

肺良性转移性平滑肌瘤 4 例及文献复习

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Benign metastasizing leiomyoma (BML) is a rare lesion characterized by benign-appearing smooth muscle tumor most frequently occurring in the lung. It is usually associated with a benign leiomyoma or intravenous leiomyomatosis (IVL) in the uterus once or at present. Tumor growth mainly depends on hormone. However, its pathogenetic mechanism has not been clarified yet. The factors lead to the changes of hormone level such as pregnancy and menopause might have important effects on the general course of BML. It rarely reported that numerous and bilateral cyst formation in the lungs or multiple metastatic sites was in association with BML. We reported 4 cases of BML and reviewed the literature as follow.

Material and results

Case 1 A 46-year-old woman with intermittent cough for 5 years and intermittent hemoptysis for 2 months was hospitalized on Apr 22nd, 2009. She denied any fever, chills, dyspnea, chest pain, or any other symptoms. She has medical history of subtotal hysterectomy 5 years prior to uterine leiomyoma. Her family history was unremarkable, and examination revealed good physical condition. Chest CT presented that multiple thin-walled cysts of various size uniformly distributed throughout both lungs and all lesions were smoothly margined and had well-defined borders (Fig 1). The patient was diagnosed via video-assisted thorascopic surgery, and then accepted left lung wedge resection. Immunohistochemical staining (streptavidin-peroxidase) for ER and PR. Des (desmin) and SMA (smooth muscle actin) were also performed (Fig 2). Follow-up information shows the nodules hasn't developed from then on.

Case 2 A 50-year-old woman who has medical

history of hysterectomy 10 years prior to uterine leiomyoma was admitted for the nodules in bilateral lungs found in medical examination on Jul 2nd, 2004. Laboratory tests were unremarkable. Chest CT presented multiple well-circumscribed masses scattered throughout both lungs. Firstly, fine needle aspiration guided by CT disclosed the carcinoma, and pathologic findings were consistent with BML, then she underwent right lung subtotal mass resection by video-assisted thorascopic surgery. The follow-up chest CT 1 year later showed multiple bilateral pulmonary lesions which increased in number and size. Therefore, left lung partial mass resection by video-assisted thorascopic surgery was performed again. The patient was admitted to our hospital for right shoulder pain during the last 2 years. A well-defined mass of 2 cm × 4.5 cm was found in the right posterolateral waist by CT. Right armpit MRI showed a mass of 5.5 cm × 6.5 cm × 9.5 cm in chest wall. The lesions were irregular margined and had well-defined borders. Both masses were resected completely and the pathologic findings were also consistent with leiomyoma. The patient was followed up, and no metastases were found again.

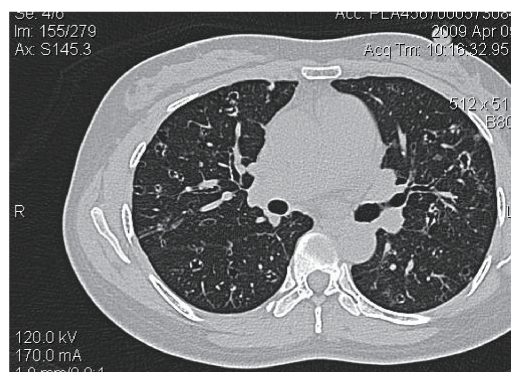


Fig 1 Chest CT showed multiple small thin-walled cysts uniformly distributed in bilateral lungs

