Refractory Pneumothorax Due to Cystic Pulmonary Metastasis of a Low-grade Endometrial Stromal Sarcoma: A Case Report

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Low-grade endometrial stromal sarcoma (LG-ESS) is a rare uterine neoplasm. Computed tomography (CT) revealed the presence of multiple small bilateral pulmonary nodules in a 58-year-old woman 1 year after surgery for LG-ESS; the clinical diagnosis was pulmonary metastasis. Hormone therapy with progesterone was initiated, after which most of the solid nodules disappeared and some transformed into cystic lesions. Seven years after hormone therapy, the patient experienced repeated pneumothorax. The cause of the pneumothorax was perforation of a metastatic focus within the wall of a small subpleural cyst that was not evident on CT images.

Key words: hormone therapy, low-grade endometrial stromal sarcoma, pneumothorax, pulmonary metastasis

INTRODUCTION

Low-grade endometrial stromal sarcoma (LG-ESS) is a rare neoplasm representing 0.2% of all malignant uterine neoplasms and 15% of all uterine sarcomas [1]. It is characterized by indolent progression and sensitivity to hormone therapy [2]. Although it has the potential to metastasize and recur, its long-term prognosis is promising [3]. Secondary pneumothorax associated with malignant tumors is well known, with an incidence of 0.05–0.5% [4]. Pulmonary metastasis of LG-ESS is less common than local recurrence [1, 5]. In contrast, the incidence of pneumothorax in patients with LG-ESS is high, reaching 19.4% [6]. Thus, pneumothorax is a potential complication in these patients, especially those with cystic pulmonary metastasis. Here, we report a case of intractable pneumothorax due to multicystic pulmonary metastasis of an LG-ESS and review the relevant literature.

CASE PRESENTATION

A 58-year-old woman was referred to our department for treatment of a right pneumothorax that had occurred three times in the past year. Her medical history included hysterectomy and unilateral salpingo-oophorectomy for LG-ESS 8 years previously, after which she was followed up at another hospital. She was a non-smoker and had no other medical history.

One year after the uterine surgery, chest computed tomography (CT) revealed that the patient had developed multiple small, solid bilateral pulmonary nodules (Fig. 1A). Although there was no pathological diagnosis, hormone therapy with progesterone was started based on the clinical diagnosis of pulmonary metastasis. Subsequently, most of the solid nodules disappeared and some transformed into cystic lesions (Fig. 1B). No signs of recurrence of any of the lesions were observed except for the lung metastasis. Initial CT at our department also showed a slightly collapsed right lung and multiple small bilateral cysts, but no lesion suggestive of the cause of the pneumothorax. Physical findings showed no particular problems.

Thoracoscopic surgery was then performed to further investigate and treat the pneumothorax. The surgical findings included multiple sporadic small blebs, which were not evident on CT, on the surface of the lungs (Fig. 2). An air leak was identified from one of them. Pulmonary wedge resections were performed, and the stapling lines were coated with polyglycolic acid sheets to prevent bullae formation near the stapling line.

Although no tumor was macroscopically visible in the resected specimens, pathological examination revealed a proliferation of short spindle cells in the cystic wall (Fig. 3A, B). These tumor cells had minimal nuclear atypia and a low mitotic index. Immunohistochemical staining showed strong nuclear staining for estrogen and progesterone receptors and diffuse cytoplasmic staining for CD10 (Fig. 3C). These features were consistent with pulmonary metastasis of the LG-ESS. The endometrial stromal sarcoma (ESS) cells had infiltrated the visceral pleura (Fig. 3A), which contributed to the development of pneumothorax.

