

An unusual case report of multiple pulmonary leiomyomatous hamartoma

Dan Cheng, MD, PhD^{a,b}, Fangcheng Zhang, MM^c, Ke Hu, MD^{a,*}

Abstract

Rationale: Multiple pulmonary leiomyomatous hamartoma (MPLH) is an extremely rare benign disease that mostly occurs in women of reproductive age.

Patient concerns: A 32-year-old female patient recently diagnosed with multiple bilateral pulmonary nodules. She has the symptoms of dry cough, chest tightness, dyspnea on exertion. Chest X-ray identified multiple bilateral pulmonary nodules in the lung, and the diameter of the largest nodule was about 3.1 cm.

Diagnoses: Pathology confirmed the diagnosis of MPLH based on morphology and immunohistochemical staining.

Interventions: The patient presented with multiple well-defined nodular shadows in chest computed tomography (CT), atypical image and symptoms were detected. Positron emission tomography/CT scan showed mild fluorine-18 fluorodeoxyglucose uptake in the lesions and no abnormal foci in any other parts of her body. She subsequently underwent a video-assisted thoracoscopic surgery with wedge resection of the biggest one of the nodules. Then the patient given symptomatic treatment, without hormone, no further treatment was prescribed.

Outcomes: The patient is in the good general condition and without obvious pulmonary symptoms after the follow-up of 1 year, chest CT scan showed no significant changes in the sizes and locations of her bilateral pulmonary nodules.

Lessons: Due to its rare presentation, the primary MPLH may be undiagnosed. Awareness of main morphologic and immunohistochemical features of MPLH is critical for the recognition of this uncommon disease.

Abbreviations: a-SMA = alpha-smooth muscle actin, CT = computed tomography, MPLH = multiple pulmonary leiomyomatous hamartoma.

Keywords: histopathology, lung, multiple leiomyomatous hamartoma, rare

1. Introduction

Multiple pulmonary leiomyomatous hamartoma (MPLH) is a rare disease characterized by diffuse or multiple nodular hyperplasia of the lung.^[1] It was thought to occur mainly in

women and first described by Logan et al in 1965.^[2] Subsequently, a few cases affecting men have been reported.^[3] MPLH is easy to be misdiagnosed as a metastatic lung tumor. Here we report an unusual case of pathologically verified multiple leiomyomatoid hamartoma of the lung, presented with the unusual presentations of computed tomography (CT) scan and exceptive histopathological features.

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^a Department of Respiratory and Critical Care Medicine, Renmin Hospital of Wuhan University, Wuhan, China, ^b Lung Biology Center, Department of Medicine, University of California, San Francisco, CA, ^c Center of Ultrapathology, Renmin Hospital of Wuhan University, Wuhan, China.

* Correspondence: Ke Hu, Department of Respiratory and Critical Care Medicine, Renmin Hospital of Wuhan University, 238 Jiefang Rd, Wuhan, Hubei, 430030, P.R. China (e-mail: huke-rmhospital@163.com).

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2. Clinical Case and Methods

A 32-year-old female presented to us with recently diagnosed multiple bilateral pulmonary nodules. Upon admission, the patient was in a good general condition, she has no prior family history of malignancy and other diseases. On review of systems, she reported a dry cough, chest pain and tightness, dyspnea on exertion. The patient was otherwise in good health. She never smokes but worked in the tunnel for 3 months before. Her lung exam was no abnormality seen. Physical examinations show everything is normal. Routine laboratory tests and any other inspections were all within normal limits, tumor marker set was negative. The lung function test showed pulmonary ventilation and diffusion function within the normal range. Thyroid ultrasonography showed bilateral cystic lobar lesions, about 1.3 × 1.5 cm on the right and 0.2 × 0.2 cm on the left. Ultrasonographic examination revealed uterine leiomyoma, about 1.6 × 1.6 cm.