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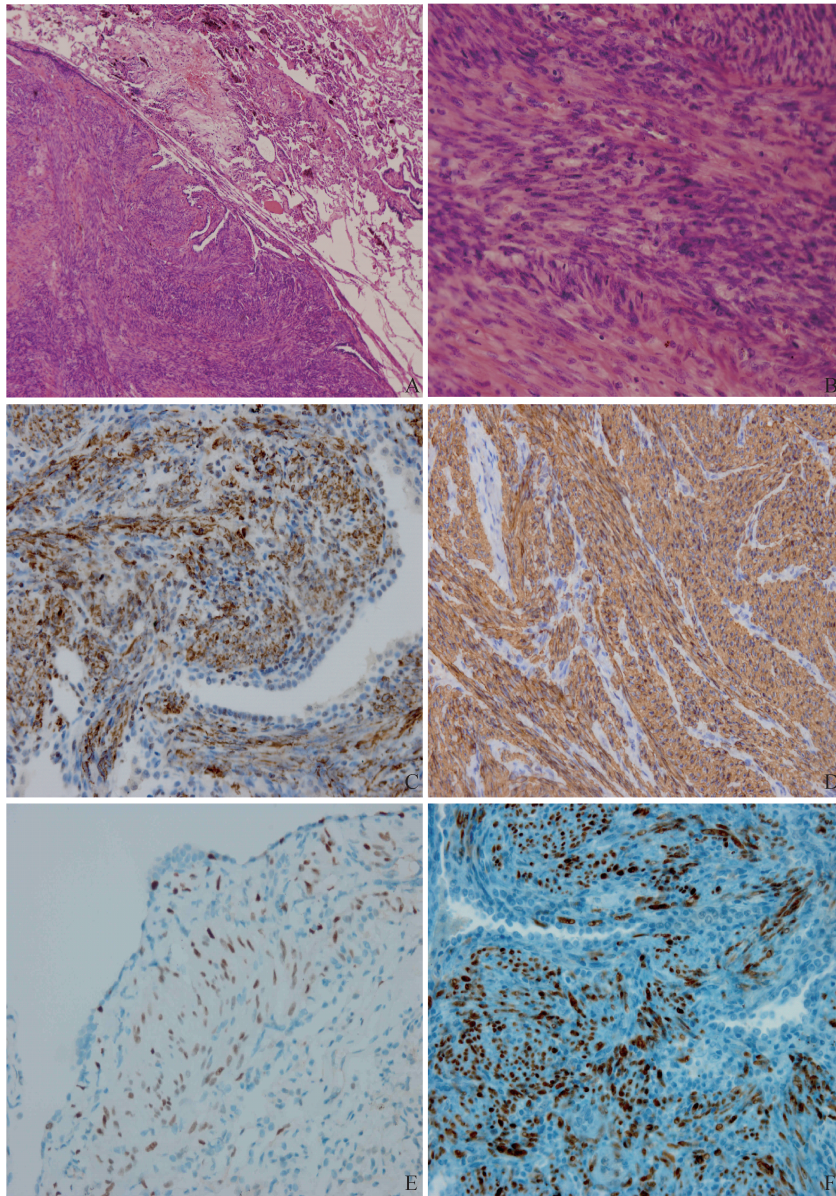


Fig 2 Histologic findings of the nodules resected from the lung by HE and immunohistochemical staining

A-B: HE staining; C-F: Immunohistochemical staining; A: Metastatic lung nodule ($\times 40$); B: Benign-appearing smooth muscle cells without nuclear atypia or mitotic index ($\times 400$); C: DES (+) throughout the pulmonary nodules ($\times 400$); D: SMA (+) throughout the pulmonary nodules ($\times 400$); E: ER (+) ($\times 400$); F: PR (+) ($\times 400$).

Case 3 A 44-year-old female complained of 2-month cough went to our hospital for pulmonary nodule suspected tuberculoma on Apr 7th, 2009. She received the hysteromyomectomy 3 years ago and subtotal hysterectomy for uterine leiomyoma 1 years ago. Physical examination revealed good physical condition. Chest CT presented a nodule of 2.0 cm \times 1.6 cm \times 2.0 cm in the left lung. Pathologic finding from left lung wedge resection revealed a diagnosis of BML in the lung. Followed-up information showed no sign of local or distant recurrence.

Case 4 A consulting patient of 36-year-old

female was found there were multiple nodules in the lungs by chest CT. Her pathological section was sent to our hospital in Nov, 2008. Physical examination was not significant. Chest CT showed multiple and bilateral masses in various sizes distributing throughout the lungs. The findings of pathological section from the left lung wedge resection were consistent with leiomyoma. There was no change of the nodules after the surgery.

Discussion BML is a rare entity with only a few reports in medical literatures, which can occur in any age group but most commonly occur between 30 and 74 years old. It was recognized by Steiner in

