Primary Pulmonary Leiomyosarcoma: A Case Report

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Abstract

Primary pulmonary leiomyosarcoma (PPL) is an exceptionally rare neoplasm with a nonspecific clinical presentation, posing a substantial risk of misdiagnosis with other malignant and non-malignant lung conditions. A comprehensive diagnostic work-up, including radiological and histological investigations, is essential to establish the diagnosis. Surgical resection remains the primary treatment modality, but radiotherapy and chemotherapy may be necessary in unresectable or metastatic cases. This report describes the case of a 68-year-old woman presenting with nonspecific respiratory symptoms. Chest X-ray demonstrated a large right upper lung mass, which was further characterized on contrast-enhanced computed tomography; the scan also revealed a right-sided pleural effusion, nodular pleural enhancement, and a pericardial effusion. Histological evaluation of tissue obtained via ultrasound-guided transthoracic needle biopsy was consistent with leiomyosarcoma. Subsequently, positron emission tomography-computed tomography (PET-CT) excluded the presence of alternative primary sites, thereby establishing the diagnosis of PPL. Given the tumour's size, presence of pleural metastases, and local mediastinal involvement, the case was deemed inoperable and was managed with three cycles of doxorubicin and ifosfamide chemotherapy. A follow-up PET-CT demonstrated interval metabolic regression of the tumour, indicating a favourable early treatment response despite stable tumour dimensions. This case highlights the importance of thorough diagnostic evaluation and demonstrates the potential role of chemotherapy in managing inoperable PPL.

Keywords: Leiomyosarcoma; Lung Neoplasms; Biopsy, Needle; Immunohistochemistry; Tomography, X-Ray Computed; Positron Emission Tomography Computed Tomography; Chemotherapy; Antineoplastic Agents; Doxorubicin; Ifosfamide

Introduction

Primary pulmonary leiomyosarcoma (PPL) is a rare malignant neoplasm arising from the pulmonary parenchyma, bronchial tree, or pulmonary arteries, in decreasing order of frequency.(1,2) First identified in 1903 by Davidsohn, PPL constitutes less than 0.5% of all pulmonary malignancies, yet remains the most prevalent primary pulmonary sarcoma, accounting for approximately 30% of cases.(3) Radiation, chemical, environmental, and occupational exposures have been identified as potential risk factors.(2,3) The disease typically presents with nonspecific respiratory symptoms including dyspnoea, cough, chest pain, and fever, though some patients may remain asymptomatic.(2,3) Given its rarity and nonspecific presentation, diagnosis is challenging and necessitates thorough investigations to exclude extrapulmonary sites, as metastatic cases are more common.(2) While surgery is the primary treatment for localized disease, radiotherapy and chemotherapy are commonly employed in unresectable or metastatic cases.(2,3) Recent advances in molecular profiling have explored targeted therapies for soft tissue sarcomas, with potential implications for PPL.(4) Here, we report a case of PPL presenting as a right upper lobe mass and managed with chemotherapy in a patient with a history of total hysterectomy 15 years earlier.

Case Report

A 68-year-old woman presented to the emergency department soon after returning from India. Her medical history was notable only for a total hysterectomy performed abroad 15 years earlier for benign fibroids.

She reported a one-week history of respiratory symptoms, which began during her travels, including exertional dyspnoea, orthopnoea, productive cough, rhinorrhoea, right-sided chest pain, and paroxysmal fever. A recent sick contact with an upper respiratory tract infection was also noted. The patient denied haemoptysis, weight loss, or night sweats.

On examination, the patient was not emaciated but appeared tachypnoeic (28 breaths/min) with a mild fever (37.8°C); other vital signs were stable. Right-sided air entry was reduced, and the remainder of the systemic examination was unremarkable.

Bedside ultrasound scan showed a right-sided pleural effusion, which was further confirmed by a chest X-ray (CXR) that also demonstrated a large, homogenous right-sided opacity suggestive of a mass.

Multiple differential diagnoses were considered, including malignant and non-malignant causes, such as tuberculosis (TB), partially treated pneumonia, and parapneumonic effusion.

Considering the CXR findings, contrast-enhanced computed tomography (CT) of the chest was performed [Figure 1]. It revealed an irregular right upper lobe lung mass measuring 15 × 11 × 10 cm, with traversing vessels, right upper bronchus obliteration, and right lower lobe collapse. Significant right-sided pleural effusion with nodular pleural enhancement and mild pericardial effusion were also present.

