Cystic, Nodular and Cavitary Metastases to the Lungs in a Patient with Endometrial Stromal Sarcoma of the Uterus

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Abstract

A 57-year-old woman, who had undergone hysterectomy for uterine myoma 11 years earlier presented with cystic, nodular and cavitary lesions simultaneously visible on computed tomography images of the chest. Histological examinations of both the resected lung and past “myoma” specimens demonstrated that the original uterine tumor was a low-grade endometrial stromal sarcoma (ESS) that had metastasized to the lungs. No previous reports have described the coexistence of cystic, nodular and cavitary lesions with pulmonary metastasis of ESS; however, we successfully correlated the radiologic appearance with the corresponding pathologic findings. Medroxyprogesterone acetate therapy has effectively kept the patient asymptomatic for approximately five years.

Key words: pulmonary metastases, endometrial stromal sarcoma, pneumothorax, progesterone


Introduction

Low-grade endometrial stromal sarcoma (ESS), a rare neoplasm comprising 0.2% of all uterine cancers and 15% of all uterine sarcomas (1), is classified separately from undifferentiated endometrial sarcoma. Low-grade ESS is histologically similar to proliferating endometrial stromal tissue, exhibits little cytological atypia or pleomorphism and is low in mitotic activity. The prognosis of patients with low-grade ESS is favorable in general, with a 10-year disease-free survival rates of 93% (2). However, approximately 40% of patients with low-grade ESS develop recurrent disease after long tumor-free intervals due to the slow-growing nature of the tumor (3). The major location of distant metastases is the lungs, with an incidence of pulmonary metastasis of 7% to 28% (4).

Pulmonary metastasis of low-grade ESS can manifest as various patterns on computed tomography (CT) images of the chest, including the presence of a solitary nodule, multiple nodules, multiple cysts and reticulonodular infiltrates (4-8). In patients with nodular pulmonary metastases of low-grade ESS, the differential diagnosis includes benign metastasizing leiomyoma (BML), carcinoid tumors, sclerosing hemangioma and metastasis of other neoplasms. On the other hand, cystic metastasis of low-grade ESS in the lungs should be carefully discriminated from lymphangioleiomyomatosis (LAM), mesenchymal cystic hamartoma and metastasis of leiomyosarcoma. However, the simultaneous coexistence of all of these imaging features in a single patient would result in a diagnostic dilemma.

In just such an experience, we encountered a patient with pulmonary metastasis of low-grade ESS who presented with cystic, nodular and cavitary lesions simultaneously. The patient had undergone hysterectomy and bilateral salpingo-oophorectomy due to uterine leiomyoma 11 years earlier. Pathologic and immunohistochemical examinations of her lung specimens greatly contributed to the ability to obtain a proper diagnosis, a rare pattern of pulmonary metastases of low-grade ESS, and provided a plausible explanation for the...
A 57-year-old woman was referred to our hospital in September 2008 for a workup of right pneumothorax. A CT scan of the chest revealed several nodules, cavitary lesions and multiple thin-walled cysts. The patient’s medical history disclosed that she was a farmer, had never smoked and had undergone hysterectomy and bilateral salpingo-oophorectomy for uterine myoma 11 years earlier. A physical examination was unremarkable. A laboratory examination showed a normal blood cell count with no biochemical abnormalities. Chest radiography demonstrated a cavitary nodule in the right upper lung field and a solid nodule in the left middle lung field (Fig. 1A). CT imaging of the chest supplemented these results by visualizing a cavitary nodule with an inhomogeneous wall thickness in the S2 area of the right lung (corresponding to the shadow indicated by the arrowhead in A) and a solid nodule (20×12 mm) in the S1 area of the left lung (corresponding to the shadow indicated by the arrow in A). Note the multiple thin-walled cysts scattered in the bilateral lung fields that are not visible on the chest radiograph.

**Case Report**

In December, the patient again developed left pneumothorax. Because her left lung was moderately collapsed, she was admitted to our hospital with a diagnosis of suspected BML of the uteri or the coexistence of an early stage of LAM and BML. Shortly after admission, right pneumothorax also developed and resolved immediately following the insertion of an intercostal chest tube. Meanwhile, the solid nodule in the S1 area of the left lung exhibited cavitary formation (not shown). In contrast to the right pneumothorax, the left lung remained in a collapsed state with a continuous air leak from the chest tube. Accordingly, video-assisted thoracoscopic surgery (VATS) was performed for treatment as well as further diagnosis. Consequently, partial resection of the lingular lobe was performed, including the cavitary nodule in the S1 area, with reinforcement of the resection line.

**Figure 1.** Radiologic findings in a patient with pulmonary metastasis of low-grade ESS. A: A chest radiograph obtained in September 2008 showed a cavitary nodule in the right upper lung field (arrowhead) and a solid nodule in the left middle lung field (arrow). B, C: Chest CT scans showing a cavitary nodule (18×15 mm) with an inhomogeneous wall thickness in the S2 area of the right lung (corresponding to the shadow indicated by the arrowhead in A) and a solid nodule (20×12 mm) in the S1 area of the left lung (corresponding to the shadow indicated by the arrow in A). Note the multiple thin-walled cysts scattered in the bilateral lung fields that are not visible on the chest radiograph.
using bioabsorbable non-woven fabric and partial ablation of the parietal pleura.

