



Case report

A case of primary pulmonary leiomyosarcoma

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A B S T R A C T

Primary pulmonary leiomyosarcoma (PPL) is a very rare malignant tumor which arises from bronchial smooth muscle and vessels. We report 48-year-old male who was diagnosed to have a small lung nodule in the right upper lung field by chest X ray film (XP). A disk shape small nodule was identified in the posterior segment of the right upper lobe by chest CT. Transbronchial lung biopsy (TBB) specimen showed a cluster of dense spindle cells with irregular shape nucleus and some necrosis. 18FluoroDeoxyGlucosePositron Emission CT (PET-CT) showed that the tumor had high value of the maximal standard uptake value (SUVmax) with no metastasis to the lymph nodes nor other organs. The right upper lobectomy and lymph node dissection were performed and microscopic examination of the specimen showed that the tumor was grade 2 leiomyosarcoma and there was no pleural invasion, nor lymph node metastasis. Post-operative staging of the tumor including its grade was Stage IIA. Immunohistochemical analysis of the specimen showed a clear transition from normal bronchial smooth muscle bundle to leiomyosarcoma in the bronchial wall. The bronchial vessels were fairly preserved. These finding suggested that the leiomyosarcoma developed from bronchial smooth muscle.

1. Introduction

PPL is very rare malignancy and found less than 0.5% of all primary malignant lung tumors [1] and is the dominant cell type of sarcomas in the lung [1,2]. Review of 38 cases in the previous literature show that the diagnoses were mostly made through TBB, surgical removal and autopsy samples [3]. Not only the staging of the tumor defined by size, lymph node and distant metastasis (TNM classification), but also the histological grading of the sarcoma are closely related to the prognosis [4]. FNCLSS grading system [5] is commonly used for sarcoma based on the subjective pathological assessment of tumor differentiation, mitotic count and necrosis. In the current report, we describe a right upper lobe leiomyosarcoma which was accidentally found by regular health checkup.

A written informed consent for the presentation and publication of the data was obtained.

2. Case report

Forty-eight-year-old male was introduced to our department because of the abnormality in chest XP. He did not have remarkable past history. He was never-smoker and had no history of exposure to the industrial materials. Physical examination showed no remarkable findings. Plain chest XP showed hazy nodular opacity in the right lung field with ill-defined margin (Fig. 1A). Chest CT showed that the tumor

was disk like-shape in the posterior segment of right upper lobe (Fig. 1B and C). The lateral branch of the posterior segment of upper lobe penetrated through the center of the tumor. The margin was not clear in some part of the tumor and spiculation was observed. Size of the tumor was 28 mm × 26 mm × 9mm. There was no lymph node swelling in the hilum and mediastinum. Blood tests including tumor marker for lung cancer were unremarkable. PET-CT showed strong positivity (SUVmax of 10) in the tumor (Fig. 1D) without metastasis to the lymph nodes, pleura and the other organs. Magnetic Resonant Imaging (MRI) with contrast media for the brain showed no abnormality. Bacteriological studies for lung tuberculosis, non-tuberculous mycobacteriosis, fungus diseases were all negative. Histological examination using Hematoxylin-Eosin (HE) staining for the specimens obtained by transbronchial lung biopsy showed dense spindle cells with irregular shape nucleus and some necrosis. The pathological diagnosis was malignant myoepithelial tumor. Preoperative staging using chest CT, PET-CT and brain MRI was stage IA (T1N0M0). Right upper lobectomy with lymph nodes dissection were performed. Fig. 2A shows the macroscopic view of the tumor. The tumor was consisted of a cluster of irregular small nodules along the airways and the part of the margin was indistinct. No invasion was found in the lymph nodes and the pleura. Microscopic examination showed that the tumor was filled with dense spindle cells with pleomorphism and division of chromosome (Fig. 2B). The pathological diagnosis was grade 2 leiomyosarcoma using FNCLCC grading system [5] as follows. The tumor differentiation was certain (score 2), mitotic

