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Case Report

A Case of Pulmonary Benign Metastasizing Leiomyoma Occurring after Uterine Myomectomy

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SUMMARY

Benign metastasizing leiomyoma (BML) is a very rare disease, and although it was reported as early as 1939 to result from metastasis of benign uterine myoma to the lungs and lymph nodes, its pathology remains obscure. Here, we describe a case of pulmonary BML occurring after uterine myomectomy in a 42-year-old woman. She presented with a 2-week history of dry cough on exertion. Chest radiography and computed tomography (CT) revealed bilateral multiple nodular lesions. The patient had a history of uterine myoma and previously underwent myomectomy. For definitive diagnosis, lung biopsy was performed by video associated thoracoscopic surgery. Histopathologic examination of biopsy specimens revealed pulmonary BML occurring after uterine myomectomy. For treatment of the pulmonary BML, gonadotropin-releasing hormone was initially administered, and 1 month later the patient underwent complete hysterectomy and bilateral salpingo-oophorectomy. Chest CT 6 months after surgery showed that the size and number of lung multiple nodular lesions did not increase compared with those before surgery. In future studies, we aim to investigate a larger number of pulmonary BML cases, as well as establish specific treatments and investigate the prognosis of the disease.

Abbreviations :
BML : benign metastasizing leiomyoma
SS : Sjögren's syndrome
CT : computed tomography
H&E : hematoxylin and eosin
VATS : video associated thoracoscopic surgery
CA : carbohydrate antigen
Ig : immunoguloblin
αSMA : α smooth muscle actin

Key Words : uterine myoma, pulmonary benign metastasizing leiomyoma, video associated thoracoscopic surgery

INTRODUCTION

Benign metastasizing leiomyoma (BML) was first described in 1939[1]. Since then, Jautzke et al[2] and Mikami et al[3] reported BML in 74 people in Western countries and 16 individuals in Japan, respectively.

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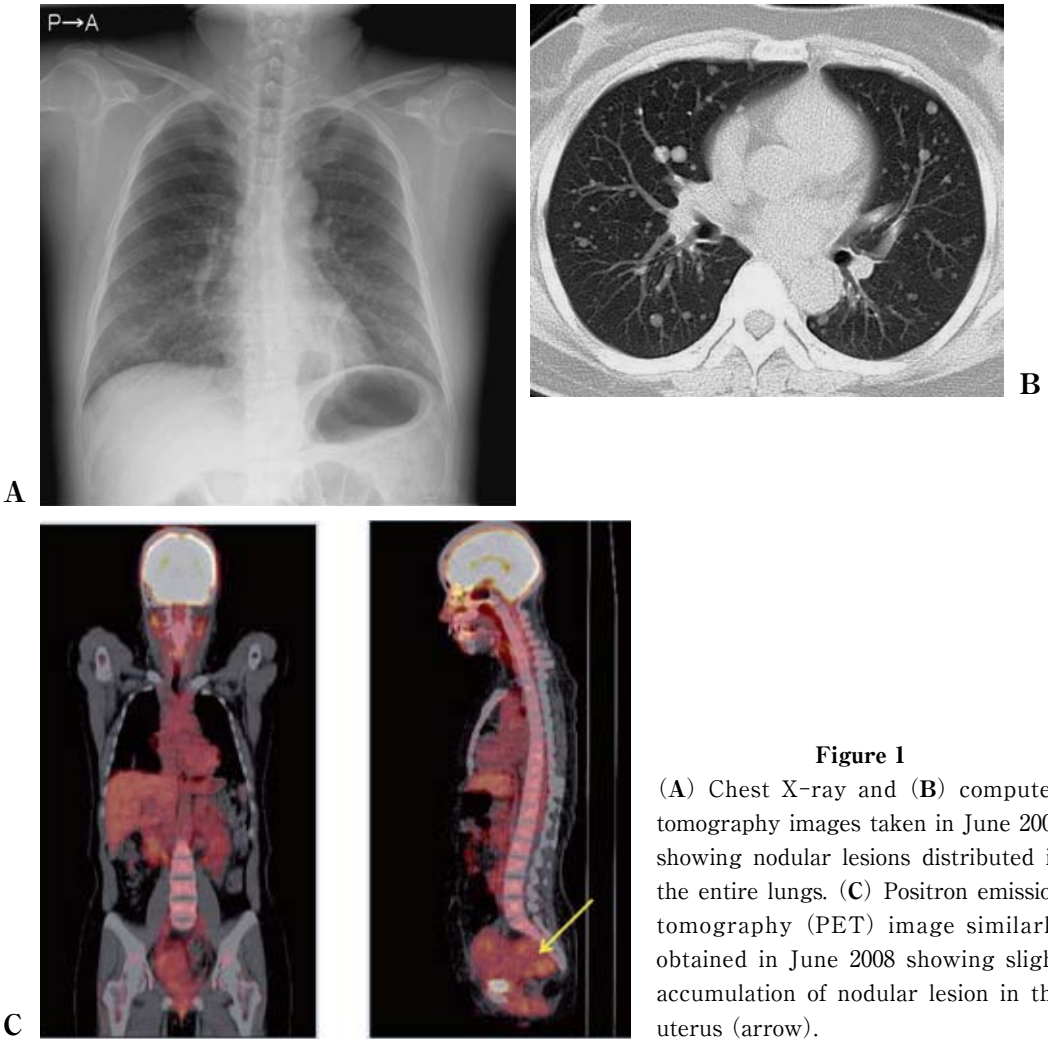

