

Author contributions: Dai HY searched and screened the literature and contributed to drafting of the manuscript; Shen J helped to search the literature; Guo SL modified the manuscript; Yang L was responsible for revision of the manuscript and for contributing important intellectual content; all authors issued final approval for the version to be submitted.

Supported by the Chongqing Science and Technology Committee, No. cstc2019jscx-msxmX0184.

Informed consent statement: Informed written consent was obtained from the patient.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an

Hai-Yun Dai, Shu-Liang Guo, Li Yang, Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400010, China

Jian Shen, Department of Cardiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400010, China

Corresponding author: Li Yang, MD, Associate Chief Physician, Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Chongqing Medical University, No. 1, Youyi Road, Yuan Jiagang, Yuzhong District, Chongqing 400010, China. yangli_018@sina.com

Abstract

BACKGROUND

Pulmonary benign metastatic leiomyoma (PBML), which is very rare, is a type of benign metastatic leiomyoma (BML). Here, we report a case of PBML, finally diagnosed through multidisciplinary team (MDT) discussions, and provide a literature review of the disease.

CASE SUMMARY

A 55-year old asymptomatic woman was found to have bilateral multiple lung nodules on a chest high-resolution computed tomography (HRCT) scan. Her medical history included total hysterectomy for uterine leiomyoma. The patient was diagnosed with PBML, on the basis of her clinical history, imaging manifestations, and computed tomography (CT)-guided percutaneous lung puncture biopsy, *via* MDT discussions. As the patient was asymptomatic, she received long-term monitoring without treatment. A follow-up of chest HRCT after 6 mo showed that the PBML lung nodules were stable and there was no progression.

CONCLUSION

For patients with a medical history of hysterectomy and uterine leiomyoma with lung nodules on chest CT, PBML should be considered during diagnosis based on the clinical history, imaging manifestations, CT-guided percutaneous lung puncture biopsy, and MDT discussions.

Key words: Pulmonary benign metastatic leiomyoma; Multidisciplinary team; Computed tomography-guided percutaneous lung puncture biopsy; Case report; Benign metastatic leiomyoma; Lung nodule

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Manuscript source: Unsolicited manuscript

Received: April 20, 2020

Peer-review started: April 20, 2020

First decision: June 2, 2020

Revised: June 16, 2020

Accepted: July 1, 2020

Article in press: July 1, 2020

Published online: July 26, 2020

P-Reviewer: Chetty R, Ferrari F

S-Editor: Liu M

L-Editor: Webster JR

E-Editor: Liu JH



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Core tip: Pulmonary benign metastatic leiomyoma (PBML) is a rare disease, and a type of benign metastatic leiomyoma, which is usually misdiagnosed. In order to avoid misdiagnosis and treat this disease effectively, we report the diagnosis and treatment of a patient with PBML as the final diagnosis based on her clinical history of uterine leiomyoma, imaging manifestations, biopsy, and multidisciplinary team discussions. A literature review of PBML was also carried out.

Citation: Dai HY, Guo SL, Shen J, Yang L. Pulmonary benign metastasizing leiomyoma: A case report and review of the literature. *World J Clin Cases* 2020; 8(14): 3082-3089

URL: <https://www.wjgnet.com/2307-8960/full/v8/i14/3082.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v8.i14.3082>

INTRODUCTION

Pulmonary benign metastatic leiomyoma (PBML) is a type of benign metastatic leiomyoma (BML) that was first reported in 1939^[1]. The etiology of PBML is related to uterine leiomyoma, and PBML mainly occurs in premenopausal women who have received a myomectomy or hysterectomy, but there are also cases of this disease occurring in women who have not received surgery, as well as in men and children^[2,3]. Typically, the appearance of PBML on imaging is multiple nodules of different sizes in the bilateral lungs, such as in our case. There are also cases that have single or unilateral lung nodules. PBML is considered benign in histopathology, but the fusiform smooth muscle cells of the uterus can be diffused by metastasis, so it is likely that the biological behavior of PBML has also been considered malignant. BML often involves the lungs, as in our case of PBML, but it may also involve the heart, skeletal system, vascular system, lymph nodes, or other organs and systems. In the described case, multiple lung nodules were found. However, most PBML patients have no clinical manifestations, while some have hemoptysis, chest pain, dyspnea, pneumothorax, or other presentations. Surgery and anti-estrogen therapy can be considered for the treatment of PBML. Although, for patients without symptoms and progression, only follow-up observation is needed, as PBML generally has a good prognosis.

