CASE REPORT

Primary Pulmonary Myxoid Sarcoma: A Rare and Challenging Diagnosis in Thoracic Oncology

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ABSTRACT

Introduction: Primary pulmonary myxoid sarcoma (PPMS) is a rare malignant mesenchymal lung tumor, with fewer than 40 cases reported worldwide. This report presents a case of PPMS with surgical difficulties.
Case: A 53-year-old male presented with a six-month history of exertional dyspnea, coughing up blood, right chest pain, anorexia, and weight loss. Thoracic CT imaging revealed an enhancing solid mass in the middle-posterior mediastinum. Histopathological examination of a core biopsy identified anaplastic lipoblast cells indicative of liposarcoma. Based on the multidisciplinary team (MDT) discussion, the patient was diagnosed with mediastinal liposarcoma and tumor excision was planned. However, during the surgery, a lung tumor with adhesions to the middle and lower lobes of the right lung was discovered, precluding complete tumor. An open biopsy was performed instead, revealing a proliferation of anaplastic cells with round to oval spindle nuclei, arranged reticularly within a myxoid stroma, along with positive Alcian blue staining. Immunohistochemical analysis demonstrated focal desmin positivity in the cytoplasm of the tumor cells. The diagnosis of PPMS was confirmed based on the criteria by the World Health Organization (WHO) in 2021, including primary lung tumor, spindle-shaped and round tumor cells in a reticular pattern within a myxoid stroma, and immunohistochemical findings that exclude other histologically similar tumors.
Conclusion: Although rare, PPMS should be considered in the differential diagnosis of thoracic tumors. This case is consistent with findings from previous cases. Most PPMS patients were treated surgically and had a good prognosis. However, tumor excision could not be performed in this patient due to the adhesion of the tumor mass to the middle and lower lobes of the right lung.

INTRODUCTION

Primary pulmonary myxoid sarcoma (PPMS) is a mesenchymal malignancy in the lungs, characterized by tumor cells originating from primitive mesenchymal cells with myofibroblastic or fibroblastic differentiation. PPMS is also known as a low-grade malignant myxoid endobronchial tumor.[1] It was first reported by Nicholson in 1999 after discovering two cases of low-grade mucinous tumors in the bronchi.[2] In 2011, Thway identified a characteristic chromosomal translocation t(2;22)(q33;q12) in this tumor, leading to the EWSR1-CREB1 gene fusion, thereby classifying PPMS as EWSR1-CREB1 gene fusion-associated.[3] Since 2021, PPMS has been categorized as a pulmonary mesenchymal tumor in the fifth edition of the World Health Organization (WHO) classification of lung tumors.[4]

As of 2021, only 37 cases of PPMS have been reported globally, with a male-to-female ratio of 19:18, and an age range from 23 to 80 years, with a median age of 44 years.[5] Smoking history is a risk factor for lung tumors, observed in about 80% of PPMS patients.[3] The diagnostic criteria for PPMS are divided into essential criteria, include a primary tumor involving the lungs, spindle-shaped to round tumor cells in a reticular pattern with prominent myxoid stroma, and an exclusion of other tumors with histologically similar

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features, and desirable criteria, including tumor localization in the endobronchial area and the presence of an EWSR1-CREB1 gene fusion.[6] The primary management of PPMS involves tumor excision, but chemotherapy and radiotherapy can be considered for patients who are not candidates for surgery.[7] This case report discusses a case of PPMS in a 53-year-old male with issues regarding diagnosis and management.

CASE

A 53-year-old male presented with a six-month history of exertional dyspnea, coughing up blood, and right chest pain. He reported a decreased appetite and a weight loss of 10 kg over the past two months. He had a history of smoking 12 cigarettes per day for 35 years.

A contrast-enhanced thoracic CT scan (Figure 1) revealed a mass in the middle-posterior mediastinum, measuring approximately 15.3 x 14.3 x 13 cm, attached to the posterior wall of the right hemithorax. The mass was sharply demarcated from the heart and displaced the heart toward the left. The mass compressed the inferior bronchus of the right lung lobe, leading to compressive atelectasis of the right lower lung lobe. Additional findings included enlargement of the right peribronchial lymph nodes and atherosclerosis of the thoracic aorta.