Over the next 3 years, the same hormone therapy was continued, pneumothorax occurred repeatedly in the left and right lungs. Three surgical and pathological findings indicated that the pneumothorax was caused by the perforation of newly appearing small

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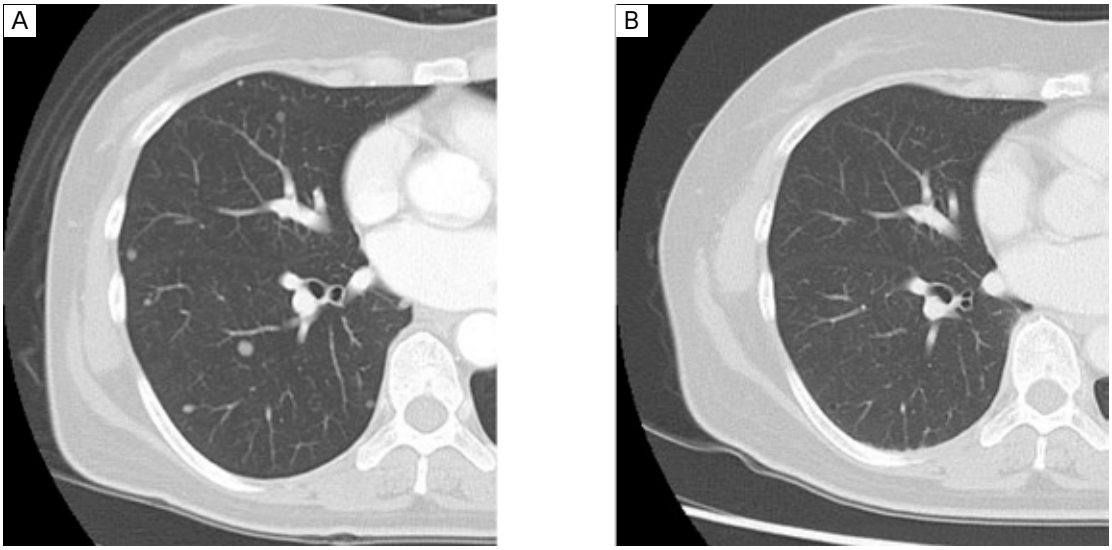

Fig. 1 Chest computed tomography (CT) reveals multiple small, solid bilateral pulmonary nodules (A), the disappearance of most of the solid tumor, multiple thin-walled cystic lesions (B).

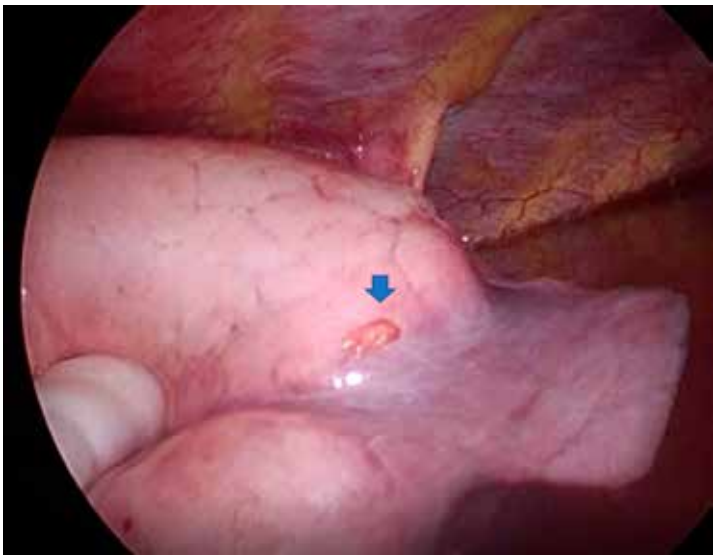

Fig. 2 Air bubbles are observed in the small bullous lesions on the pulmonary surface.

metastatic cystic lesions as before. The morphology of the tumor cells (e.g., nuclear atypia, mitotic index) in the resected specimens had not changed over time. Pleurodesis using an autologous blood patch was performed only once to prevent a prolonged postoperative air leak. CT during the past 3 years showed a slight increase in the number and size of the cystic lesions (Fig. 4A, B). Although the patient had no other recurrent lesions, these findings suggested the presence of slowly progressive metastatic pulmonary lesions. Except for pneumothorax, there were no other abnormal findings, and there was no limitation in the patient's daily activities. Currently, there are no additional metastatic lesions or recurrent pneumothoraxes.

DISCUSSION

We experienced a case with ESS with repeated pneumothorax, that we were able to follow the long-term course of CT findings and evaluate detailed pathological findings of resected lungs.