CASE PRESENTATION

Chief complaints

A 55-year-old asymptomatic Chinese woman was found to have multiple nodules in both lungs during a health checkup.

History of present illness

No symptoms present.

History of past illness

Her medical history included total hysterectomy for uterine leiomyoma 14 years previously.

Personal and family history

She was a non-smoker without relevant family history or recent weight loss.

Physical examination

She had no obvious abnormalities on physical examination.

Laboratory examinations

Lung cancer tumor marker was normal, and other auxiliary examination results were unremarkable.

Imaging examinations

On a chest high-resolution computed tomography (HRCT) scan (Figure 1A-C), the largest nodule of 7 mm in diameter was detected in the right lower lobe.

Further diagnostic work-up

Lung cancer metastasis or metastatic lung cancer was suspected, and she was admitted to our department. Following informed consent, she underwent a computed tomography (CT)-guided percutaneous lung puncture biopsy (Figure 1D) with pneumothorax complication (Figure 2A), and recovered after thoracic puncture and aspiration (Figure 2B). Her lung puncture biopsy smear found neither cancer cells nor tuberculosis. Histopathological examination of a lung puncture biopsy specimen of the largest nodule in the right lower lobe showed the following manifestations (Figure 3A-D): A few spindle cells (spindle cell tumor was considered); and immunohistochemistry results of Desmin(+), CD34 blood vessel(+), Bcl-2(+), SMA(+), Vim(+), S-100(-), CD99(+), STAT-6(-), and CR(-). The immunohistochemical smooth-muscle markers SMA and Desmin were positive, suggesting the origin was smooth muscle; however, because Bcl-2 and CD99 showed positive staining, a synovial origin was not excluded. Positron emission tomography-CT (PET-CT) (Figure 4A, 4B) showed multiple nodules in both lungs and no uptake of fluorodeoxyglucose (FDG), which is usually taken up by tumor lesions; there were no suspicious tumor lesions elsewhere on PET-CT.

FINAL DIAGNOSIS

After a multidisciplinary team (MDT) discussion, which involved personnel from six hospital departments (respiratory, oncology, obstetrics and gynecology, imaging, pathology, and nuclear medicine) and comprehensive consideration of past history, clinical manifestations, and histopathological results, the patient was finally diagnosed with PBML from uterine leiomyoma.

TREATMENT

Because her lesions were small and she had no symptoms, she received follow-up monitoring without treatment.

OUTCOME AND FOLLOW-UP

Six months later, she underwent chest HRCT (Figure 5A-C), which showed no progression.

DISCUSSION

PBML is a rare disease, with only around 100 cases reported worldwide. In 2006, Pacheco-Rodriguez *et al*^[4] reviewed the current knowledge on BML. Research papers and case reports on PBML before and after 2006 have been collated for this literature review.

The etiology of PBML is still unclear, but there are three main hypotheses: (1) The mainstream hypothesis states that after myomectomy or hysterectomy, smooth muscle cells are transported through blood and lymph vessels to the lungs and other sites (“transport theory”). But this hypothesis does not explain why non-surgical patients also develop PBML. The study performed by Patton *et al*^[5] showed positive expression of estrogen receptor (ER) and progesterone receptor (PR) in PBML tissue, which supports the hypothesis that PBML is transferred from uterine fibroids to the lungs; (2) The second hypothesis is that PBML metastasizes to other organs and systems because it is a low grade, malignant, and highly differentiated leiomyosarcoma^[6]; and (3) Others have hypothesized that PBML has multifocal origins, as some PBMLs have been found before or at the same time as uterine fibroids. Thus, in this hypothesis, PBML is considered a multiple smooth muscle hamartoma, not a metastasis^[7].