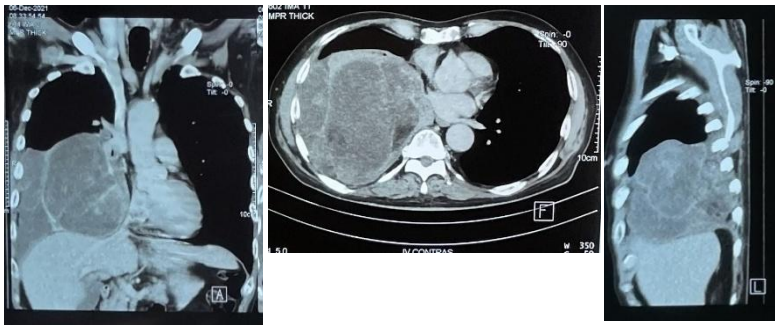

Figure 1. Thoracic computed tomography scan showing an enhanced solid mass in the middle-posterior mediastinum

Histopatological examination of a core biopsy (Figure 2) revealed anaplastic lipoblast cells with oval to spindle-shaped nuclei, vacuolation, severe pleomorphism, coarse chromatin, prominent nucleoli, and abundant cytoplasm. Among them, bizarre cells with multiple nuclei were observed, suggesting the presence of a liposarcoma.

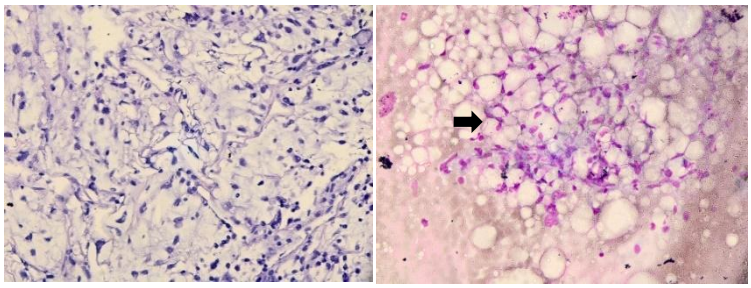

Figure 2. Histopathological examination showing anaplastic lipoblast cells indicative of liposarcoma (black arrow)

Based on the multidisciplinary team (MDT) discussion, the patient was diagnosed with mediastinal liposarcoma and tumor excision was planned after confirming the presence of distant metastasis. A comprehensive evaluation, including a bone survey, abdominal ultrasound, and head magnetic resonance imaging (MRI), showed no evidence of metastatis.

Although tumor excision was initially planned, a lung tumor, rather than a mediastinal mass, was accidentally discovered during the surgery. The lung tumor caused adhesions in the middle and lower lobes of the right lung (Figure 3). As a result, excision could not be performed, and an open biopsy was performed instead.

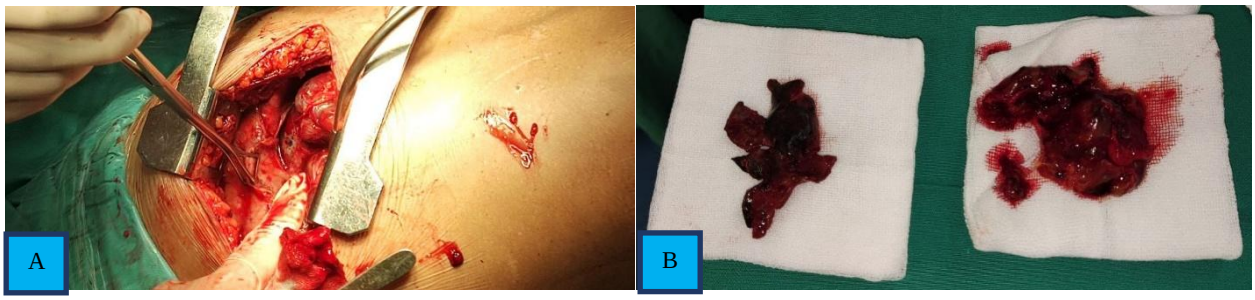

Figure 3. A) Intraoperative photo; B) The findings of the open biopsy

Histopathological examination of the open biopsy (Figure 4) revealed a tumor growth pattern arranged in a reticular pattern within a myxoid stroma, with some areas forming lobules. The tumor consisted of a proliferation of anaplastic cells with oval to spindle-shaped nuclei, pleomorphism, coarse chromatin, prominent nucleoli, and abundant cytoplasm. Mitosis was observed at a rate of more than 20 per 10 high-power fields. Extensive necrotic areas and hemorrhagic regions were also present, and Alcian blue staining was positive in the myxoid stroma.