The World Health Organization currently recognizes four endometrial stromal tumor types: endometrial stromal nodule (ESN), LG-ESS, high-grade ESS, and undifferentiated uterine sarcoma [7]. Based on their histological characteristics, ESNs and LG-ESSs are considered low-grade malignant tumors. However, unlike ESNs, LG-ESSs have the potential for metastasis, including myometrial, vascular, and lymphatic invasion. Approximately 40% of patients with endometrial stromal tumors experience recurrence after a long disease-free interval [3]. Recurrence is most common in the pelvis and abdomen and less common in the lungs and vagina [1, 5]. Because estrogen and progesterone regulate the proliferation and differentiation of LG-ESS cells, hormone therapy is effective for recurrent and metastatic tumors [2]. LG-ESS has a generally favorable prognosis, with a 5-year disease-specific survival rate of 80–90% [8].

Pulmonary metastasis exhibits various patterns on CT. Multiple solid lesions (50%) are common, and

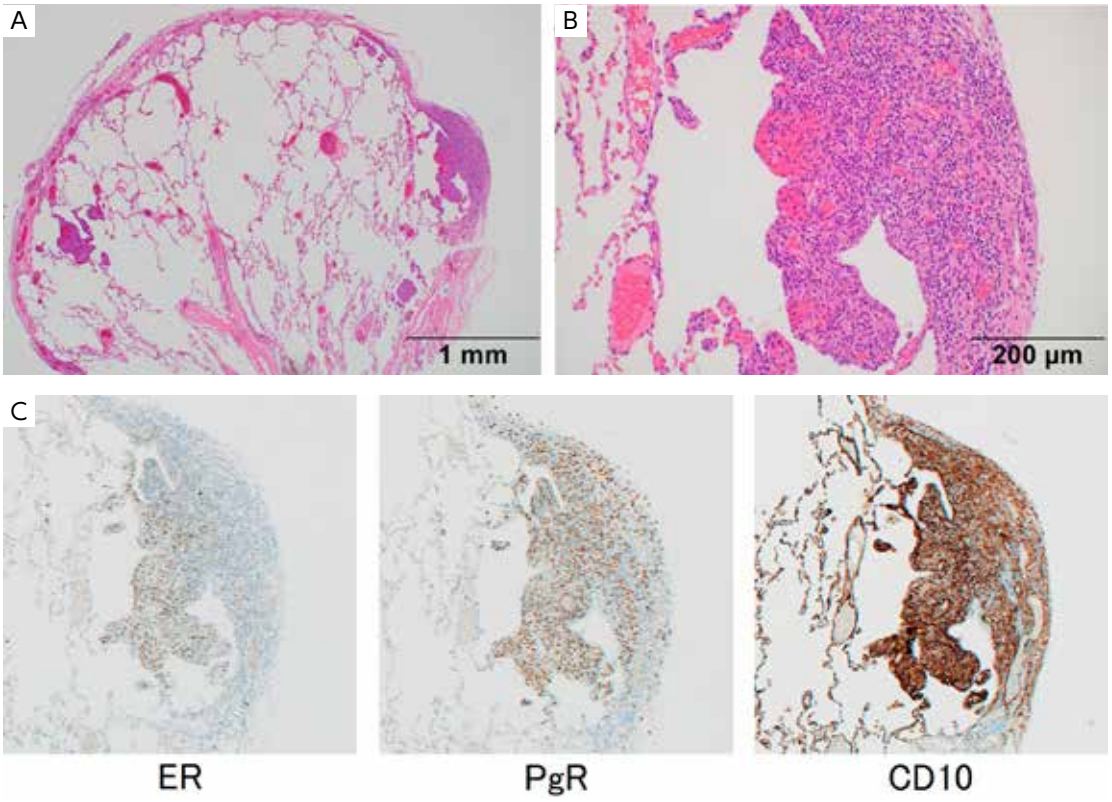

Fig. 3 (A, B) Pathologic examination of the resected specimens reveals a proliferation of short spindle cells in the cystic wall (hematoxylin and eosin staining). (C) Immunohistochemistry shows strong nuclear staining for estrogen and progesterone receptors and diffuse cytoplasmic staining for CD10.

