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## Contents

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## EXPERT RECOMMENDATIONS

- 2893 Recommendations for perinatal and neonatal surgical management during the COVID-19 pandemic  
*Ma LS, Zhao YL, Wei YD, Liu C*

## MINIREVIEWS

- 2902 Clinical applicability of gastroscopy with narrow-band imaging for the diagnosis of *Helicobacter pylori* gastritis, precancerous gastric lesion, and neoplasia  
*Cho JH, Jeon SR, Jin SY*

## ORIGINAL ARTICLE

## Clinical and Translational Research

- 2917 Identification of APEX2 as an oncogene in liver cancer  
*Zheng R, Zhu HL, Hu BR, Ruan XJ, Cai HJ*

## Retrospective Cohort Study

- 2930 Restenosis after recanalization for Budd-Chiari syndrome: Management and long-term results of 60 patients  
*Zhang W, Tian YL, Wang QZ, Chen XW, Li QY, Han JH, Chen XD, Xu K*

## Retrospective Study

- 2942 Comparison of microendoscopic discectomy and open discectomy for single-segment lumbar disc herniation  
*Pang JY, Tan F, Chen WW, Li CH, Dou SP, Guo JR, Zhao LY*
- 2950 Clinical characteristics of patients with COVID-19 presenting with gastrointestinal symptoms as initial symptoms: Retrospective case series  
*Yang TY, Li YC, Wang SC, Dai QQ, Jiang XS, Zuo S, Jia L, Zheng JB, Wang HL*

## Observational Study

- 2959 Effects of policies and containment measures on control of COVID-19 epidemic in Chongqing  
*Liang XH, Tang X, Luo YT, Zhang M, Feng ZP*
- 2977 Role of shear wave elastography in the evaluation of the treatment and prognosis of supraspinatus tendinitis  
*Zhou J, Yang DB, Wang J, Li HZ, Wang YC*
- 2988 Endoscopic retrograde cholangiopancreatography in elderly patients: Difficult cannulation and adverse events  
*Tabak F, Wang HS, Li QP, Ge XX, Wang F, Ji GZ, Miao L*

- 3000** Diagnostic value of orbicularis oculi muscle electromyography in functional epiphora

*Lu H, Liu PD, Yao X, Wang ZF, Gao LF, Wang SP*

### META-ANALYSIS

- 3006** Diagnostic value of liquid-based cytology and smear cytology in pancreatic endoscopic ultrasound-guided fine needle aspiration: A meta-analysis

*Pan HH, Zhou XX, Zhao F, Chen HY, Zhang Y*

### SCIENTOMETRICS

- 3021** Bibliometric analysis of randomized controlled trials of colorectal cancer over the last decade

*Wang CY, Zhou SC, Li XW, Li BH, Zhang JJ, Ge Z, Zhang Q, Hu JH*

### CASE REPORT

- 3031** Spontaneous pneumothorax in a single lung transplant recipient-a blessing in disguise: A case report

*Deshwal H, Ghosh S, Hogan K, Akindipe O, Lane CR, Mehta AC*

- 3039** Endoscopic third ventriculostomy in obstructive hydrocephalus: A case report and analysis of operative technique

*Munda M, Spazzapan P, Bosnjak R, Velnar T*

- 3050** Underwater endoscopic mucosal resection for neoplasms in the pyloric ring of the stomach: Four case reports

*Kim DH, Park SY, Park CH, Kim HS, Choi SK*

- 3057** Successful treatment of basaloid squamous cell carcinoma in the rectosigmoid colon: A case report and review of literature

*Lee TG, Yoon SM, Kim MJ*

- 3064** Synchronous sporadic bilateral multiple chromophobe renal cell carcinoma accompanied by a clear cell carcinoma and a cyst: A case report

*Yang F, Zhao ZC, Hu AJ, Sun PF, Zhang B, Yu MC, Wang J*

- 3074** Intra-abdominal hemorrhage during pregnancy: Four case reports

*Yang L, Liu N, Long Y*

- 3082** Pulmonary benign metastasizing leiomyoma: A case report and review of the literature