Immunohistochemical analysis of the tumor cells using CK, S100, desmin, and CD34 antibodies yielded the following results: CK was negative in the cytoplasm, S100 was negative in the nucleus and cytoplasm, desmin was focally positive in the cytoplasm, and CD34 was negative in the cell membrane. While focal positivity for desmin is characteristic of PPMS, the negative results for CK, S100, and CD34 can help rule out diagnoses other than PPMS.[5,7]

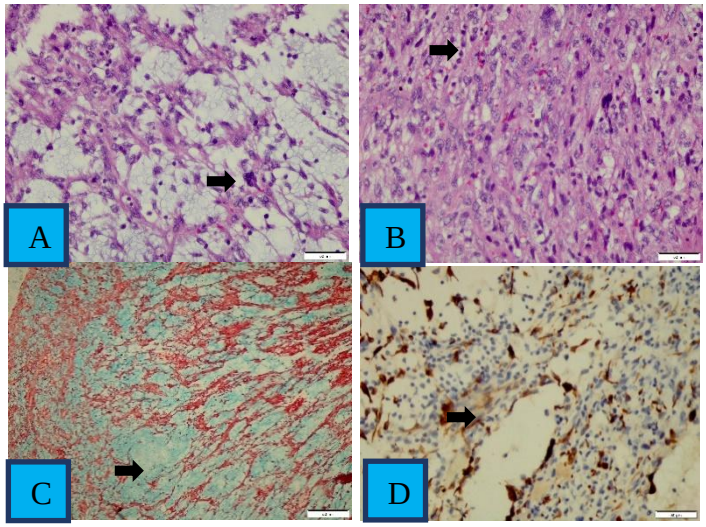

Figure 4. A) Histopathological examination showing proliferation of anaplastic cells arranged reticularly within the myxoid stroma; B) Tumor cells with high mitosis; C) Positive Alcian blue staining in the myxoid stroma; D) Immunohistochemical analysis demonstrating focal desmin positivity in the cytoplasm of tumor cells

DISCUSSION

Currently, no gold-standard diagnostic examination and staging system exist for PPMS. The diagnostic criteria for PPMS based on the fifth edition of the WHO lung tumor classification are categorized into essential criteria and desirable criteria. The essential criteria include a primary tumor involving the lungs, spindle-shaped to round tumor cells in a reticular pattern with prominent myxoid stroma, and an exclusion of other tumors with histologically similar features. The desirable criteria include tumor localization in the endobronchial area and the presence of an EWSR1-CREB1 gene fusion.[6]

This case fulfills the essential criteria for the diagnosis of PPMS based on the WHO 2021 criteria, which include a primary tumor involving the lungs, spindle- and round-shaped tumor cells in a reticular pattern within myxoid stroma, and immunohistochemical findings that exclude other tumors with histologically similar features. However, genetic testing for the EWSR1-CREB1 gene fusion via the fluorescence in situ hybridization (FISH) was not performed due to its unavailability.

The clinical manifestations of PPMS are nonspecific. Some patients present with symptoms such as productive cough, hemoptysis, and weight loss, while others remain asymptomatic, with incidental tumor masses identified during radiological examination of the chest.[1,5,8] In this case, a 53-year-old male with a 35-year history of smoking presented with hemoptysis (coughing up blood) as the primary complaint. The patient also reported intermittent shortness of breath, especially during physical exertion, a sensation of heaviness in the right chest, loss of appetite, and a weight loss of 10 kg over the past two months. Smoking is a risk factor for lung tumors.