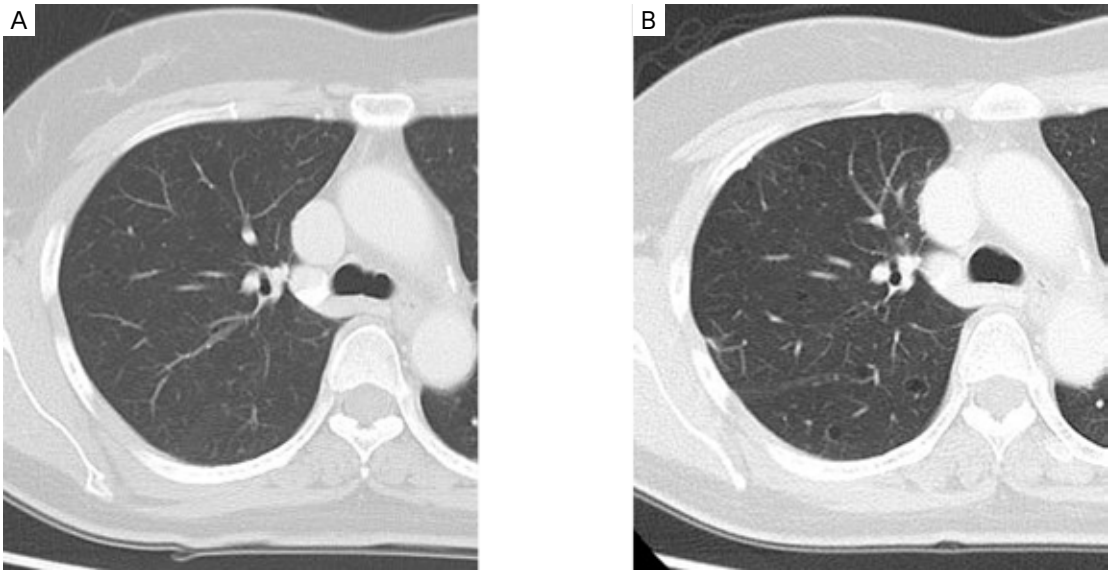

Fig. 4 Chest computed tomography (CT) reveals an increase in the number and size of the cystic lesions compared with those 3 years earlier (A, B).

solitary (15%) and cystic (15%) lesions are also present [1, 7]. The cystic type of lung metastasis is especially associated with the development of pneumothorax. In this case, a series of CT images showed that the pulmonary metastases first appeared as solid lesions. After initiating hormone therapy (progesterone), most of the solid lesions disappeared and some transformed into cystic lesions, as shown via CT. The tumor cells in specimens obtained later (i.e., during pneumothorax surgery) expressed estrogen and progesterone receptors. Therefore, hormone therapy was an appropriate choice for this patient.

When we first managed the patient's pneumothorax, she had already been on hormone therapy for 7 years. The diameter of the cystic lesions remaining after therapy was approximately 1 cm on CT images, and it was unclear whether tumor cells remained in the cystic wall. We initially thought that the remaining

thin-walled cysts were formed by the therapy-induced disappearance of ESS cells from the solid tumors. The pneumothorax appeared to be clinically unrelated to the metastasis; instead, the surgical findings suggested that it was caused by the rupture of a small subpleural cystic lesion that was not evident on CT. However, pathological examination of the subpleural lesions revealed that the tumor cells were locally present on the cystic pleural side and that pulmonary metastasis accounted for pneumothorax development. The previous literature has reported on patients with ESS who presented with pneumothoraxes [9–11]. However, differently from these previous reports, we have followed the long-term CT findings and evaluated the detailed pathological findings of the resected lung in this case.

Three years after the surgery for pneumothorax, we noted a slight increase in the number and size of the cystic lesions compared with those on previous CT images. This observation suggests that the pulmonary metastasis had progressed slowly. The pathological findings of the resected specimens of the subpleural lesions over 3 years, all newly appearing metastatic tumor cells were of the low-grade malignant form and localized within the cyst wall just below the pleura. There were no tumor thrombi in the blood vessels. These findings suggest that the metastasis occurred via the lymphatic vessels just below the pleura and that the subpleural cyst was formed by a check-valve mechanism related to tumor invasion of the bronchioles rather than by destruction of the lung parenchyma by the tumor [12].