Figure 1
(**A**) Chest X-ray and (**B**) computed tomography images taken in June 2008 showing nodular lesions distributed in the entire lungs. (**C**) Positron emission tomography (PET) image similarly obtained in June 2008 showing slight accumulation of nodular lesion in the uterus (arrow).

However current reports describe BML as a very rare disease with little information regarding its pathology. Here, we report a case of pulmonary BML occurring after uterine myomectomy.

CASE REPORT

A 42-year-old woman presented with a 2-week history of dry cough on exertion upon visiting our hospital in June, 2008. Chest radiography and computed tomography (CT) revealed bilateral multiple nodular lesions (Fig. 1A and B). The patient had a history of uterine myoma and previously underwent myomectomy in 2003.

Physical examination revealed no abnormalities and her oxygen saturation while breathing room air was 96 %. Laboratory test results were as follows : white blood cells 6900/μl ; neutrophils 60.0 % ; eosinophils 5.0 % ; lymphocytes 30.0 % ; serum C-reactive protein 0.1 mg/dl (normal, ＜0.3 mg/dl) ; creatinine 0.69 mg/dl (0.46-0.82 mg/dl) ; lactate dehydrogenase 145 IU/l (200-400 IU/l) ; carcinoembryonic antigen＜1.0 ng/ml (＜5.0 ng/ml) ; carbohydrate antigen (CA) 19-9 8 U/ml (＜37 U/ml) ; CA125 14 U/ml (＜37U/ml) ; squamous cell carcinoma related antigen 1.6 ng/ml (＜1.5 ng/ml) ; sialyl stage-specific embryonic antigen-1 35U/ml (＜38 U/ml) ; soluble interleukin-2 receptor 316U/ml (220-530 U/ml) ; immunoguloblin (Ig) G 1204 mg/dl (870-1700 mg/dl) ; IgA 101 mg/dl (107-363 mg/dl) ; IgM 139 mg/dl (46-260 mg/dl) ; cytoplasmic-anti-neutrophil cytoplasmic antibody＜10EU ; perinuclear-anti-neutrophil cytoplasmic antibody＜10EU ; anti-nuclear antibody 20x ; anti-Sjögren's syndrome (SS) A (anti-SSA/Ro) negative (＜20 index) ; β-D glucan 3.2 pg/ml (＜10 pg/ml) ; Crypto-