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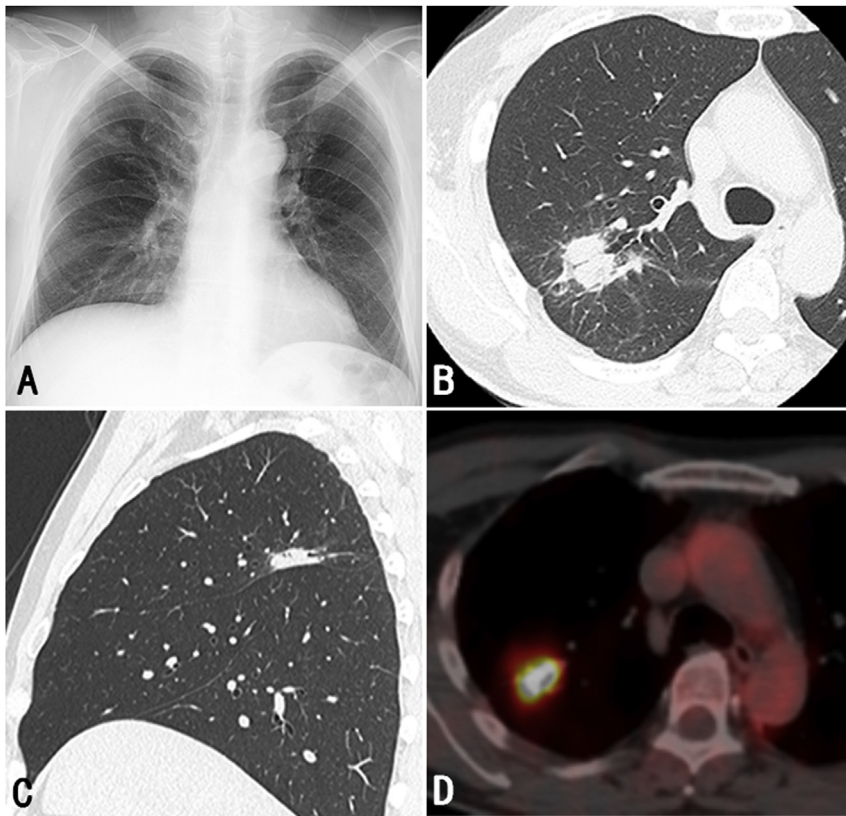


Fig. 1. Radiological examination. A: Plain chest X-ray film. 22 × 17mm tumor with unclear margin was observed in the upper lung field. B and C: Computed tomography of the chest in Axial and Sagittal slices. Tumor was disc-like shape spreading along the airways. D: PET-CT showed high SUVmax for the tumor and no metastasis was observed in the lymph nodes and other organs.

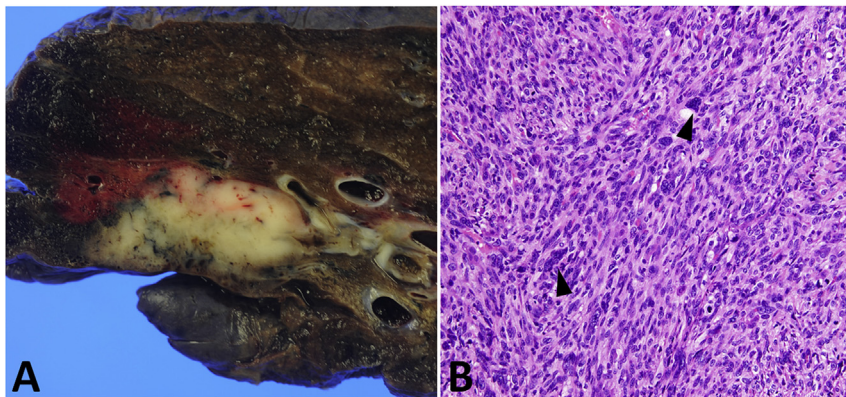


Fig. 2. Histological examination. A: Macroscopic view of excised surgical specimen. The tumor was irregularly developed around the airway. A part of the tumor consisted with small nodules. B: Histology of the tumor with HE staining. Densely populated pleomorphic spindle cells were observed. The spindle cells were eosinophilic and arranged in interweaving bundles. Pleomorphic elongated nucleus strongly stained with Hematoxylin and nuclear divisions were observed (arrow head).