1939 for the first time, and was believed to be a primary lung neoplasm and named as metastasizing fibroleiomyoma of the uterus^[1]. Although it is most commonly seen in the lung, other sites of involvement include lymph nodes, peritoneum, retroperitoneal structures, abdomen and bones^[2-3]. Women who have undergone hysterectomy for leiomyomas are the most commonly affected population and are usually asymptomatic at presentation. The origin of this rare disorder has been somewhat controversial, someone claims a pathogenetic hypothesis of monoclonal origin of both the uterine and pulmonary tumors. Lee^[4] analysed the chromosome of both uterine and pulmonary tumor tissues, and found significant overlapping genetic abnormalities in both lesions, suggested that both lesions were histogenetically related to each other. Case 2 in our report may support this point. She was diagnosed leiomyoma in the lung and leiomyoma were found both at waist and chest wall in the following 2 years. Because we could not compare the pathologic specimens of the three surgeries and this just is our guess. However, pulmonary BML and the uterine tumor are discovered at the same time sometimes. Another possibility of surgically induced mechanical displacement from the preexisting benign uterine tumor has been suggested, because the development of BML usually follows a few years after the excision of uterine leiomyoma in most cases^[4-5]. So BML has been recognized as originating from uterine leiomyoma of an unknown malignant potential^[6]. Besides, tumor growth mainly depends on hormone. Still others suggest multifocal independent proliferation of smooth muscle tissue. Regarding different clinical behavior of the tumor, not every case seems to have the same histogenesis, and they can be heterogenous. In other word, we should compare pathologic specimens of the hysterectomy and lung biopsy in the future.

A few cases of BML may be associated with respiratory symptoms, such as dyspnea, cough and chest pain, most of them are generally asymptomatic and diagnosed coincidentally by routine chest CT for other reasons. However, it can lead to respiratory failure even death^[7-8]. Regarding the imaging findings, BML characteristically presents as numerous well-defined pulmonary

nodules of various sizes ranging from a few millimetres to several centimetres. But tiny calcification can rarely be seen^[7]. To our knowledge, multiple thin-walled cysts of various sizes uniformly distributed throughout both lungs, as case 1, has been rarely described previously. However, the explanation for multiple thin-walled cysts of various sizes in image is obscure. The cyst lesion may be explained as follows: (1) chronic inflammation; (2) continuous secretion of the cyst wall. The reason of the cyst formation requires further investigation. And we don't find similar report before. Pulmonary nodules usually show little change and may even spontaneously regress sometimes. But case 2 demonstrated that solid nodules grew in number and size and metastasize to parenchyma in a short time, which made it an unusual case.

According to the differential diagnosis, several diseases should be considered: Pulmonary hamartomas are lesions composed of normal tissues arranged in a disorderly pattern. Presence of fat, cartilage and calcium is frequent. They rarely occur in multiple lesions on radiographic examination. The histopathology of the lung samples show several scattered well-demarcated nodules composed of smooth muscle bundles without cellular pleomorphisms or mitotic activity.

Lymphangioleiomyomatosis is the proliferation of smooth muscle cells from lymphatic walls in the lung and lymph nodes. Young women can present with a spontaneous pneumothorax, chylous pleural effusion, or progressive dyspnea. Imaging finding includes honeycomb pattern on chest radiographs and numerous thin-walled lung cysts on CT. Case 1 diagnosed as lymphangioleiomyomatosis at first should be differentiated from this disease.

Leiomyosarcomas often leads to biologically malignant behavior. There are cellular pleomorphism and increased mitotic figures in the lung samples. Besides, BML also should be differentiated from inflammatory pseudotumor, tuberculoma, sarcoidosis and pulmonary histiocytosis X-ray.

If feasible, surgical resection has been advocated as the treatment of first choice. Estrogen and progesterone receptors have been identified in lung lesions, and this has led to hormonal therapy,

such as gonadotrophin-releasing hormone (GnRH) antagonists, medroxyprogesterone, ovarian ablation, and even adjuvant chemotherapy. However, in case of symptomatic or progressive disease, both hormonal therapy and wedge thoracotomy would be the appropriate^[2,7,9-10]. Lung lesions tend to remain stable with occasional regression after surgery, so further therapy may not always be suggested. For the 4 cases, we just did lung wedge resection without any other therapy, and all of them are well up to now. Because of the limited number of therapeutic options, new drugs and new therapeutic modalities should be considered. Some of the new drugs like Gleeevel (Novartis pharmaceuticals) have been suggested to have some effect on this tumor^[9]. Further extensive molecular, cytogenetic and chromosomal abnormalities studies of these tumors are needed to confirm pathogenetic mechanism of the transportation.

Median survival of the BML patients was 94 months after the excision of intrapulmonary lesions, and prognosis is favorable in most patients with BML.

BML is a rare disease, although the fact that uterine leiomyomas in the general population is of high frequency. BML should be considered in any asymptomatic patient presenting with pulmonary nodules and a history of a leiomyomatous uterus. Strengthening the recognition of the characteristics of BML is essential to avoiding mis-diagnosis and over-treatment.

【关键词】 benign pulmonary metastasizing leiomyoma; pulmonary nodule; estrogen; progesterone

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