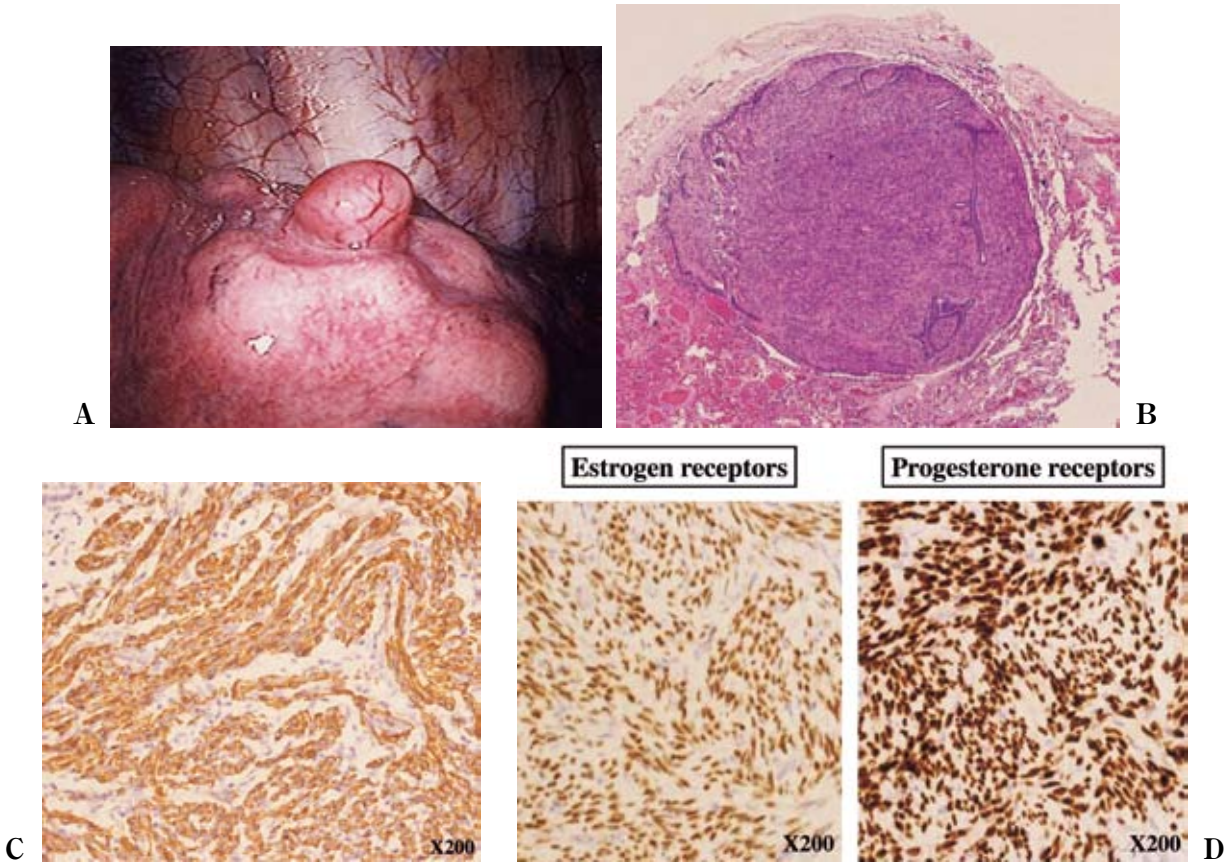

Figure 2

(**A**) Video associated thoracoscopy of the lung surface performed in July 2008 showing multiple elevated smooth lesions. (**B**) Hematoxylin and eosin (H&E) staining (original magnification, ×65) showing scattered nodular lesions of up to 3 mm diameter composed of bundles of spindle cells and columnar epithelial cells incorporated into the nodule resembling hamartoma. Few mitotic figures can be seen and the proliferating cells fall short of anaplasia which might lead to a diagnosis of a spindle cell sarcoma. (**C**) Immunostaining for α smooth muscle actin in spindle cells (original magnification, ×200). (**D**) Histologic examination of progesterone and estrogen receptors in spindle cells found in lung nodular lesions.

coccus neoformans antigen negative. Urinary examinations were normal.