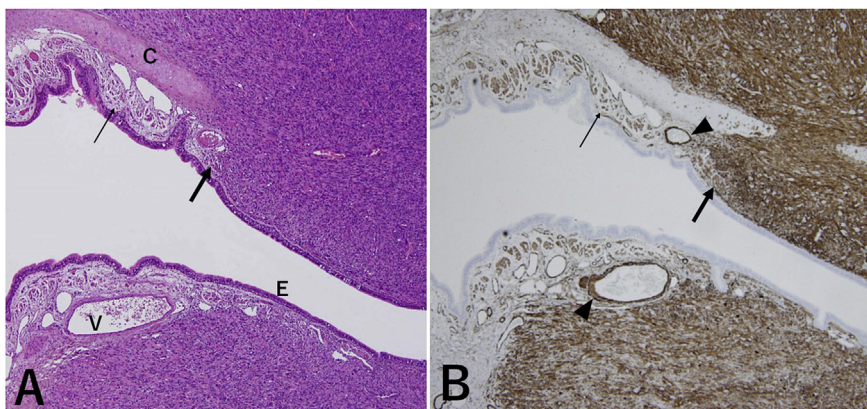


Fig. 3. HE and Immunohistochemical stainings. A: Histology with HE staining. C, E and V stand for bronchial cartilage, epithelium and vessel. The thin arrow shows the normal structure of bronchial smooth muscle bundle. The thick arrow shows the transient area of normal structure of bronchial smooth muscle to leiomyosarcoma. B: Immunohistochemical staining for H-Caldesmon. Normal bronchial smooth muscle (thin arrow) and leiomyosarcoma (thick arrow) were stained. In the area of leiomyosarcoma, staining was denser than normal muscle bundle area showing dense population of malignant cells. Smooth muscle within the vessel was also normally stained (arrow head).

Table 1
Immunohistochemistry.

Cytokeratin MNF116	(-)
Cytokeratin5/6	(-)
P40	(-)
TTF1	(-)
Napsin A	(-)
CD56	(-)
Synaptophysin	(-)
Chromogranin A	(-)
S-100	(-)
D2-40	(-)
CD34	(-)
Desmin	(-)
Calponin	(-)
Vimentin	(+)
H-Caldesmon	(+)
α -SMA	(+)
HHF35	(+)

MIB-1 labeling index 67.7%.

count was 2–3/10 hyperpower fields (score 1) and tumor necrosis was 20% (score 1), the total score, all together, was 4. Post-operative staging with PET-CT and pathological grading was Stage IIA. The clear transition from normal smooth muscle bundle (Fig. 3A, thin arrow) to a cluster of malignant spindle cells was observed (Fig. 3A, thick arrow). Immunohistochemical staining routinely used for diagnosis of histological types of carcinoma such as CytokeratinMNF116, Cytokeratin5/6, P40 for the squamous cell carcinoma, TTF1, Napsin A for the adenocarcinoma, CD 56, Synaptophysin, ChromograninA and S100 for the neuroendocrine carcinoma [6] were all negative (Table 1). Staining using CD 34 and D2-40 for vascular and mesothelial malignancies were also negative [6]. On the other hand, although Desmin and Calponin were negative, Vimentin, H-Caldesmon, α -SMA and HHF35 were strongly stained suggesting that the origin of the tumor was smooth muscle. MIB-1 labeling index was 67.7%. Fig. 3B shows positive staining of H-Caldesmon for sarcoma cells as well as normal bronchial smooth muscle. Structure of the vessels in the tumor was preserved and smooth muscle cells of the vessels were normally stained (Fig. 3B, arrow heads). The Elastica HE staining (not shown) showed that destruction of elastic fibers was more prominent in bronchial walls than vessels.

