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【 CASE REPORT 】

A Fast-growing Benign Metastasizing Leiomyoma Mimicking Malignancy

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Abstract:
We herein report a rare case of fast-growing benign metastasizing leiomyoma. A 52-year-old woman was admitted to our hospital with abnormal chest shadows. Chest computed tomography showed well-circumscribed cystic tumors. Because malignancy could not be completely distinguished in fast-growing tumors, video-assisted thoracic surgery was performed. The pathological findings revealed many cysts and the proliferation of smooth muscle cells. According to the Stanford criteria, the tumor was diagnosed as benign metastasizing leiomyoma. One possible reason for the fast growth of the tumor was enlargement of the cysts. Malignant diseases characterized by cystic tumors are rare but occasionally reported. Therefore, differentiation by a pathological examination is essential.

Key words: benign metastasizing leiomyoma, fast-growing tumor, cystic tumor

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Introduction

Benign metastasizing leiomyoma (BML) is a rare condition of uterine leiomyoma with pathologically benign findings but pulmonary metastasis. Fast-growing cystic BML is extremely rare. Many patients with BML have a medical history of myomectomy or hysterectomy.

The mean time from the primary surgery to the diagnosis of BML was 14.9 years. BML usually progresses quite slowly. In our case, the fast-growth of a tumor in a short period of one year was able to be observed by imaging over time. A fast-growing tumor is primarily considered malignant. However, this is a valuable case of a fast-growing benign tumor. To our knowledge, the causes of fast-growing BML have been poorly documented. We also investigated three possible causes of fast-growing BML, including the presence of malignant tumors, hormone-dependent tumors, and rapid expansion of cysts.

Case Report

A 52-year-old woman was admitted to our hospital for a further examination of her chest abnormal shadow. She had undergone uterine myomectomy 15 years earlier and had recently taken low-dose pills and iron supplements for iron deficiency anemia due to hypermenorrhea caused by residual uterine myoma.

She was 155 cm tall and weighed 50 kg. Other physical examinations revealed no significant findings. Although many laboratory tests, including tumor markers, were normal, the hemoglobin level was low (9.9 g/dL). Her chest roentgenogram showed a mass in the left hilum of the lung (Fig. 1A), and a chest roentgenogram taken about one year earlier also showed a slight mass at the same site. The tumor had grown rapidly over the past year (Fig. 1B). Chest computed tomography (CT) revealed well-circumscribed high-density masses in the left superior lingular segment and right lower lobe (Fig. 2A). T2-weighted images of magnetic resonance imaging also showed a high-intensity pattern, suggesting a cystic mass (Fig. 2B).

Because the patient had multiple lesions, pulmonary metastasis of malignant disease was initially suspected. Sputum cytology was performed, but the result was class II. Systemic CT was also performed for the primary malignant lesion search. However, no primary malignant tumor was de-

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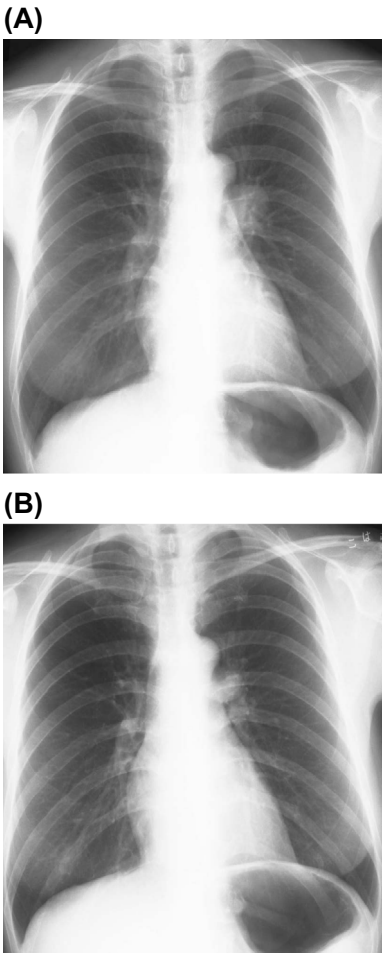