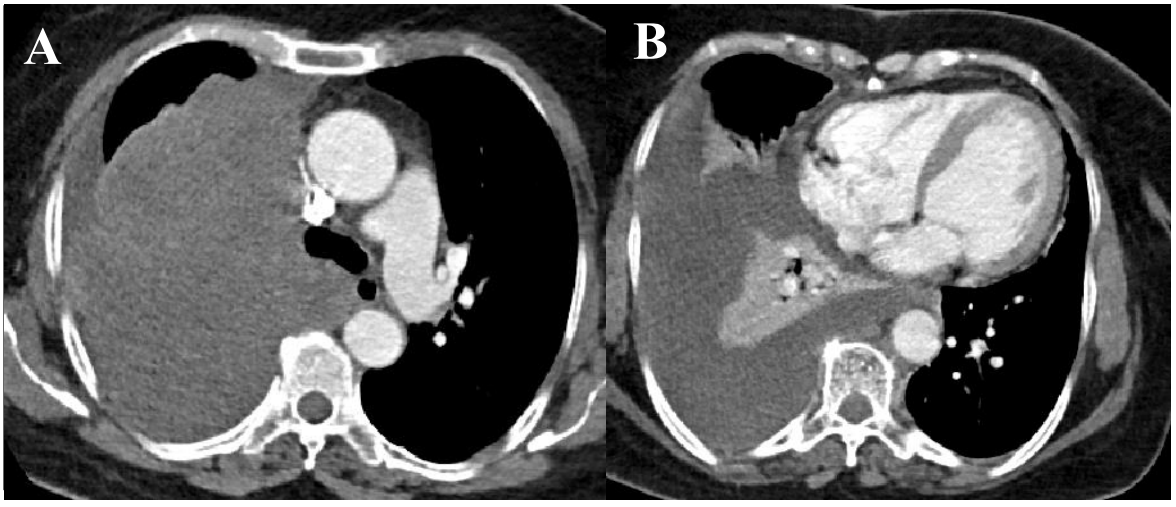

Figure 1: Axial mediastinal window images from a contrast-enhanced chest CT demonstrating a large right upper lobe mass **(A)**. Adjacent right-sided pleural effusion with nodular pleural enhancement is visible, along with collapse of the right lower lobe **(B)**. Mild right-sided pericardial effusion is also present.

Microbiological investigations, including for TB, were negative. Tumour markers revealed elevated CA 15-3 (42 U/mL; normal 0-33), CA 125 (68 U/mL; normal 0-35), and CEA (1.1 µg/L). Additionally, pleural fluid cytology demonstrated inflammatory and reactive mesothelial cells without evidence of malignant cells.

Accordingly, ultrasound-guided transthoracic needle biopsy of the right lung mass was performed. Tumour histology revealed spindle-shaped cells with marked nuclear pleomorphism and a mitotic count of 11 per 10 high-power fields, without epithelial differentiation. Immunohistochemistry was positive for Desmin and H-caldesmon, markers of smooth muscle differentiation, and negative for PanCK, TTF1, Napsin A, S100, STAT6, and CD34. The morphology and immunoprofile of the tumour supported a diagnosis of a high-grade leiomyosarcoma, and ruled out other spindle cell malignant neoplasms. The tumour was classified as Grade 2 based on the French Federation of Cancer Centers Sarcoma Group (FNCLCC) grading system. [Figure 2]