CT scan findings in PPMS may reveal nodules and solid masses extending into the tracheobronchial system. PPMS is more frequently located in the right lung (62%) and near the bronchus (85%). Tumor sizes typically range from 1.5 cm to 14 cm, with an average size of 5 cm.[1,5,8] In this case, the CT scan identified a solid mass with fat and cystic components. The mass exhibited well-defined borders, was loculated and septated, with a septum thickness of approximately 0.4 cm in the posterior mediastinum, and measured approximately 13.2 x 15.0 x 12.2 cm. It was observed to displaced the heart toward the left and the right inferior bronchus, resulting in adjacent compressive atelectasis in the right inferior lung.

Histopathological examination of tissue, followed by immunohistochemical staining, can assist in diagnosing PPMS. Generally, the macroscopic appearance of PPMS is nodular with well-defined borders. The cut surface is white-gray to pale yellow, soft, mucus-like, and lobulated, with or without fibrous pseudocysts. Microscopically, tumor cells in PPMS are composed of spindle-shaped, polygonal, and stellate cells arranged in a mesh or strips within a myxoid stroma. The mitotic count is typically less than five per 10 high-power fields. The stroma is often accompanied by lymphocytic and plasma cell infiltrates. PPMS does not express specific immunohistochemical markers. Immunohistochemical stains that can be used in the diagnosis of PPMS include vimentin, EMA, CD99, and desmin. PPMS does not express CK, TTF1, S100, calponin, SMA, ALK, CD31, and CD34.[5,7]

Histopathological examination of the core biopsy in this patient revealed anaplastic lipoblast cells with oval to spindle-shaped nuclei, vacuolation, severe pleomorphism, coarse chromatin, prominent nucleoli, and abundant cytoplasm, including bizarre cells with multiple nuclei, supporting a diagnosis of liposarcoma. After a multidisciplinary team (MDT) discussion, the patient was diagnosed with mediastinal liposarcoma, and it was decided to proceed with tumor excision. Microscopic examination of the open biopsy showed lung parenchymal tissue with tumor growth consisting of proliferative anaplastic cells with round, oval, and spindle-shaped nuclei arranged in a reticular pattern within a myxoid stroma. Immunohistochemical staining revealed focal desmin positivity in the cytoplasm of tumor cells, while CK, S100, and CD34 antibodies were negative.

The EWSR1-CREB1 gene fusion or EWSR1 gene rearrangement is an important genetic feature in PPMS and plays a crucial role in its diagnosis. Genetic testing the FISH can aid in diagnosis, with 84% of PPMS cases showing EWSR1 gene rearrangement and approximately 78% showing EWSR1-CREB1 gene fusion through RT-PCR. Therefore, it is important to fully consider the histopathological characteristics, immunohistochemical findings, and FISH results when diagnosing PPMS.[5,9,10]

In this case, the planned tumor excision procedure revealed that the mass was not found in the mediastinum, but was instead was located in the lung, causing adhesions to the right middle and inferior lobes. As a result, tumor excision could not be performed, and only an open biopsy was conducted. Several cases of PPMS have been reported in the literature. Smith et al. reported a case in a 28-year-old male with a main symptom of hemoptysis for four months.[8] Similarly, Thway et al. reported two cases involving a 63-year-old former smoker presenting with hemoptysis as the main symptom and a 28-year-old male non-smoker who presented with hemoptysis accompanied by fever and weight loss.[3]

Agaimy et al. reported a case of PPSM in a 48-year-old Caucasian male with a significant smoking history and chronic obstructive pulmonary disease (COPD) who presented with shortness of breath. A CT scan revealed a large mass (>14 cm) in the right hemithorax, extending into the right main bronchus, compressing the left main bronchus and reaching the trachea. Histopathological examination of the tumor tissue from bronchoscopy revealed medium-sized epithelioid spindle and round cells arranged in a reticular pattern, with fewer than two mitoses per 10 high-power fields. The cellular areas were solid and mixed with myxoid components. Immunohistochemical staining showed diffuse expression of vimentin and varying expression of EMA and CD10, while pan-cytokeratin and other specific markers were negative. Genetic analysis using the FISH for EWSR1, FUS, NR4A3, and SMARCB1 probes showed no translocations or copy number alterations of the genes.[9]