3. Discussion

Since PPL is very rare, most of the reports were isolated case reports or review of previous cases [3,7]. PPL is classified as intraluminal type [7], pulmonary vascular type [8,9] and intrapulmonary type as our case. In the current report, the tumor was accidentally found on chest XP examination during yearly health checkup without any symptoms. Chest CT showed that the tumor was thin disk-shape appearance and did not form a concentric development as usually seen in bronchial carcinoma (Figure 1B and C). Pathological diagnosis using TBB was myoepithelial malignancy and preoperative staging of the tumor using CT, PET-CT and MRI was Stage IA. Pathological diagnosis using a post-operative specimen, however, was grade 2 leiomyosarcoma by FNCLCC grading [5] and postoperative stage was Stage IIA. It was reported that MIB-1 labelling index is more objective assessment of mitosis than mitotic counts using FNCLCC grading system and gives better prognostic estimation of soft tissue tumor [10]. Since MIB-1 labelling index in our case was 67.7%, mitotic score increased to 3. By adding this value to the other FNCLCC scores for differentiation (score 2) and necrosis (score 1), the total score became 6 showing that our case was grade 3 leiomyosarcoma and prognosis may be poorer than expected from conventional FNCLCC grading.

Although adequate amount of specimen is necessary for the pathological grading of the tumor, TBB often obtains only small and

crushed specimens preventing precise assessment of grade. Recent study by Rakheja et al. compared PET-CT and histological markers of sarcoma and reported that SUVmax was significantly correlated to mitotic count and necrosis of sarcoma [11]. These findings suggested that PET-PET may be one of the potential surrogate markers for assessing the grade of sarcoma. In the study of 493 patients with different histological subtypes of bone and soft tissue sarcomas, histologically high-grade tumors had SUVmax over 5 [12]. Therefore, PET-CT could provide useful information about not only identification of sarcomas in the lung and metastasis to lymph nodes or other distant organs but also estimating its grade. In case of pulmonary arterial leiomyosarcoma, differentiation of sarcoma from pulmonary embolism may be difficult without PET-CT [13]. Compared with conventional methods for diagnosing sarcoma using CT and MRI, adding PET-CT provides more than 20% benefit in staging of the tumor especially by detecting occult distant metastasis [12]. Anatomical origin of sarcoma has been reported to influence the difference in SUVmax and leiomyosarcoma from gynecological origin tended to have higher SUVmax compared that from non-gynecological origin [12]. Although leiomyosarcoma in our case was non-gynecological origin, SUVmax was very high suggesting the histological grade was supposed to be high. The final pathological diagnosis of leiomyosarcoma was made using postoperative specimen and the histological grade, in deed, was grade 2 (FNCLCC grading system) or grade 3 (MBI grading system) as expected from high SUVmax.

Although diagnosis of leiomyosarcoma could morphologically be made by HE staining, the immunohistochemical examination confirms the diagnosis. In our case, Vimentin, as a mesenchymal marker, was positive and epithelial markers for different types of carcinoma were all negative and H-Caldesmon, α -SMA and HHF35 were strongly positive confirming that the origin of tumor was smooth muscle [14]. Histological observation using HE and H-Caldesmon staining in our case provided another information about the structural origin of leiomyosarcoma in the airway. Fig. 3 shows normal smooth muscle (thin arrow) bundle with normal epithelium and bronchial vessels. On the other hand, diffuse leiomyosarcoma area is shown at the transient from normal smooth muscle bundles (thick arrow). The bronchial vessels adjacent to leiomyosarcoma looked normal both in HE and H-Caldesmon staining (Fig. 3B, arrow head). These findings lead us to believe that the origin of the leiomyosarcoma of our case was from the bronchial smooth muscle not from bronchial vessels.

Conflicts of interest

There is no conflict of interests.

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