Pathologically, PBML may present as an extrauterine smooth-muscle cell

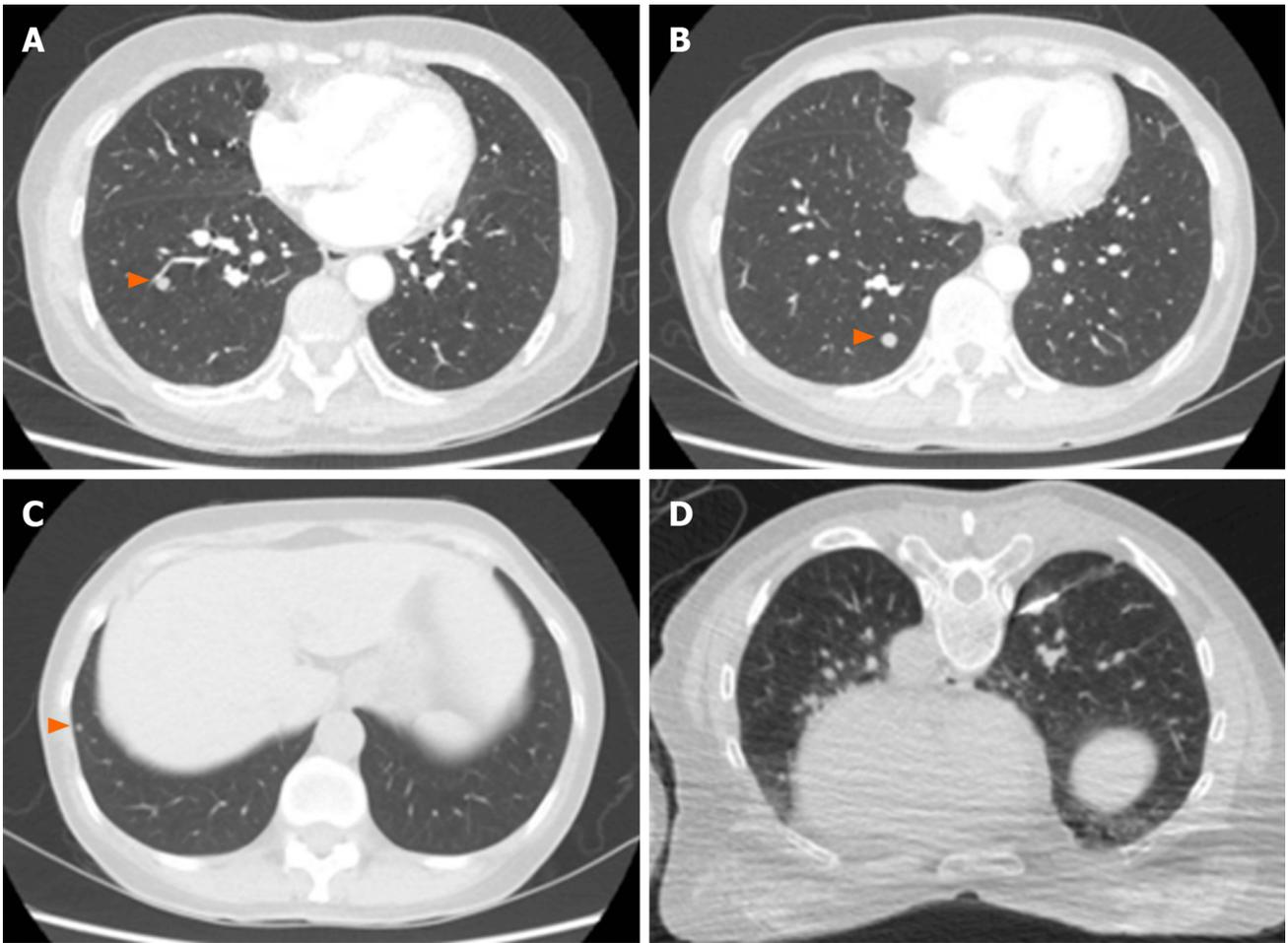


Figure 1 Chest high-resolution computed tomography imaging. A-C: The three largest lung nodules on chest high-resolution computed tomography; D: Computed tomography-guided percutaneous lung puncture biopsy of the largest nodule in the right lower lobe.