*Dai HY, Guo SL, Shen J, Yang L*

- 3090** Mucoepidermoid carcinoma in the infratemporal fossa: A case report

*Zhang HY, Yang HY*

- 3097** Intra-abdominal inflammatory pseudotumor-like follicular dendritic cell sarcoma associated with paraneoplastic pemphigus: A case report and review of the literature

*Zhuang JY, Zhang FF, Li QW, Chen YF*

- 3108** Multiple recurrent cystic echinococcosis with abdominal aortic involvement: A case report  
*Taxifulati N, Yang XA, Zhang XF, Aini A, Abulizi A, Ma X, Abulati A, Wang F, Xu K, Aji T, Shao YM, Ahan A*
- 3114** Dental focal infection-induced ventricular and spinal canal empyema: A case report  
*Xue H, Wang XH, Shi L, Wei Q, Zhang YM, Yang HF*
- 3122** Effect of chidamide on treating hepatosplenic T-cell lymphoma: A case report  
*Wang XT, Guo W, Sun M, Han W, Du ZH, Wang XX, Du BB, Bai O*
- 3130** Acute esophageal obstruction caused by reverse migration of gastric bezoars: A case report  
*Zhang FH, Ding XP, Zhang JH, Miao LS, Bai LY, Ge HL, Zhou YN*



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

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### 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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**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.

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## INTRODUCTION

Pulmonary benign metastatic leiomyoma (PBML) is a type of benign metastatic leiomyoma (BML) that was first reported in 1939<sup>[1]</sup>. 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<sup>[2,3]</sup>. 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

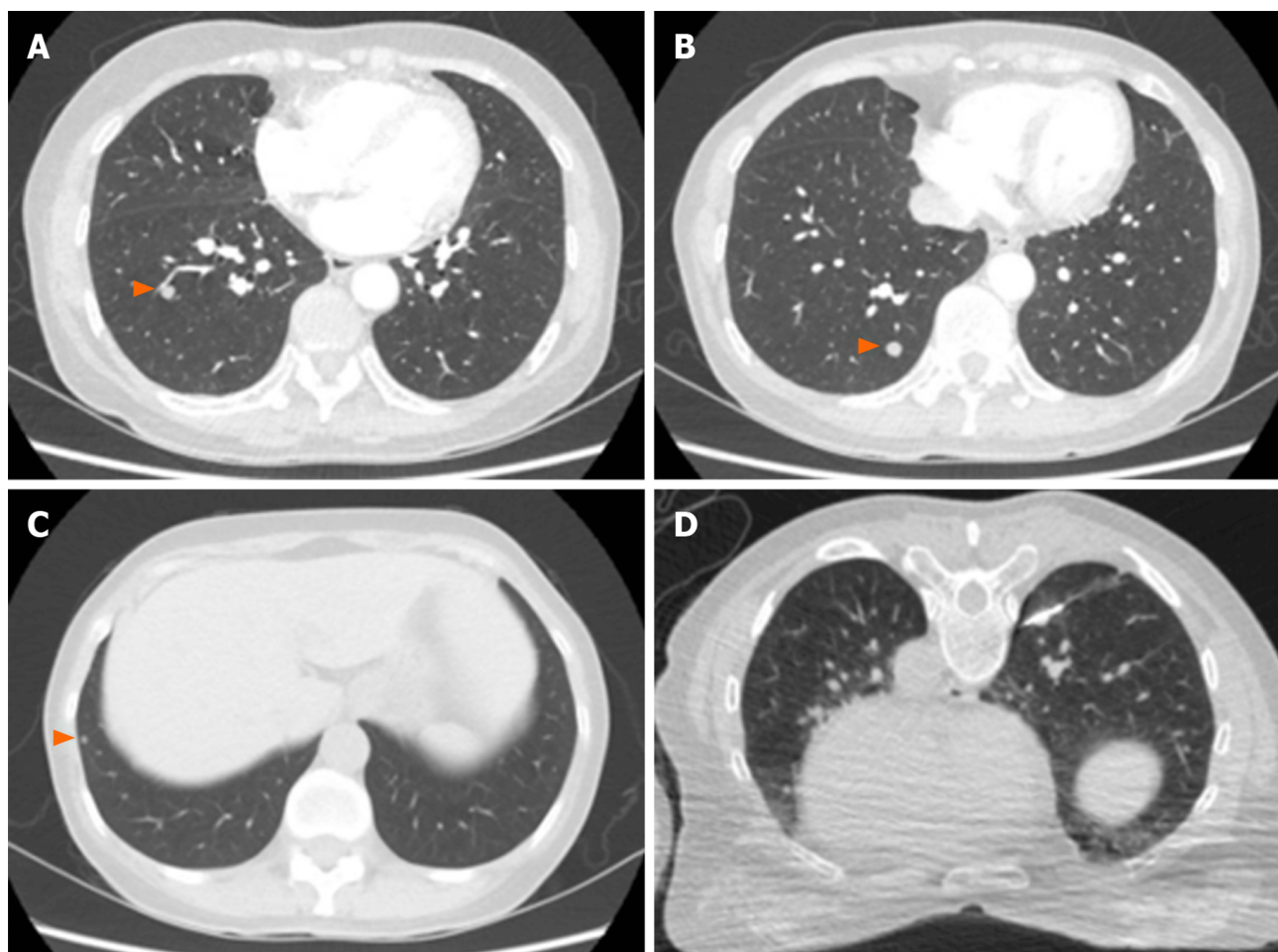
Six months later, she underwent chest HRCT (Figure 5A-C), which showed no progression.