Chest X-ray and CT identified multiple well-defined nodular shadows in her lungs, and the diameter of the largest nodule was

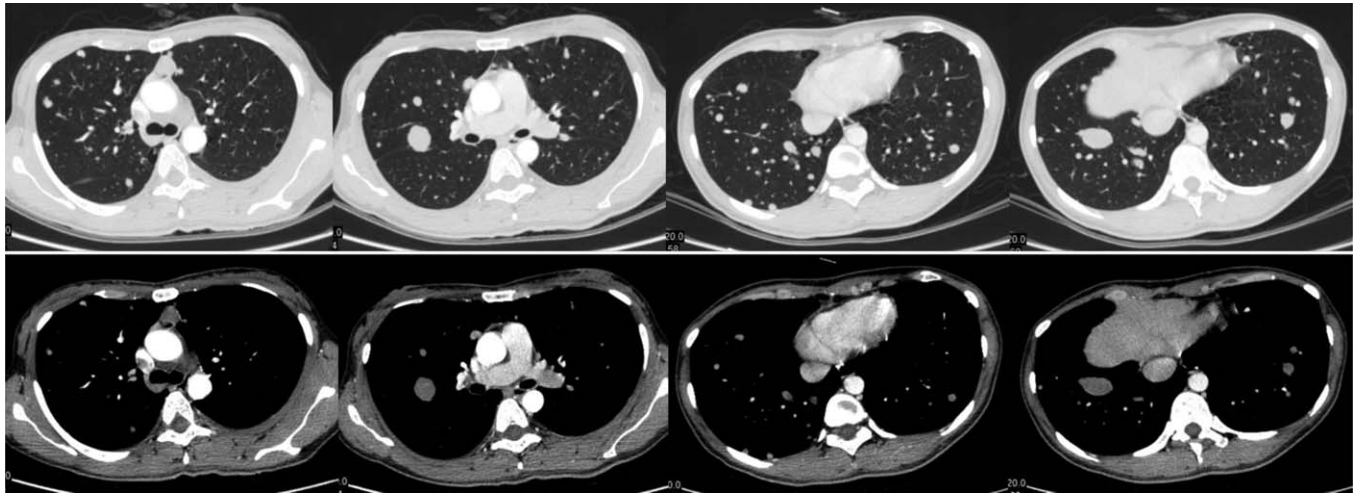


Figure 1. Chest CT scan showed diffused bilateral nodules in the lungs, the diameter of the largest nodule is about 3.1 cm, and with local thickening of bilateral pleura. CT = computed tomography.

about 3.1 cm (Fig. 1). Pulmonary metastases from an unknown primary tumor were suspected. But the bronchoscope and transbronchial lung biopsy did not establish a diagnosis. The patient subsequently underwent a positron emission tomography/CT scan. The pulmonary nodules were mildly fluorine-18 fluorodeoxyglucose avid (maximal standardized uptake value = 3.9), and no abnormal foci were observed in any other parts of her body. Because of the uncertain property nodules and the obvious symptoms, thoracoscopic surgery was proposed based on the morphology and pathological examination (Fig. 2A).

3. Results

Immunohistochemical staining was performed. The mesenchymal component was positive for alpha-smooth muscle actin (a-SMA) (Fig. 2B), desmin (Fig. 2C), caldesmon, and WT-1, but was negative for CD117, CD34, PAX8, CK20, STAT6, and S-100 protein. The epithelial component was positive for thyroid transcription factor, epithelial membrane antigen, CK7, and NapsinA, but was negative for SMA, desmin, caldesmon, and STAT6. Also, cells in the mesenchymal component were negative for estrogen receptor. Ki67 was expressed with labeling indexes of 1% in the mesenchymal components (Fig. 2D). Finally, the patient was diagnosed with MPLH. Then the patient was given symptomatic treatment, such as antitussive, the medicine for relieving chest tightness, without hormone. After the follow-up of 1 year, the general condition of this patient is very well she has no obvious respiratory symptoms and is not restricted in her daily physical activities, the chest CT scan showed no significant changes in the sizes and locations of her bilateral pulmonary nodules.