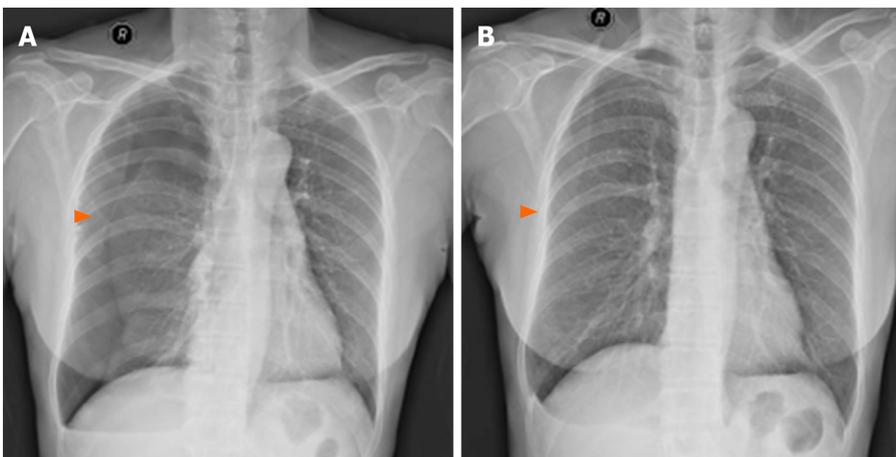


Figure 2 Chest X-ray imaging. A: Complication of pneumothorax after computed tomography-guided percutaneous lung puncture biopsy; B: The patient recovered after thoracic puncture and aspiration.

proliferation^[8,9], and, as seen in our case, with a few spindle cells on histopathological examination. Uterine smooth muscle cells express ER and PR, as do PBML cells^[8]. Cells of PBML have a low mitotic index; therefore, PBML nodules grow slowly and may remain unchanged for a long time. Cells have no nuclear atypia and necrosis, and no invasion to the surrounding tissue, while BML cells can destroy the lumbar vertebrae; therefore, some people believe that the biological behavior of PBML is malignant^[10]. As shown in our case, PBML is often immunohistochemically positive for the typical