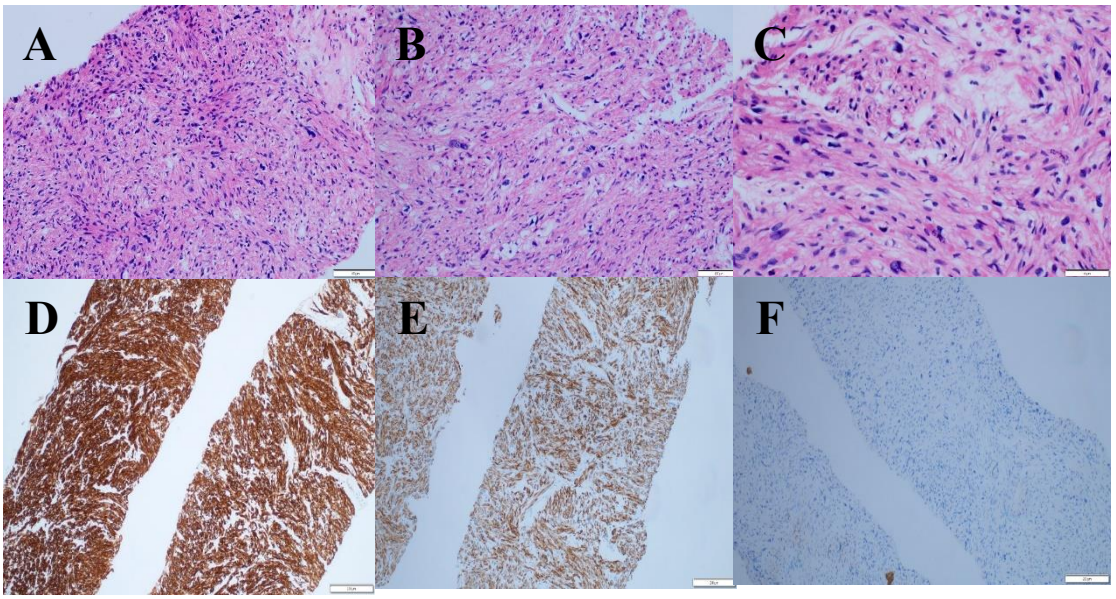

Figure 2: (A) Haematoxylin and eosin-stained section of the core biopsy at 10× magnification revealing a spindle cell neoplasm composed of interwoven fascicles of spindled cells with cigar-shaped, pleomorphic, hyperchromatic nuclei and moderate eosinophilic cytoplasm. **(B)** At 20× magnification, increased cellular detail is observed. **(C)** Mitotic figures, some of which are atypical, are identified at 40× magnification. The spindled cells demonstrates strong, diffuse immunoreactivity for H-caldesmon **(**D**)** and desmin **(**E**)**, while tumour cells are negative for the epithelial marker pan-cytokeratin **(**F**)**.

In view of PPL's rarity, the patient's prior hysterectomy, and the absence of a histopathology report, metastatic uterine leiomyosarcoma was considered. A multidisciplinary team meeting recommended further investigations to identify an alternative primary site. Whole-body fluorine-18 fluorodeoxyglucose positron emission tomography–computed tomography (^{18}F-FDG PET-CT) was performed, demonstrating no abnormal uptake apart from the right lung mass and an incidental right thyroid nodule [Figure 3], thereby confirming the diagnosis of PPL.