## DISCUSSION

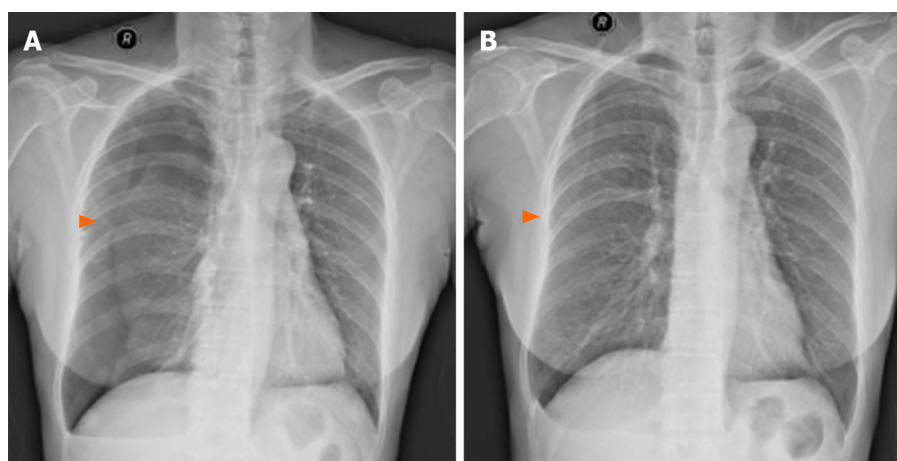
PBML is a rare disease, with only around 100 cases reported worldwide. In 2006, Pacheco-Rodriguez *et al*<sup>[4]</sup> reviewed the current knowledge on BML. Research papers and case reports on PBML before and after 2006 have been collated for this literature review.

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*<sup>[5]</sup> 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<sup>[6]</sup>; 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<sup>[7]</sup>.