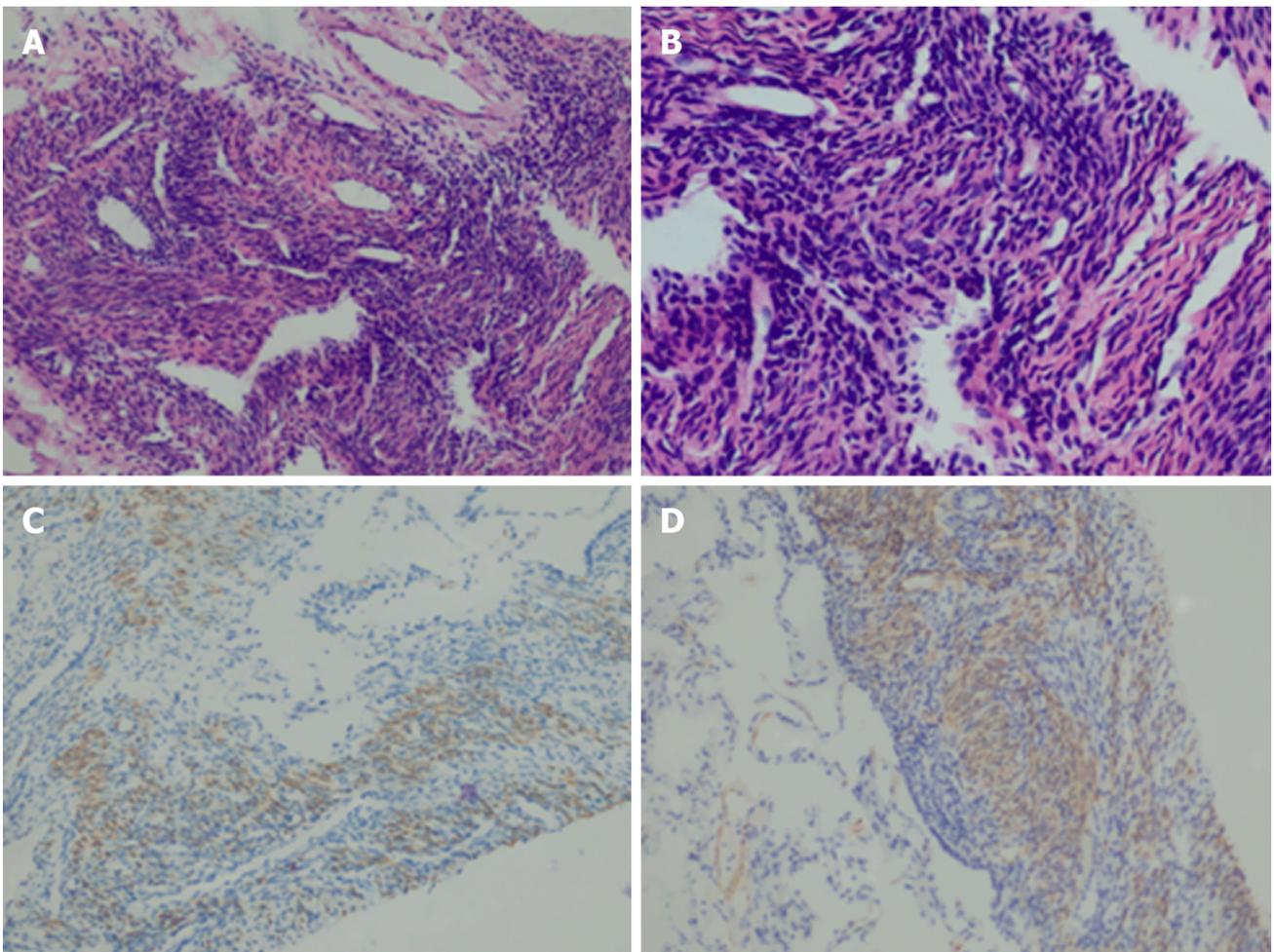


Figure 3 Histological findings. A-D: Histopathological examination of the lung puncture biopsy specimen: A few spindle cells were seen, and a spindle cell tumor was considered; immunohistochemical smooth-muscle labeling revealed Desmin(+) and SMA(+), suggesting smooth muscle origin.

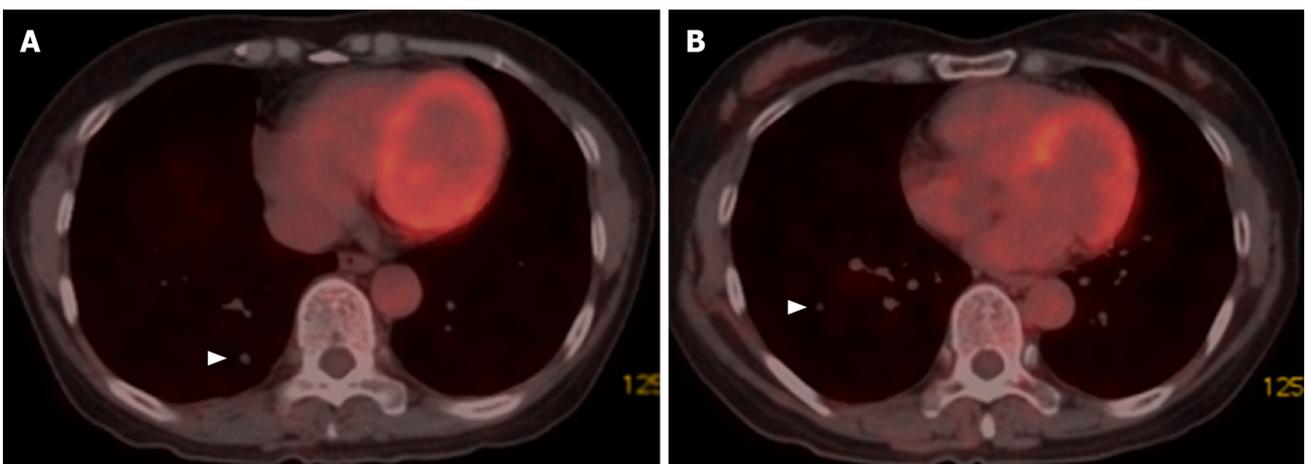


Figure 4 Positron emission tomography-computed tomography imaging. A and B: Positron emission tomography-computed tomography showed multiple nodules in both lungs with no uptake of fluorodeoxyglucose.

muscle-cell markers SMA and Desmin.

As in the described case, PBML patients are often asymptomatic, and almost 30% of PBML patients have pulmonary manifestations, such as dyspnea, cough, and chest pain. Moreover, pneumothorax and cysts may occur in PBML patients, who should be differentially diagnosed for lymphangioliomyomatosis (LAM), as this disease has the clinical characteristics of recurrent pneumothorax and cysts^[11]. Rarely, PBML can cause