Positron emission tomography (PET) performed in June, 2008 showed the absence of nodular lesion accumulation in the entire lung but slight accumulation in the uterus (Fig. 1C). Although bronchoscopy with accompanying bronchoalveolar lavage and transbronchial lung biopsy was performed, a definitive diagnosis could not be made. Subsequently, video associated thoracoscopy was carried out the following month, which demonstrated multiple elevated smooth lesions on the lung surface (Fig. 2A). Histological examination of hematoxylin and eosin (H&E)-stained biopsy specimens obtained by video associated thoracoscopic surgery (VATS) from the right S4 region demonstrated scattered nodular lesions of up to 3 mm diameter composed of bundles of spindle cells and columnar epithelial cells incorporated into the nodule resembling hamartoma (Fig. 2B). Mitotic figures were scarce, but the proliferating cells fell short of anaplasia which could indicate a diagnosis of spindle cell sarcoma. Immunostaining revealed the expression of α smooth muscle actin (αSMA) (Fig. 2C). Furthermore, spindle cells were positive for estrogen and progesterone receptors (Fig. 2D). From these histopathologic features, a definitive diagnosis of pulmonary BML of uterine origin was made. As for BML treatment, gonadotropin-releasing hormone was initially administered, and 1 month later in August, 2008, the patient underwent both complete hysterectomy and bilateral salpingo-oo-