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



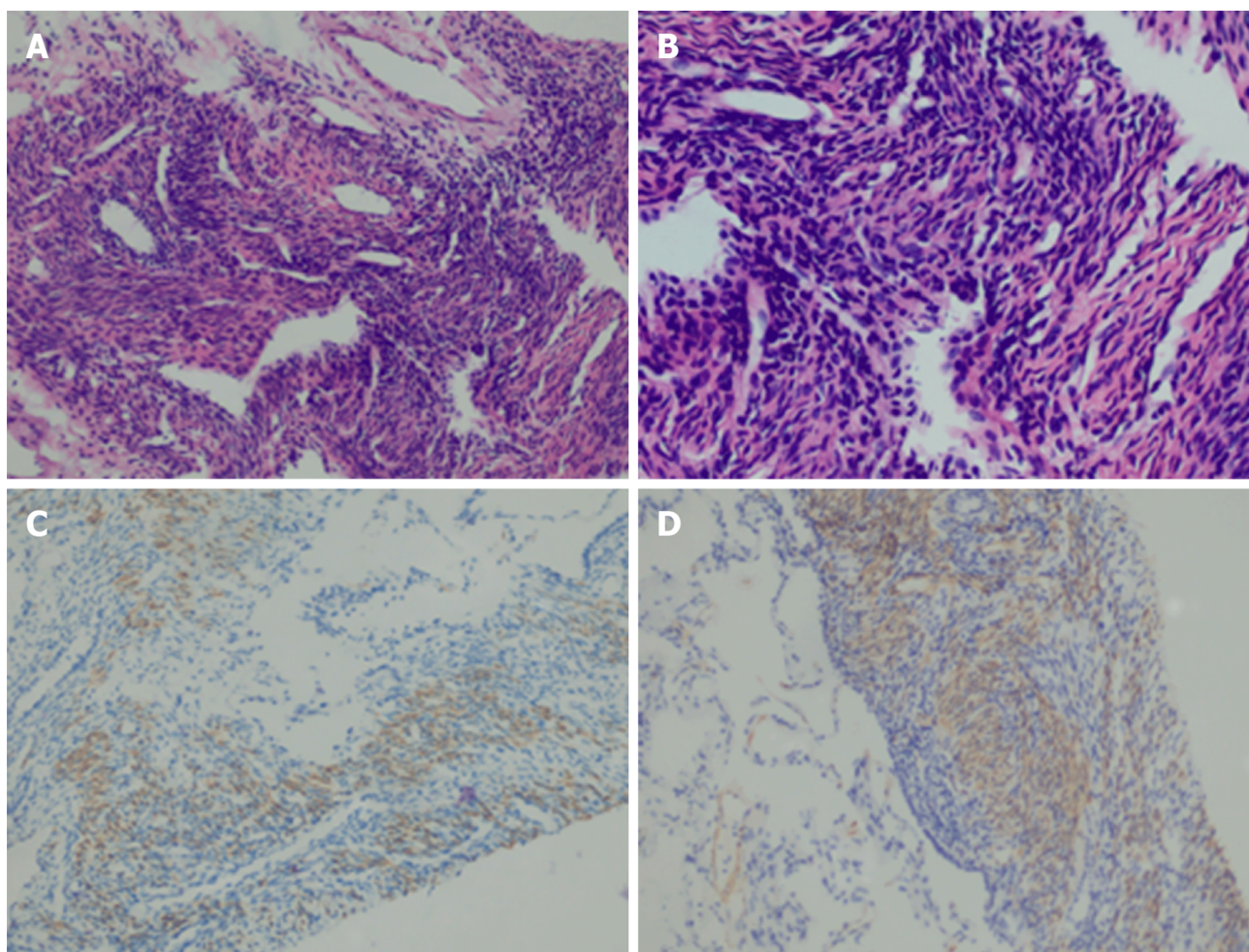
**Figure 1 Chest high-resolution computed tomography imaging.** A-C: The three largest lung nodules on chest high-resolution computed tomography; D: Computed tomography-guided percutaneous lung puncture biopsy of the largest nodule in the right lower lobe.