4. Discussion

Multiple pulmonary hamartomas are rare, mostly appear in females, and are usually leiomyomatous.^[4] The MPLH is a special pulmonic lesion, and the individual lesions of which are composed of a mixture of smooth muscle and glandular elements.^[5] The pathogenesis of MPLH is not clear, it is not

associated with specific pathological conditions of the lung, some investigators have reported that uterine leiomyoma can be found in many cases of MPLH and suggested that MPLH is not a real hamartoma but represents metastasizing uterine leiomyoma.^[6,7] However, there is still controversy whether MPLH represents the metastasizing uterine leiomyoma, as MPLH could not be distinguished pathologically from metastasizing uterine leiomyoma.^[8] The clinical process of MPLH also remains unclear. Patients are usually asymptomatic, whereas some patients may have respiratory symptoms such as cough, chest tightness, and expiratory dyspnea.^[9] MPLH are frequently discovered on chest imaging examination, in which they typically appear as single or multiple diffuse nodules.

The imaging examination is the main method for the diagnosis of pulmonary nodules. MPLH lack of specific imaging features and usually characterized by different sizes of well-bounded nodules. There was no obvious or slight enhancement after contrast agent, and without cartilages or calcifications in the lesions. Horstmann et al^[10] reported that multiple solid nodules were most common, about 70% in the 23 patients, and lobular or cavitory lesions could be seen in few cases. The unilateral multiple masses accounted for about 17%, while unilateral independent mass was about 13% and the diffused bilateral nodules were rare. In our present case, the radiographic findings were diffused bilateral nodules in her lungs, all the nodules are in different sizes, and the diameter of the largest node is about 3.1 cm. This imaging representation is very rare in former published cases and literatures, it is reported that the various clinical courses and the different imaging features seems to depend on the status of estrogen. It has been described that the benign leiomyomatous hamartoma always progressed in pre-menopausal females, but it is indolent in post-menopausal women.^[11] In addition, the level of hormonal changes in pregnancy and menopause women also affect the growth of nodules.^[12]

Immunohistochemical characteristics are essential in differentiating MPLH. The a-SMA, S-100 protein, and desmin are the commonly used markers in confirming the histomorphologic findings in leiomyomatous hamartoma.^[13,14] The histological