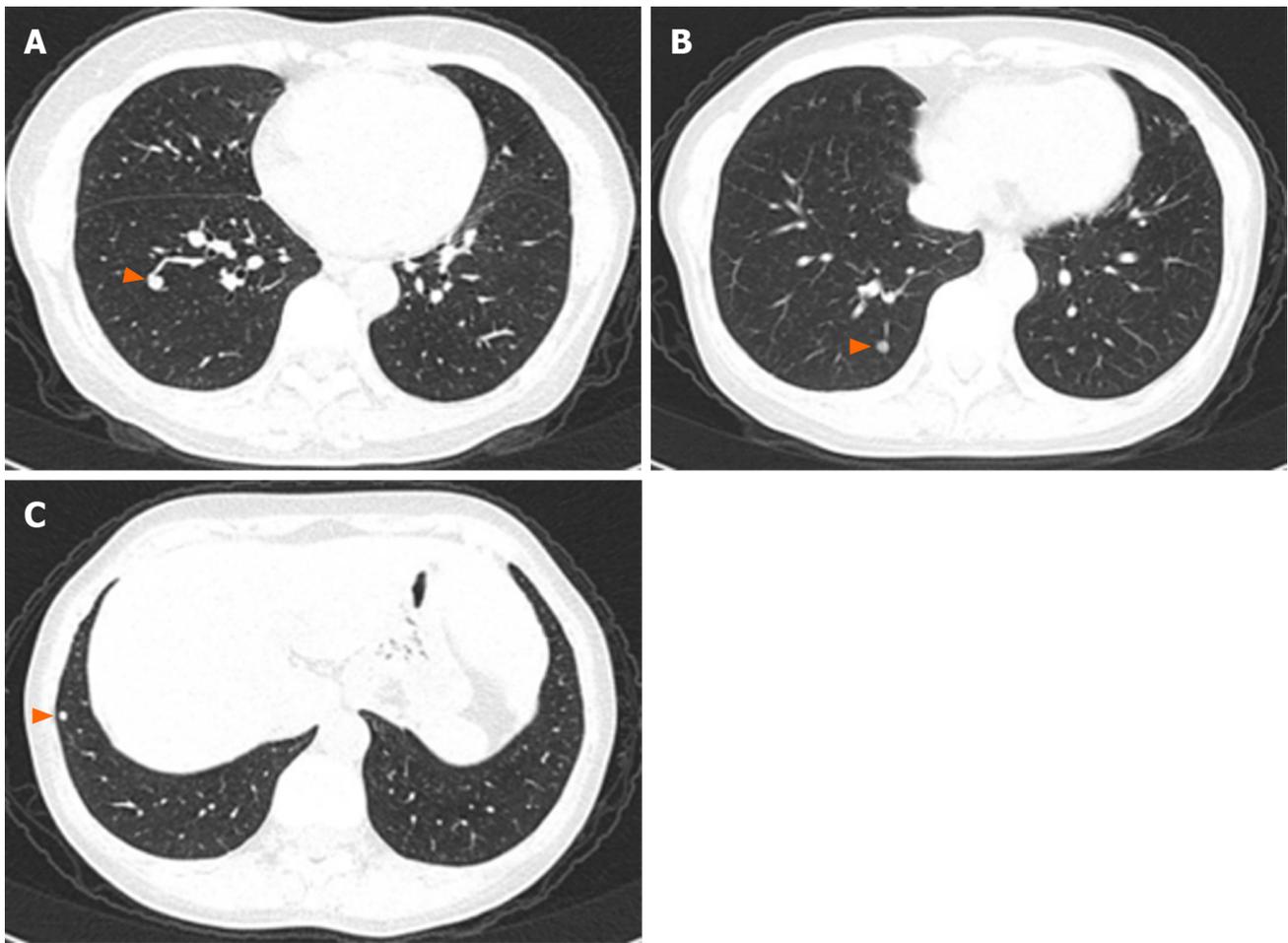


Figure 5 Follow-up with chest high-resolution computed tomography imaging after 6 mo. A-C: No progression.

respiratory failure^[12] and present as progressive pneumothorax^[13]. In addition, BML can affect other organs and systems in PBML patients; therefore, other systems may manifest clinical symptoms, such as leg aches and paresthesia due to spinal BML^[14]. Uterine leiomyoma itself could result in gynecological symptoms, including abnormal uterine bleeding and pelvic pressure or pain.