The pathologic examination of the resected lung specimen revealed dense and uniform proliferation of tumor cells with oval-shaped nuclei (Fig. 2A) in both the nodular portion and cavity wall of the left S’ cavitary nodule (Fig. 3A). There was little cytological atypia or pleomorphism, and mitosis was scanty. However, tumor cells appeared in a whorl-like arrangement around the vessels. An immunohistochemical examination demonstrated the tumors cells to be negative for α-smooth muscle actin (SMA) (Fig. 2B) and HMB45 (Fig. 2C) and strongly positive for CD10 (Fig. 2D). The cell nuclei were strongly positive for estrogen receptor (ER) (Fig. 2C) and strongly positive for CD10 (Fig. 2D). The cell nuclei were strongly positive for estrogen receptor (ER) (Fig. 2C) and strongly positive for CD10 (Fig. 2D). The cell nuclei were strongly positive for estrogen receptor (ER) (Fig. 2C) and strongly positive for progesterone receptor (PR) (Fig. 2F). Since the immunohistochemical findings of the lungs indicated low-grade uterine ESS, we reviewed the hysterectomized specimen that had been diagnosed as a uterine myoma at a local hospital 11 years earlier. That tumor also consisted of oval-shaped cells in a whorl-like arrangement around the vessels and exhibited expansive growth with a partly irregular border and venous invasion at the periphery. Immunoreactivity for ER, PR and CD10 was positive, while that for both SMA and HMB45 was negative (not shown). Therefore, we concluded that the uterine tumor resected 11 years previously was a low-grade ESS that had subsequently developed pulmonary metastasis.

The cystic lesions scattered in the specimen from the resected lingular lobe were composed of ESS cells and normal alveolar septal cells. It is notable that the ESS cells frequently occupied airways leading into cysts and only connecting portions of the cyst wall, whereas most of the cyst wall was composed of normal alveolar septal cells (Fig. 3B). On the other hand, numerous small nodules composed of ESS cells, which were not evident on CT images, lay in the parenchyma (Fig. 3C). In addition, ESS cells had infiltrated the visceral pleura in some places, which may have contributed to the development of pneumothorax (Fig. 3D).

After establishing this diagnosis, we initiated the treatment with medroxyprogesterone acetate (MPA) administered orally at a dose of 400 mg/day. The solid and cavity nodules disappeared within three to six months according to CT images of the chest. Some small cysts disappeared, although most remained unchanged. As of this writing, the patient has continued the MPA regimen and remained asymptomatic for approximately five years since its initiation. No new metastatic lesions have been identified.
This report describes the case of a patient with low-grade ESS and pulmonary metastasis whose CT images of the chest showed cystic, nodular and cavitary lesions coexisting simultaneously. Although low-grade ESS of the uterus generally has a favorable prognosis, the tumor tends to develop pulmonary metastasis; metastasis occurs even if the primary tumor is resected and the patient experiences a long tumor-free interval. Aubery et al. reported intervals from hysterectomy to subsequent pulmonary metastasis ranging from 2.5 to 20 years (4). Since low-grade ESS is frequently present for long intervals before the appearance of pulmonary metastasis and CT scans show such varied patterns as the presence of a solitary nodule, multiple nodules, multiple cysts and reticulonodular infiltrates (4-8), selecting the correct diagnosis is often a challenge, especially when several radiologic manifestations coexist. In this context, our patient is a very rare example. Her simultaneous expression of cystic, nodular and cavitary lesions was not only unique, but also made the diagnosis problematic.

The mechanisms underlying the coexistence multiple lesions on radiologic examinations await final substantiation. However, based on the results of the histopathologic examinations in this case and the patient’s clinical course, the following explanations have merit. First, the patient’s cavitary lesions apparently evolved from the nodular proliferation of ESS cells, since a nodule in the S1 area of the left lung demonstrated cavitary changes. Other researchers have asserted that the pathological mechanisms underlying the cavitary formation of a neoplasm include internal desquamation of tumor cells with subsequent liquefaction (9). Furthermore, we presume that the thin-walled cysts observed in this case developed due to the proliferation of ESS cells along peripheral small airways followed by the destruction of pa-
renchyma and air trapping. The detection of elastolysis, as demonstrated on Elastica van Gieson staining, in the patient’s tissues supports the presence of parenchymal destruction by ESS cells. Bronchiolitis and ensuing air trapping during cystic formations have been implicated in the pulmonary manifestations of Sjögren’s syndrome and other diffuse cystic lung diseases (10). Morgan et al. reported the potential of an elastic recoil force from normal alveolar tissue around a demolished area to cause thin-walled cysts (11). This mechanism appears to support the finding that most cysts remained intact in our patient, although the cavitory lesions and nodules composed of ESS cells disappeared following the administration of MPA therapy. However, the disappearance of some cysts was noted, which indicates that the air trapping generated by proliferating ESS cells along small airways was dominant, whereas parenchymal damage, if any, was minimal in some cysts.

The optimal treatment for low-grade ESS with pulmonary metastasis has not been established as of yet. However, several case reports have been published regarding the efficacy of progesterone and aromatase inhibitors in the treatment of metastatic low-grade ESS (12-16), and the guidelines for uterine neoplasms proposed by the Japan Society of Gynecologic Oncology recommend the use of hormonal therapy, including progesterone and aromatase inhibitors, in cases of recurrent low-grade ESS (17). For such patients, the median overall survival from recurrence is 41 to 62 months (12-16). Our patient has responded very well to MPA therapy, tolerating the treatment well with no adverse events for approximately five years. During this time, no new metastatic lesions have been identified. Consistent with the findings of previous reports (12-16), MPA therapy should be the first-line therapy for pulmonary metastases of low-grade ESS.

In conclusion, our patient with pulmonary metastasis of low-grade ESS 11 years after hysterectomy and bilateral salpingo-oophorectomy, manifested cystic, nodular and cavitary lesions simultaneously. Each of these radiologic findings individually is known to reflect pulmonary metastasis of low-grade ESS; however, the coexistence of these imaging features should also be considered indicative of pulmonary metastasis of low-grade ESS in cases involving a past history of resection of “leiomyoma of the uterus.”

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

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References