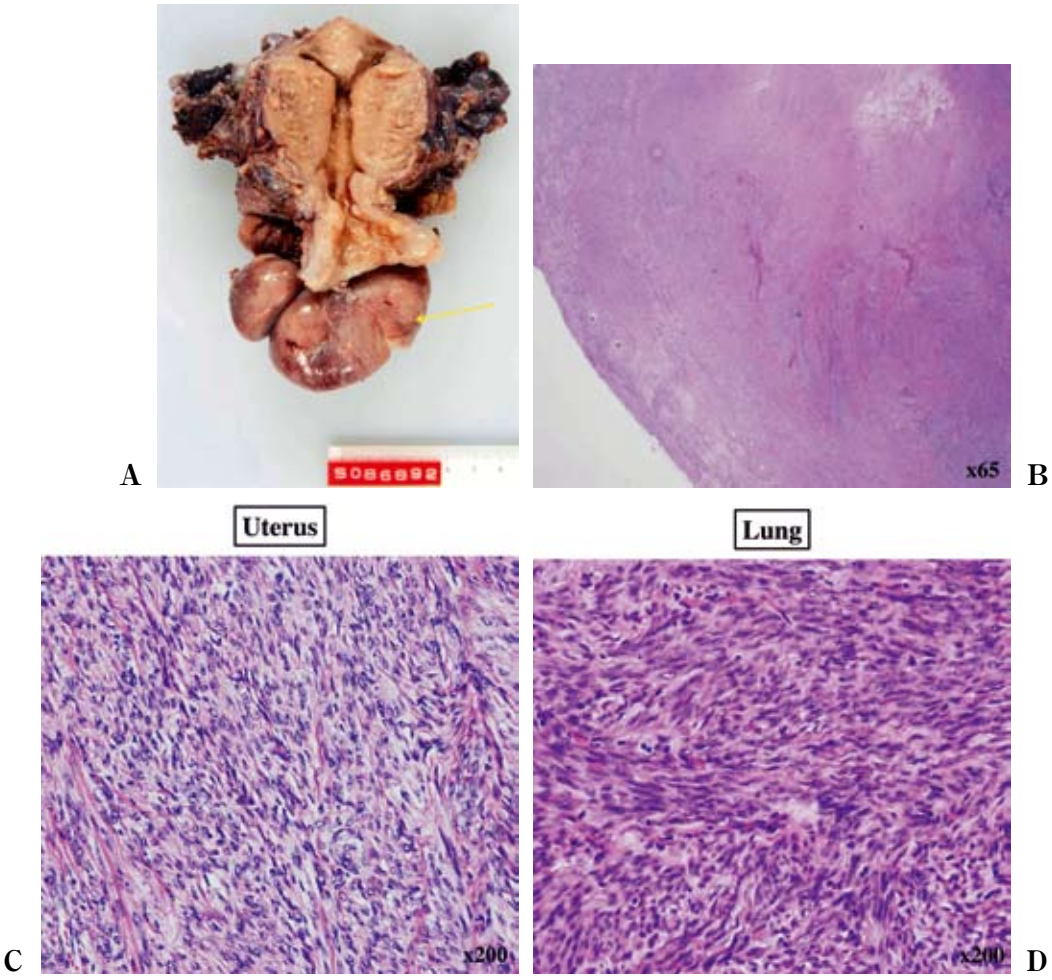

Figure 3

(**A**) Complete hysterectomy and bilateral salpingo-oophorectomy were performed in August 2008 as treatment for BML. Grossly, two uterine myomas (arrow) were found, as well as myomas with < 1 cm diameter in the uterine fundus [**B** (original magnification, ×65) and **C** (×200)] and lung tissue [**D** (×200)]. Histopathologic findings in lung tissue were consistent with those in typical uterine leiomyoma.

phorectomy. Bilateral ovarian findings revealed neither cystic lesions nor any abnormalities. Grossly, two myomas were observed in the uterine body, as well as < 1 cm myomas in the uterine fundus (Fig. 3A). Histopathologic findings in lung tissue (Fig. 3D) were consistent with those in typical uterine leiomyoma (Fig. 3B, 3C). On follow-up examination in November, 2008, her serum progesterone and estradiol levels were 0.19 ng/ml (< 0.44 ng/ml) and 10 pg/ml (< 21 pg/ml), respectively, a clinical state resembling postmenopause. Six months after surgery, chest CT showed that both the size and number of lung multiple nodular lesions did not increase compared with those before surgery.

DISCUSSION

The pathogenesis of pulmonary leiomyoma is considered to result from metastasis of benign uterine leiomyoma via unknown mechanisms, as well as low-grade uterine leiomyosarcoma, primary multiple leiomyoma or hamartoma. Caballes reported that BML develops in patients who previously underwent surgery for uterine leiomyoma [4] and suggested that leiomyoma cells metastasize into the lungs after surgery through the hematogenous route and thereafter undergo tumor progression [4]. On the other hand, patients have also shown good recovery from BML following metasectomy [5]. In particular, most BML patients are

women aged 36-64 years (average 44 years), and they are given an additional life expectancy of approximately 0 to 24 years following hysterectomy or myomectomy [6~9]. Bilateral, unilateral, and single lung lesion patterns have been demonstrated in 70%, 17%, and 13% of BML cases [10]. In histopathologic examinations, the diagnosis of myoma must be differentially specified as either leiomyoma or leiomyosarcoma. A recent trend in the classification of uterine smooth muscle neoplasms into clinically benign or malignant groups has been to move from exclusive reliance on using mitotic index to other approaches [11]. The presence or absence of coagulative tumor cell necrosis and cytologic atypia has been regarded as important in the classification of smooth muscle neoplasms [11].

For BML treatment, several studies have reported the efficacy of surgery for lung lesions, as well as bilateral salpingo-oophorectomy and/or hormonal therapy using gonadorelin acetate and progesterone [5]. However, specific and highly effective treatments have not yet been established. In some BML cases, convalescence has been observed without treatment [3,6]. In the present case, histopathologic examination of the lung showed low cytologic atypia, absence of coagulative tumor cell necrosis, αSMA expression, and positivity for progesterone and estrogen receptors in spindle cells. Moreover, the histopathologic features of the lung nodular lesions were similar to those of the uterine leiomyoma obtained by complete hysterectomy, leading to a definitive diagnosis of pulmonary BML originating from uterine leiomyoma. The clinical features of this case, such as reproductive age and postmyomectomy, were also consistent with previous reports of BML [6]. Complete hysterectomy and bilateral salpingo-oophorectomy following hormonal therapy were used as treatment in the present case, and this therapy induced a subsequent decrease in the serum level of progesterone and estrogen to the standard level corresponding to postmenopause. Although the level of efficacy of this treatment was not fully clarified, it has at least suppressed the progression of lung multiple nodular lesions. It is imperative that lesion progression must subsequently be followed by radiography and CT.

When lung multiple nodular lesions are encountered in women, a detailed clinical history regarding previous uterine surgeries must be taken. And BML is suspected when PET showed the absence of nodular lesion accumulation in the entire lung but accumulation in the uterus [12]. To arrive at a definitive diagnosis of BML, histopathogic examination following VATS instead of bronchoscopy is recommended.

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