Wu et al. reported a case of PPMS in a 44-year-old male with nonspecific symptoms. Physical examination identified bilateral thyroid enlargement. A contrast-enhanced CT scan of the chest revealed a solid nodule measuring 2 cm in the right upper lung near the azygos vein. Microscopically, the tumor cells were

round and spindle-shaped, arranged in a reticular or ribbon-like pattern within a myxoid stroma, accompanied by extensive lymphocytic and plasma cell infiltration. Immunohistochemical analysis showed diffuse positivity for vimentin and EMA, focal weak positivity for Bcl6, low Ki-67 labeling index, and negativity for AE1/AE3, ALK Ventana, CD34, CD68, SMA, and CD99. FISH analysis revealed an EWSR1 gene rearrangement.[5]

The primary management of PPMS involves tumor excision, which may include lung segmentectomy, lobectomy, or pneumonectomy.[7] Surgery can be performed for patients whose tumors are of a resectable tumor and have not spread to other organs or lymph nodes, and who have good lung and cardiac function.[11,12,13] In this case, tumor excision could not be performed due to the adherence of the tumor mass to the right middle and inferior lobes, preventing its complete removal. For patients who are not candidates for surgery, chemotherapy and radiotherapy can be considered. Preoperative neoadjuvant therapy could potentially reduce tumor size, enabling complete surgical excision. However, no data on patients who underwent neoadjuvant therapy are available.[14,15] In this case, the patient was planned for radiotherapy and palliative care.

In a case reported by Wu et al., the patient underwent a right upper lobectomy and lymph node dissection, without post-surgical radiotherapy. No signs of recurrence or metastasis were observed within 12 months after the surgery.[5] Meanwhile, in a case reported by Agaimy et al., surgery was not feasible due to a large tumor (>14 cm) in the right hemithorax extending to the right main bronchus, compressing the left main bronchus and reaching the trachea. No regional or distant metastasis was found. The patient received palliative chemotherapy with doxorubicin and trabectedin, followed by palliative radiotherapy. Post-chemoradiotherapy CT scan indicated stable disease. However, 13 months later, a new cerebellar metastasis was detected, and the patient continued palliative care.[9]

Although PPMS is considered a low-grade sarcoma, no specific histological or clinical features can reliably predict prognosis or therapeutic outcomes of patients. Histologically, some cases may show atypical nuclei, necrosis, and high mitotic activity, but these do not necessarily correlate with a worse prognosis. Molecular testing may provide prognostic insights. Patients with EWSR1 gene rearrangement or EWSR1-CREB1 gene fusion may have a better prognosis compared to those without EWSR1-CREB1 fusion or those with wild-type EWSR1. The relationship between genetic characteristics and survival rates in PPMS requires further investigation.[16-18]

Approximately 90% of patients were reported to recover well after surgery, without recurrence or metastasis. However, five patients had developed metastasis after surgery: one with brain metastasis, one with kidney metastasis, one with contralateral lung metastasis, one with cerebellar metastasis, and one with pleural and bone metastasis. Patients with metastasis typically survive for 23 to 72 months, with only the patient with brain metastasis reported to have died a few months after its detection. Patients without metastasis were reported to survive for up to 15 years.[5,19,20]

CONCLUSION

PPMS is a rare condition. The clinical manifestations in this patient included hemoptysis, shortness of breath, chest pain, loss of appetite, and weight loss. The patient's examination results fulfilled the essential criteria for PPMS according to the WHO 2021 diagnostic criteria, which include a primary tumor in the lung, spindle- and round-shaped tumor cells arranged in a reticular pattern within a myxoid stroma, and immunohistochemical findings that exclude other tumors with histologically similar features. Tumor excision could not be performed in this patient due to an attachment of the tumor mass to the middle and lower lobes of the right lung. As a result, the patient was planned for radiotherapy and palliative care. Patients who cannot undergo surgery require multidisciplinary treatment. This case underscores the importance of long-term monitoring, the potential role of genetic testing in guiding management, and the need for further research on treatment strategies.

Consent

Written informed consent was obtained from the patient.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Authors' Contributions

All authors contributed and approved the final version of the manuscript.

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