Figure 1. **(A) The initial chest roentgenogram revealed a round mass in the left hilum. (B) A chest roentgenogram taken about a year ago revealed a slight lesion in the same area, which had clearly grown rapidly in the past year.**

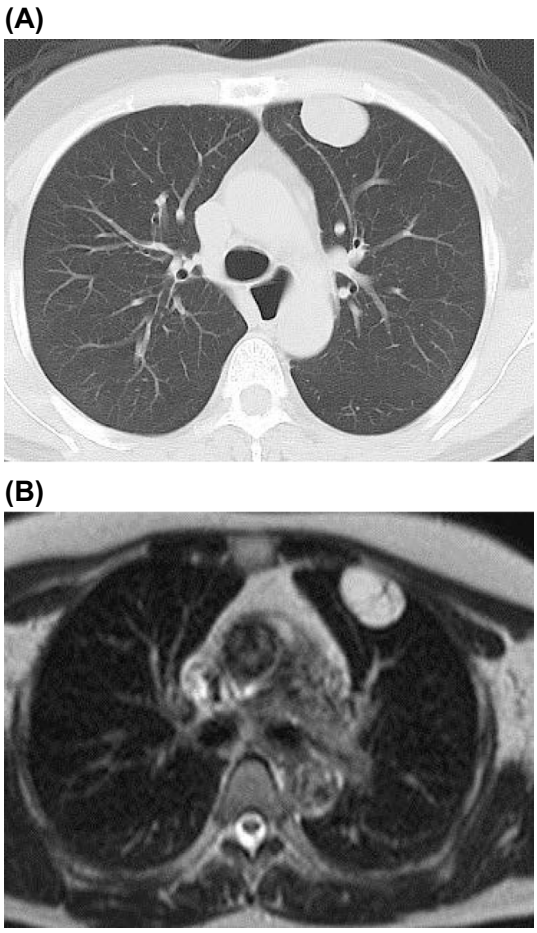

Figure 2. **(A) Initial chest computed tomography showed a well-circumscribed high-density mass in the left superior lingular segment. (B) The high-intensity pattern on T2-weighted magnetic resonance imaging indicated a cystic mass.**

tected aside from uterine leiomyoma. 18-fluoro-2-deoxy-D-glucose positron emission tomography/CT did not identify any abnormal uptake in the lung lesions or other sites. These findings suggested that the lung tumor was a benign disease.

However, the clinical course of a fast-growing tumor in a short period did not completely rule out malignancy, and several diagnostic methods for the pathological diagnosis of lung tumors were investigated. Bronchoscopy was initially planned for a definitive diagnosis but could not be performed because the part of the bronchus that was associated with the tumor could not be identified. Finally, video-assisted thoracic surgery was performed. We resected only the lesion in the left lingular segment for a definitive diagnosis.

The macroscopic findings of the resected specimen showed cystic tumors (Fig. 3A), and the cyst fluid was clear and colorless (Fig. 3B). The cell classification of the cyst fluid was as follows: macrophages 85%, lymphocytes 14%, and neutrophils 1%. No bacteria were detected in the fluid culture, and the cytology was class II. The cellular components of the cyst fluid were almost the same as those of normal bronchoalveolar lavage fluid. The pathological findings revealed simple columnar epithelium components in the smooth muscle cell (Fig. 4A). The space surrounded by the simple columnar epithelium components was expanded in some places, and large and small cysts had formed. (Fig. 4B). The simple columnar epithelial components were positive for thyroid transcription factor-1 and cytokeratin 7 (Fig. 4C) and negative for estrogen receptor and progesterone receptor on immunohistochemistry, indicating proliferation of alveolar epithelial cells. The solid components were positive for smooth muscle actin (Fig. 4D), indicating smooth muscle cells, and were also positive for desmin, estrogen, and progesterone receptor (Fig. 4E) and negative for CD10, HMB45, S100, and MIB-1 on immunohistochemistry (Table). According to the Stanford Criteria (1), the patient was diagnosed with leiomyoma rather than leiomyosarcoma based on a comprehensive assessment of three indicators: cytologic atypia, coagulative necrosis, and the mitotic index. Previous systemic CT had shown residual uterine myoma (Fig. 5). A diagnosis of BML of the lung was made based on the above pathological and clinical findings and surgical history of uterine myomectomy. Unfortunately, a specimen from uterine myomectomy performed 15 years earlier was