In previous reports, CT showed the presence of cystic lesion on the surface of the lungs [9–11]. However, pneumothorax treatment in this case was problematic owing to underestimation of pneumothorax recurrence. Because we focused only on the CT images, we could not predict that new metastatic lesions not detectable via CT would develop on the lung surface over time. Therefore, as with pneumothorax in general, chemical pleurodesis was considered unnecessary. Pneumothorax caused by multiple pulmonary cystic metastases from an LG-ESS differs from pneumothorax associated with other malignancies. In this case, although the cystic lung metastasis progressed, subpleural small cystic lesions on the lung surface also proliferated, causing pneumothorax. Therefore, if the progression of cystic pulmonary metastasis is suspected, procedures such as chemical pleurodesis [9] should be performed early to prevent recurrence caused by new subpleural lesions.

We need to pay close attention to the possibility of recurrent pneumothorax.

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CONFLICT OF INTEREST

There were no conflicts of interest.

REFERENCES

1) Aubry MC, Myers JL, Colby TV, Leslie KO, Tazelaar HD. Endometrial stromal sarcoma metastatic to the lung: A detailed analysis of 16 patients. Am J Surg Pathol 2002; 26: 440–9.
2) Kim GW, Basek SK, Han JJ, Kim HJ, Sung JY, Maeng CH. Pulmonary metastasizing low-grade endometrial stromal sarcoma: Case report and review of diagnostic pitfalls. Diagnostics (Basel) 2022; 12: 271.
3) Leath CA 3rd, Huh WK, Hyde J Jr, Cohn DE, Resnick KE, Taylor NP, *et al*. A multi-institutional review of outcomes of endometrial stromal sarcoma. Gynecol Oncol 2007; 105: 630–4.
4) Dines DE, Cortese DA, Brennan MD, Hahn RG, Payne WS. Malignant pulmonary neoplasms predisposing to spontaneous pneumothorax. Mayo Clin Proc 1973; 48: 541–4.
5) Chang KL, Crabtree GS, Lim-Tan SK, Kempson RL, Hendrickson MR. Primary uterine endometrial stromal neoplasms: a clinicopathologic study of 117 cases. Am J Surg Pathol 1990; 14: 415–38.
6) Xu Y, Liang ZX, Guo JT, Su X, Lu YL, Guan XZ. Cystic and solitary nodular pulmonary metastases in a patient with low-grade endometrial stromal sarcoma: a case report and literature review. Oncol Lett 2019; 18: 1133–44.
7) Ferreira J, Felix A, Lennerz JK, Oliva E. Recent advances in the histological and molecular classification of endometrial stromal neoplasms. Virchows Arch 2018; 473: 665–78.
8) Feng W, Hua K, Gudlaugsson E, Yu Y, Zhou X, Baak JP. Prognostic indicators in WHO 2003 low-grade endometrial stromal sarcoma. Histopathology 2013; 62: 675–87.
9) Dedalian A, Tran K, Lee C, Chopra S, Hu J Pneumothorax presentation in endometrial sarcoma patients receiving chemotherapy: A case series. Rare Tumors 2020; 12: 2036361320972865.
10) Chong SG, Mitchell P, Fabre A, *et al*. Recurrent pneumothoraces in a 65-year-old female: an unusual case of cystic lung disease. Eur Respir Rev 2014; 23(132): 271–272.
11) Shah DJ, Phadke VK, Oprea-Ilies G, *et al*. Spontaneous pneumothoraces due to metastatic endometrial stromal sar coma in a woman infected with HIV. Am J Respir Crit Care Med 2016; 193(1): 96–97.
12) Le Garff G, Lena H, Corbineau F, Kerbrat P, Delaval P. Unusual cause of recurrent pneumothorax: Excavated metastasis of osteosarcoma. Ann Thorac Surg 2001; 72: 2111–3.