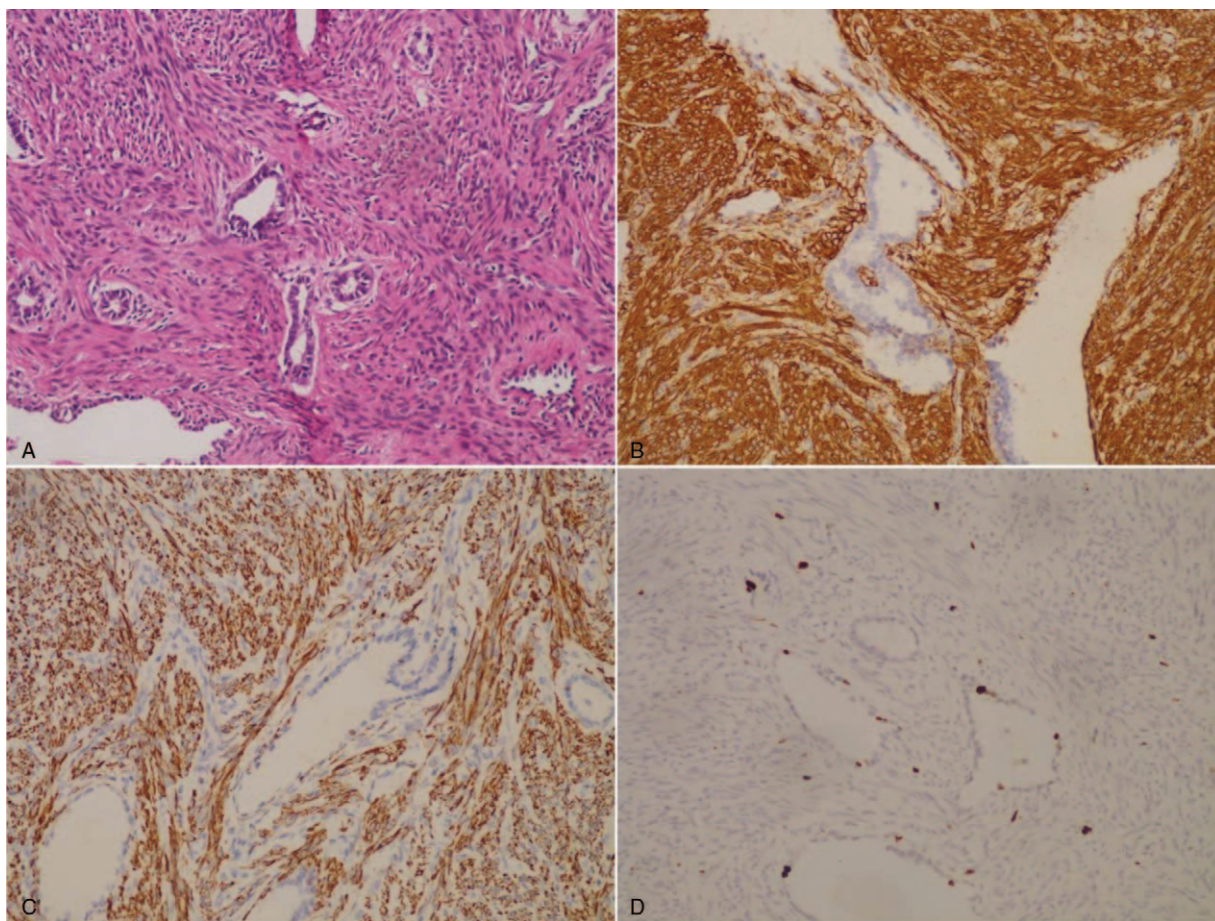


Figure 2. HE staining showed the nodule consisted of smooth muscle cells with numerous epithelial inclusions, no mitosis (A). Immunohistochemical staining indicated the α -SMA (B) and desmin (C) were diffuse positive expression, and the labeling indexes of Ki67 was about 1% (D). Magnification was $\times 200$ for each image. α -SMA = alpha-smooth muscle actin, HE = hematoxylin and eosin.

characteristics of currently referred benign metastasizing leiomyoma are as follows:

- (1) well circumscribed nodule composed of smooth muscle cells with numerous epithelial inclusions, which were hyperplastic, bunched, glandular epithelium or some may be associated with metaplasia and
- (2) no degeneration or vascular invasion, no cellular dysplasia or mitotic figures.^[15]

The histopathology of this patient revealed proliferation of smooth muscle cells, which were positive for α -SMA, desmin, caldesmon, and the extension of the bronchial epithelium into the alveolar septa were observed. Neither cellular atypia nor mitotic figures were present.

MPLH is a benign tumor that usually has no malignant tendency and with a good prognosis. However, because of the peculiar hamartomatous proliferation of the pulmonary smooth muscle cells, the lesion maybe progressive and even lead to fatal in some women during the reproductive age under certain conditions.^[3] The solitary tubercle is feasible for lobectomy and multiple nodules are mainly treated conservatively. It has been reported that the nodules may recede in female patients during pregnancy or after ovariectomy, suggesting that MPLH may be related to hormones.^[10,16] Other anti-estrogen therapies, such as selective estrogen receptor modulators, prostaglandins,

and aromatase inhibitors, have also been recommended.^[17] This present patient only given symptomatic treatment, without hormone, no further treatment was prescribed, and she remains in the good general condition and without obvious pulmonary symptoms during the follow-up of 1 year, the chest CT scan showed no significant changes in the sizes and locations of her bilateral pulmonary nodules.

In conclusion, multiple pulmonary leiomyomatoid hamartoma is an unusual disease, it should be considered in the differential in patients who present with multiple pulmonary nodules, especially with a history of uterine leiomyoma. The pathological examination and additional stains, such as estrogen/progesterone receptors, may need to be done to confirm the diagnosis.

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Author contributions

Data curation: Dan Cheng, Ke Hu.

Funding acquisition: Dan Cheng.

Methodology: Fangcheng Zhang.

Project administration: Dan Cheng.

Resources: Dan Cheng.

Supervision: Ke Hu.

Writing – original draft: Dan Cheng.

Writing – review and editing: Ke Hu.

Dan Cheng orcid: 0000-0002-5488-1937.

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