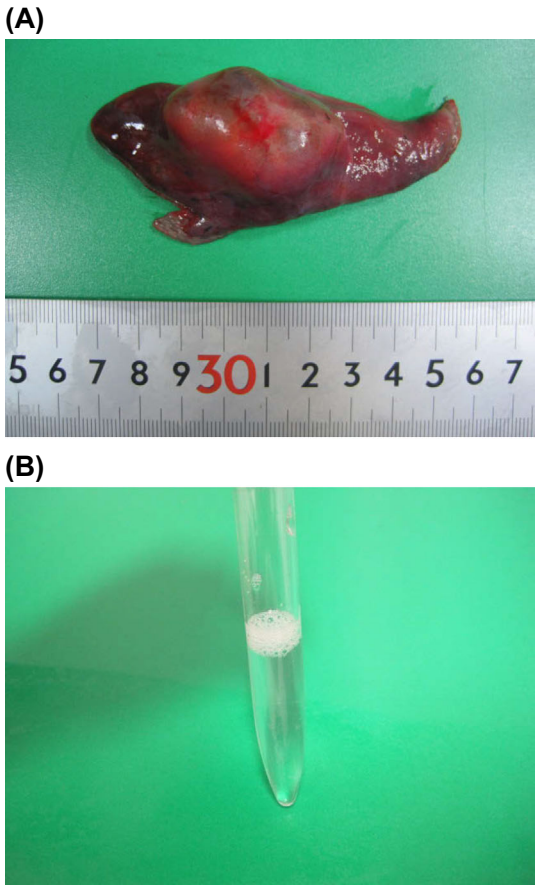

Figure 3. **(A) Macroscopic findings of the resected specimen showed a cystic mass. (B) The fluid in the cyst of the resected specimen was clear, and its cellular components were almost the same as those of normal bronchoalveolar lavage fluid.**

not available and thus could not be compared with this resected specimen.

The patient was referred to the gynecology department and is now being followed up as an outpatient. According to the patient's gynecologist, the residual lesion on the right side grew later and then has been removed, but the histological findings were similar. No new lesions have appeared since then.

Discussion

We herein report an extremely rare case of fast-growing BML of the lung mimicking malignancy. Pulmonary leiomyomas are divided into primary and metastatic tumors. Most primary pulmonary leiomyomas are solitary, have negative hormone receptors on immunohistochemistry, and contain no epithelial components. However, the present case findings conflicted with all of the above conditions, being more consistent with metastatic leiomyoma than primary leiomyoma.

BML is usually detected at a median of 14.9 years after hysterectomy or myomectomy and is usually stable in size or grows very slowly (2). To our knowledge, this is the first report of BML growing so fast within a short period of one year and requiring differentiation from malignancy. There are three possible reasons for the fast-growing BML in our patient: the presence of malignancy, the presence of a hormone-dependent tumor, and the expansion of a cyst.

Regarding the possible involvement of malignancy, several reports of malignant transformation from uterine leiomyoma to leiomyosarcoma have recently been published (3-5). Although this case showed features that tended to indicate a benign tumors, such as the presence of intratumoral cysts and clear tumor margins on chest CT, malignant transformation might nevertheless have occurred. Therefore, a histological examination in this case was considered to be essential. Fortunately, this notion was dismissed in our patient, as BML was diagnosed using Stanford's criteria. According to Wolff et al., BML appears bland on light microscopy but may exhibit mitotic activity on electron microscopy, indicating cellular immaturity and suggesting that BML is a low-grade metastatic leiomyosarcoma (6). Though BML assumed to be low grade malignancy grows over several years, it does not compatible with the clinical course of rapidly growing tumor like our case. For these reasons, it is unlikely that the fast-growing tumor in this case developed due to malignancy.