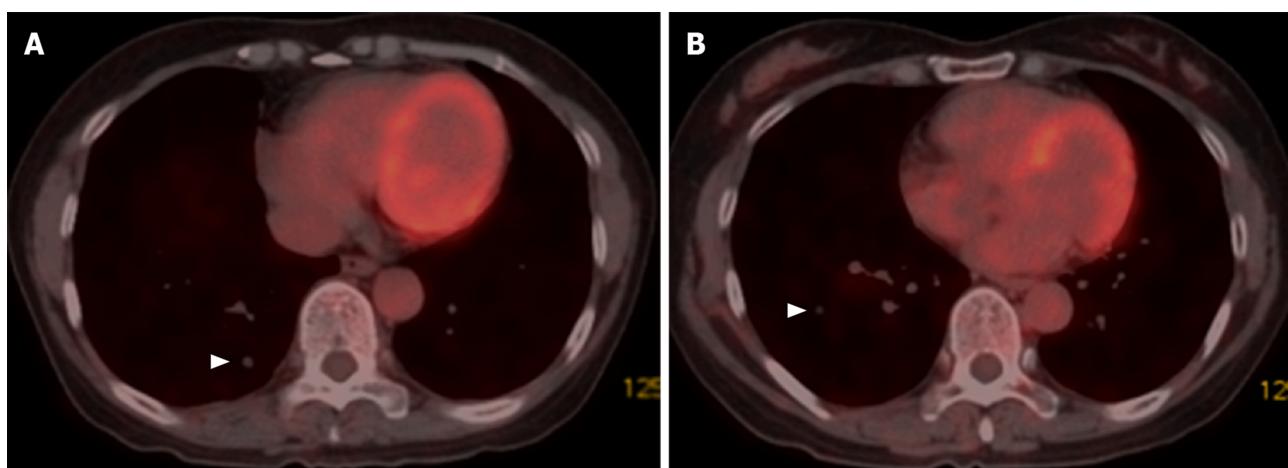
**Figure 2 Chest X-ray imaging.** A: Complication of pneumothorax after computed tomography-guided percutaneous lung puncture biopsy; B: The patient recovered after thoracic puncture and aspiration.

proliferation<sup>[8,9]</sup>, 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<sup>[8]</sup>. 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<sup>[10]</sup>. As shown in our case, PBML is often immunohistochemically positive for the typical