With regard to imaging, chest X-ray, CT, 18F-fluorodeoxyglucose-PET/CT (18F-FDG-PET/CT), and magnetic resonance imaging can be used to investigate PBML. Usually, as in our case, the imaging results show pulmonary abnormalities, and multiple well-circumscribed nodules in the bilateral pulmonary fields are characteristic manifestations of chest CT^[15]. The nodules may vary in size and can also be solitary or multiple but only affect one lung. Rarely, PBML presents as diffuse miliary lesions in the lungs. The nodules are mostly solid with no calcification but can also be cavitated^[16-19]; the edges are smoother and clearer without enhancement than those of general malignant metastasis but may also be lobulated and enhanced on contrast-enhanced CT^[10]. On 18F-FDG-PET/CT, most pulmonary nodules of PBML show low or no metabolic activity, as in our case; therefore, 18F-FDG-PET/CT may be used to differentiate PBML from malignant metastases. A case reported by Sawai *et al.*^[20] showed that metastatic lesions had high metabolic activity with maximum standard uptake values of 20.1, which is the same as the value for the diagnosis of pulmonary nodules. HRCT is more sensitive for the diagnosis of small PBML lesions.

There are no standardized diagnostic criteria for PBML. PBML is diagnosed by three major aspects (Figure 6): The clinical history (history of prior hysterectomy or myomectomy); Imaging manifestations (most significant diagnostic stage); Biopsies (CT-guided percutaneous lung puncture biopsy, bronchial biopsy, surgical lung biopsy); and Histopathological evaluation (uterine leiomyoma-like spindle-shaped cells, smooth muscle markers on immunohistochemistry, ER, and PR). However, these three aspects sometimes show atypical manifestations. In such cases, an MDT, mostly involving specialists from respiratory, oncology, obstetrics and gynecology, imaging, pathology, and nuclear medicine fields, is needed to diagnose PBML. The differential

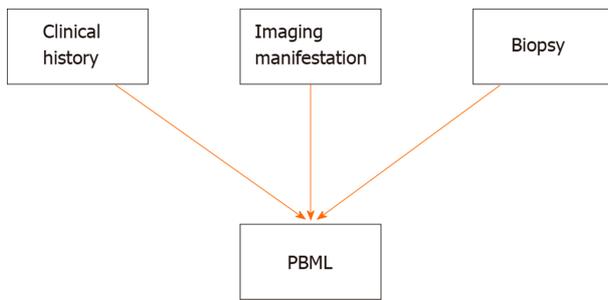


Figure 6 Three major diagnostic aspects for pulmonary benign metastatic leiomyoma. PBML: Pulmonary benign metastatic leiomyoma.

diagnosis of PBML, mainly includes diseases that manifest as diffuse multiple pulmonary nodules or occasionally cavities on chest imaging, such as metastatic lung cancer^[21], sarcoidosis, silicosis, infectious diseases, LAM, pulmonary Langerhans cell histiocytosis, and Birt-Hogg-Dubé syndrome^[22]. Research into typical PBML biomarkers for diagnosis is needed in the future.

For the treatment of PBML patients, there are three major approaches. Firstly, for asymptomatic PBML patients, long-term observation and follow-up with imaging examination without treatment can be chosen, as most PBML lesions are stable for long periods. Changes in hormones affect the development of BML lesions, thus, these lesions often shrink after the menopause and during pregnancy^[23,24]. Therefore, antiestrogen therapy, including bilateral oophorectomy, gonadotropin-releasing hormone agonists, selective estrogen receptor modulators, and aromatase inhibitors, should be considered as second-line treatment options, especially for younger patients who have clinical manifestations^[25]. Thirdly, for PBML patients with symptoms, especially symptoms secondary to the lesions (*e.g.*, compression symptoms), who do not respond to antiestrogen therapy, surgical resection of PBML can be considered^[26]. In one case report, a 36-year-old woman received seven procedures to remove 87 PBML lesions^[27]; thus, mini-invasive local therapies, such as ablation, might be worthy of research.

Further characteristics of PBML patients are shown in [Supplementary Tables 1 and 2](#).

CONCLUSION

In summary, the typical imaging manifestations of PBML are multiple nodules in the bilateral pulmonary fields, which are usually asymptomatic; uterine leiomyoma or a history of uterine leiomyoma; low or no metabolic activity on PET/CT; and extrauterine smooth-muscle cell proliferation on histopathology of biopsy samples. PBML can usually be diagnosed using these observations. Antiestrogen therapy and surgical resection should be considered for the treatment of PBML, which often has a good prognosis.

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