Regarding the possible involvement of a hormone-dependent tumor, spontaneous regression of uterine leiomyomas has been reported in both pregnant (7) and menopausal patients (8), with decreased levels of endogenous hormones such as estrogen and progesterone. Thus, uterine leiomyomas themselves are hormone-sensitive tumors. We considered that the BML in the present case might also have grown rapidly due to the influence of estrogen or progesterone hormones. However, our patient had been taking low-dose pills for menorrhagia due to uterine leiomyoma; low-dose pills have been reported to reduce the menstrual blood volume by more than half. The mechanism underlying the decrease in menstrual blood volume involves a decrease in endogenous estrogen and progesterone by low-dose pill administration. These mechanisms are presumed to explain the low serum estrogen and progesterone levels in our patient. Therefore, we suspected that a hormone-dependent rapid tumor growth was not involved in our patient. However, the actual truth of the matter was unclear, as the blood levels of estrogen and progesterone were not measured in our patient.

Regarding the possible involvement of cyst expansion, as observed in the present case (Fig. 4A), BML is characterized by a mixture of smooth muscle cell components and spaces lined with bronchial epithelial components. Shin et al. reported that cysts of BML show a space surrounded by dilated bronchi located near smooth muscle cells. These dilated bronchi may be the result of destruction of the elastic tissue of the bronchial epithelium and air trapping due to proliferation of peribronchial smooth muscle cells (9). Since BML contains only two components - dilated bronchial luminal components and smooth muscle cell components - the rapid tumor growth may be attributed to fast-expanding bronchial epithelial luminal components. In addition, Her-