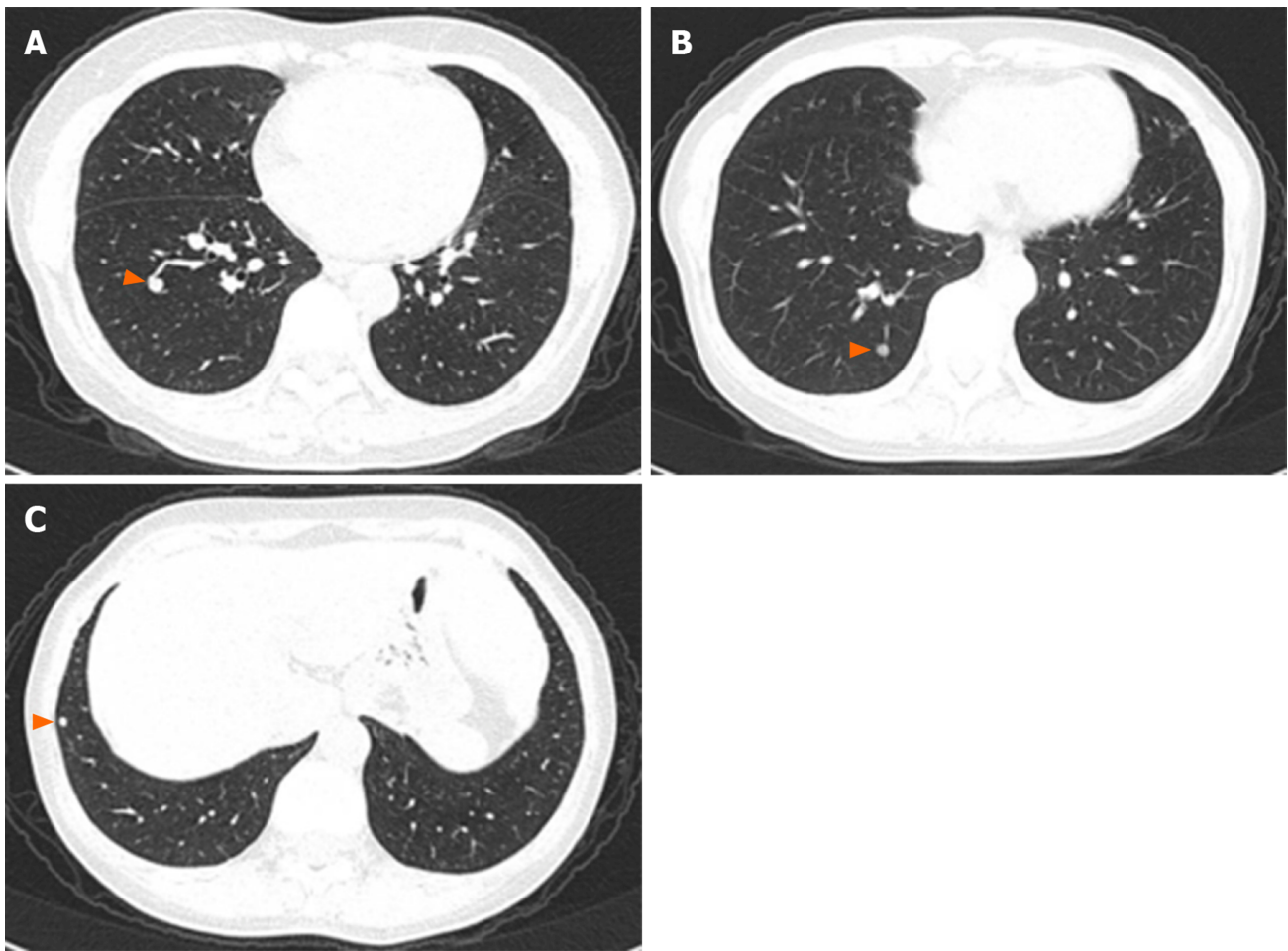
**Figure 3 Histological findings.** A-D: Histopathological examination of the lung puncture biopsy specimen: A few spindle cells were seen, and a spindle cell tumor was considered; immunohistochemical smooth-muscle labeling revealed Desmin(+) and SMA(+), suggesting smooth muscle origin.



**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 lymphangioleiomyomatosis (LAM), as this disease has the clinical characteristics of recurrent pneumothorax and cysts<sup>[11]</sup>. Rarely, PBML can cause



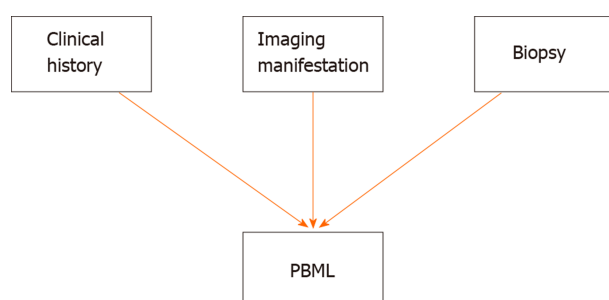
**Figure 5** Follow-up with chest high-resolution computed tomography imaging after 6 mo. A-C: No progression.

respiratory failure<sup>[12]</sup> and present as progressive pneumothorax<sup>[13]</sup>. 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<sup>[14]</sup>. 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<sup>[15]</sup>. 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<sup>[16-19]</sup>; 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<sup>[10]</sup>. 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*<sup>[20]</sup> 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<sup>[21]</sup>, sarcoidosis, silicosis, infectious diseases, LAM, pulmonary Langerhans cell histiocytosis, and Birt-Hogg-Dubé syndrome<sup>[22]</sup>. 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<sup>[23,24]</sup>. 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<sup>[25]</sup>. 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<sup>[26]</sup>. In one case report, a 36-year-old woman received seven procedures to remove 87 PBML lesions<sup>[27]</sup>; 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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