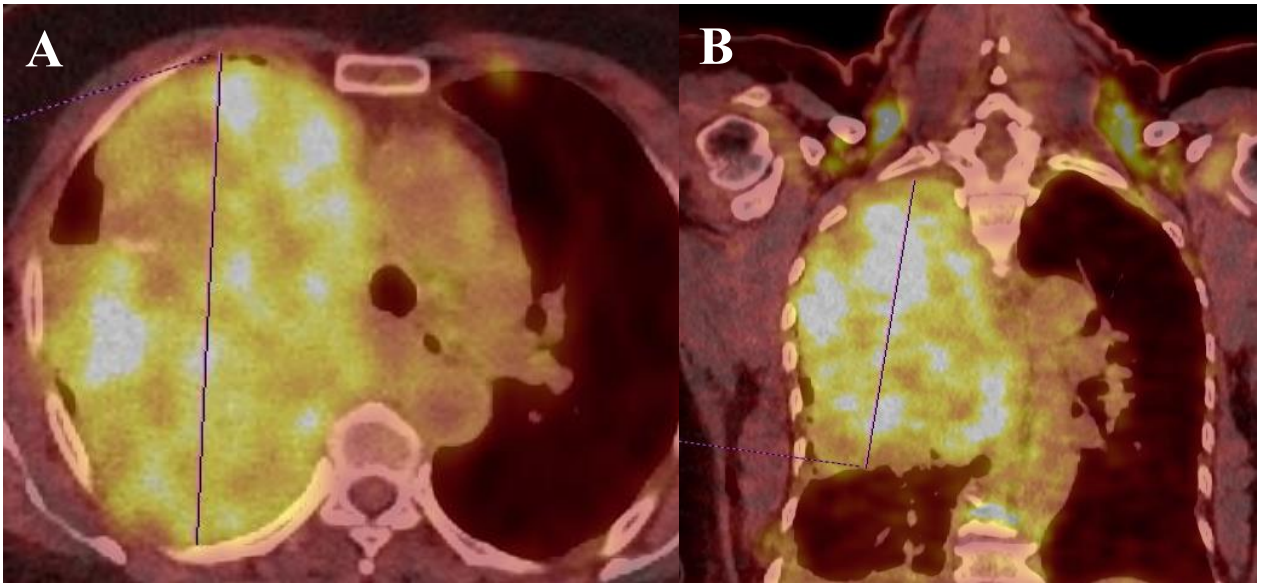

Figure 3: Axial **(A)** and coronal **(B)** 18F-FDG PET-CT images demonstrating a large, FDG-avid heterogenous right lung mass measuring 16.7 × 10.6 cm in cross-section and 15.4 cm craniocaudally, with a maximum standardized uptake value (SUVmax) of 10.6. The mass is contiguous with the right hilum, mediastinum, and subcarinal region. Additionally, diffuse FDG-avid right pleural thickening is noted, with an SUVmax of 8.7.

Given the tumour's size, presence of pleural metastases, and local mediastinal involvement, surgical resection was deemed unfeasible. The patient underwent three cycles of doxorubicin/ifosfamide chemotherapy.

Follow-up PET-CT showed encouraging interval metabolic regression, indicating a positive treatment response despite stable tumour dimensions.

Discussion

Primary pulmonary leiomyosarcoma presents a complex diagnostic challenge due to its rarity and the absence of specific clinical and radiological features.(2,3) Histopathological evaluation of core lung biopsy specimens—obtained via ultrasound-guided transthoracic needle biopsy in this case—remains the gold standard for establishing a preoperative diagnosis and excluding differentials such as bronchogenic carcinoma and other soft tissue sarcomas.(2,5,6) Given that most pulmonary leiomyosarcomas are metastatic in origin, it is crucial to rule out extrapulmonary primary sites before confirming a diagnosis of PPL, (2) which was achieved in this instance using ^{18}F-FDG PET-CT.

Surgical resection remains the mainstay treatment for PPL; however, when preoperative evaluation reveals inoperable local disease or metastatic spread, radiotherapy and/or chemotherapy may be required.(1–3) Cases involving neoadjuvant chemotherapy for PPL are scarce, but Tanaka et al.(7) reported successful use of neoadjuvant doxorubicin monotherapy to achieve a resectable tumour size. In our case, a favourable metabolic response was observed following three cycles of doxorubicin/ifosfamide chemotherapy. Emerging evidence also supports the use of targeted therapies such as pazopanib, a multi-targeted tyrosine kinase inhibitor, in advanced PPL, with reported tumour size reduction and disease stabilization, highlighting the growing role of personalized treatment in sarcoma management.(2,4)

Regarding prognosis, the tumour's histological grade remains the most reliable predictor of long-term survival, compared to the site (endobronchial vs. parenchymal) or size.(6) However, outcomes are generally poor for tumours exceeding 10 cm or demonstrating more than 8 mitotic figures per 10 high-power fields.(6,8,9) A population-based cohort study by Bao-Dong et al., involving 231 patients with PPL, reported a median overall survival of approximately 14 months. Notably, patients who underwent cancer-directed surgery experienced an additional median survival benefit of nearly 29 months.(10) Currently, there is insufficient evidence to draw definitive conclusions regarding the prognostic impact of chemotherapy or radiotherapy in PPL.

Conclusion

Primary pulmonary leiomyosarcoma is an extremely rare malignant neoplasm originating from the pulmonary parenchyma, bronchial tree, or pulmonary arteries. Its diagnostic complexity stems from both its rarity and the lack of specific clinical or radiological features. Nonetheless, histological evaluation, including immunohistochemistry, is pivotal in establishing the diagnosis. Surgical intervention remains the cornerstone of treatment and is associated with improved prognosis. However, in inoperable or metastatic cases, radiotherapy and/or chemotherapy may be considered. Further research on PPL, including emerging targeted therapies, optimal management strategies, and the prognostic impact of non-surgical treatments, is warranted.

Disclosure

The authors declare no conflicts of interest. Informed consent was obtained from the patient.

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