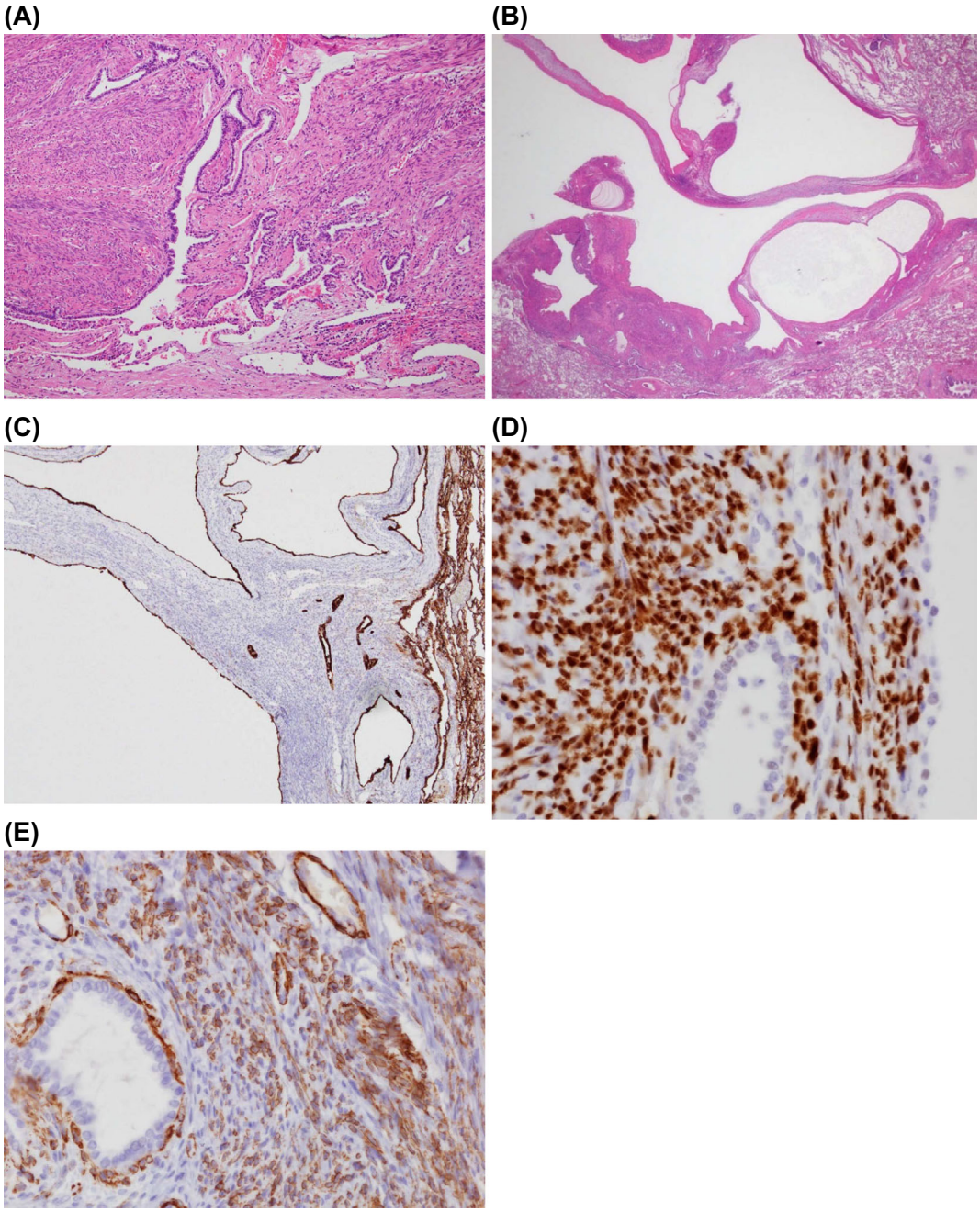

Figure 4. **(A) Histology of the resected specimen showed a mixture of smooth muscle cell components and spaces lined by bronchial epithelium [Hematoxylin and Eosin (H&E) staining, ×100]. (B) The spaces lined by bronchial epithelium had partially expanded to form both large and small cysts (H&E staining, ×100). (C) The bronchial epithelium surrounding the cyst was positive for cytokeratin-7 on immunohistochemistry (×200). (D) The solid lesion was positive for smooth muscle actin on immunohistochemistry and indicated smooth muscle cells (×400). (E) The solid lesion was also positive for estrogen and progesterone receptor on immunohistochemistry (×400).**

rera et al. showed through electron microscopy that the bronchial epithelium within the BML contained Clara cells and type II alveolar epithelial cells (10). The fluid produced by these cells accumulated without outflow, resulting in the enlargement of the bronchial lumen and formation of both large and small cysts. The cellular components of the cyst fluid were almost the same as those of normal bronchoalveolar lavage fluid. These findings may thus support the validity of the mechanism of cyst development observed in this case. Based on the above, we suspect that the rapid growth of the tumor in the present case was due to cyst enlargement, but the reason for the rapid growth of the cyst is still unclear. We hope to clarify the associated mechanism by accumulating similar cases in the future.

Conclusion

This is the first report of fast-growing cystic BML monitored by imaging. Malignant tumors that manifest as cystic

Table. **Immunohistochemistry for the Two Components of the Tumor.**

	The simple columnar epithelial components	The Solid components
Thyroid transcription factor-1	+	-
Cytokeratin 7	+	-
Estrogen receptor	-	+
Progesteron receptor	-	+
Smooth muscle actin	-	+
Desmin	-	+
CD10	n.d.	-
HMB45	n.d.	-
S100	n.d.	-
MIB-1	n.d.	-

n.d.*: not done

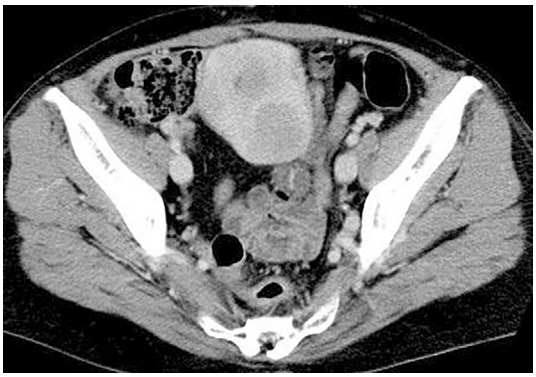

Figure 5. **Pelvic computed tomography showed residual uterine leiomyoma.**

tumors are rare but have occasionally been reported (11, 12). In a fast-growing cystic tumor, imaging cannot differentiate benign lesions from malignant ones. Therefore, a histopathological examination is essential for confirming the differential diagnosis.

The authors state that they have no Conflict of Interest (COI).

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