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Atypical Presentation of Pleomorphic Liposarcoma in the Intrathoracic Extrapulmonary Region

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Abstract

Liposarcoma (LPS) is a malignant tumor of mesenchymal origin derived from adipocytic lineage. Among its histological subtypes, pleomorphic liposarcoma (PL) represents a rare and highly aggressive variant. PL typically affects the extremities and is most often diagnosed in patients over the age of 50. Its occurrence within the thoracic cavity, especially in young adults, is exceptionally uncommon and frequently associated with pulmonary metastasis. We present the case of a 32-year-old male with no notable medical history who reported symptoms of dyspnea, left-sided posterior thoracic pain, and a non-productive cough. Radiological evaluation revealed a large extrapulmonary, intrathoracic mass originating from the left pleura, causing significant compression of the heart and left lung, leading to atelectasis, though without invasion of the pulmonary parenchyma or chest wall. Initial differential diagnoses included hemothorax, empyema, and pleural effusion based on the mass's location and radiodensity; however, drainage attempts produced only minimal fluid.

Thoracotomy performed for presumed pleural decortication unexpectedly revealed a solid mass with localized pleural adhesions. Histopathological examination of the biopsied tissue confirmed a diagnosis of high-grade pleomorphic liposarcoma, characterized by extensive necrosis and the presence of pleomorphic lipoblasts. The patient was initiated on the AIM chemotherapy regimen (adriamycin/doxorubicin, ifosfamide, mesna), and further oncologic care was coordinated through a specialized treatment center. Several aspects of this case were particularly atypical, including the patient's young age, the intrathoracic extrapulmonary tumor location, the absence of significant pulmonary invasion or distant metastasis, and the lack of identifiable genetic or environmental risk factors. Given the aggressive biology and poor prognosis associated with pleomorphic liposarcoma, treatment typically necessitates a multimodal approach, which can be especially complex due to limited data and guidelines for

this rare variant. This case not only illustrates an unusual clinical manifestation of sarcoma but also highlights current therapeutic challenges and underscores the urgent need for research into targeted, subtype-specific treatment protocols.

Keywords: Atypical Lipomatous Tumor, Alcohol, Liposarcoma, Mild Leukocytosis

Introduction

Liposarcoma (LPS) is a malignant tumor of mesenchymal origin arising from lipoblasts or adipocytes and remains relatively rare among neoplasms. However, it is the most frequently encountered malignant soft tissue tumor, accounting for up to 20% of all soft tissue sarcomas[1]. Depending on the histological subtype, LPS can develop in various deep soft tissue compartments, including the extremities, retroperitoneum, mediastinum, paratesticular areas, head and neck region, and even the esophagus[2]. Notably, benign lipomas very rarely undergo malignant transformation into liposarcomas[3].

There are four primary histological subtypes of liposarcoma: atypical lipomatous tumor (ALT)/well-differentiated liposarcoma (WDL), dedifferentiated liposarcoma (DDL), myxoid liposarcoma (ML), and pleomorphic liposarcoma (PL)[2]. ALT/WDL and DDL are the most prevalent subtypes and are characterized by amplification of the 12q14-15 chromosomal region[2]. ALT typically arises in surgically accessible locations such as the extremities, allowing for complete excision and potential cure[4]. In contrast, tumors found in less accessible sites like the retroperitoneum, mediastinum, or paratesticular regions are classified as WDL, given their higher likelihood of recurrence and invasive behaviour[4]. Myxoid liposarcoma, the third most common variant, also frequently originates in the extremities and is associated with a characteristic FUS-CHOP gene fusion resulting from a translocation involving chromosome 12[5]. DDL shares the same genetic hallmark as ALT/WDL (12q14-15 amplification) and most often arises in the retroperitoneum, either de novo or as a progression from a pre-existing ALT/WDL lesion[6]. Pleomorphic liposarcoma, the rarest and most genetically complex subtype, exhibits variable clinical behaviour and remains poorly understood.

Pleomorphic liposarcoma (PL) represents less than 5% of all liposarcoma cases and is the least characterized among the major subtypes, with most literature emerging only in the 21st century[7-9]. It typically arises between the fifth and seventh decades of life and is most frequently located in the soft tissues of the lower extremities[8]. Genetically, PL is often associated with mutations in TP53, RB1, and NF1, but it also exhibits a wide array of chromosomal abnormalities, making it more genetically and morphologically complex than other LPS subtypes, which tend to have well-defined molecular profiles[2]. These factors, along with a limited understanding of effective targeted treatments, contribute to its poor prognosis—the worst among LPS subtypes—with a five-year survival rate of approximately 57%[7]. While PL commonly presents in older individuals with extremity tumors and subsequent pulmonary metastases[2], this case is noteworthy for its rare manifestation as a primary intrathoracic, extrapulmonary tumor in a young adult.

Case Presentation

A 32-year-old male with a medical history of well-controlled asthma and attention deficit hyperactivity disorder presented to the emergency department with progressively worsening shortness of breath. The dyspnea had been ongoing for three months but had acutely intensified two days before presentation. The patient also reported the sudden onset of sharp, localized pain in the left posterior thoracic region, which began two days prior and was not associated with radiation.

Additionally, he experienced a dry, non-productive cough that started three days before admission.

He was not on any regular medications and reported no history of tobacco, alcohol, or illicit drug use. There were no known occupational or environmental exposures, and his family history was negative for malignancies or major medical conditions. His asthma had remained asymptomatic since childhood. He denied experiencing extremity swelling, claudication, palpitations, gastrointestinal symptoms, fatigue, or syncopal events. Notably, he had never experienced a similar episode in the past.

On physical examination, the patient appeared in mild distress but remained alert and oriented. He was tachycardic, with a heart rate of 130 beats per minute, and had an oxygen saturation of 87% on room air; other vital signs were within normal limits. Respirations were mildly labored, and auscultation revealed clear breath sounds bilaterally, accompanied by mild tachypnea. An electrocardiogram (ECG) showed sinus tachycardia. Initial laboratory findings, summarized in Table 1, revealed normocytic anemia, mild leukocytosis, and a slightly elevated prothrombin time. The basic metabolic panel (Chem 6) showed normal levels of carbon dioxide, chloride, creatinine, potassium, sodium, and blood urea nitrogen.

Table 1: Relevant lab values

Relevant Labs	Lab Values	Normal Reference Values
Hemoglobin (g/dL)	11.5	13.2 – 16.6 (males)
Total Iron Binding Capacity (mcg/dL)	232	250 – 450
Prothrombin Time (seconds)	17	11 – 15
Leukocytes (cells/microliter)	15,000	4,500 – 11,000
Troponins (ng/mL)	0.2	0 – 0.4

A non-contrast chest CT scan (depicted in Figure 1 and Figure 2) revealed a sizable, heterogeneous mass of intermediate density located in the left posterior thoracic cavity, outside the lung parenchyma. The lesion appeared extrapulmonary and was most consistent with a pleural-based origin. It caused anterior displacement and mild compression of the heart, along with anterior displacement of the left lung and associated atelectasis. The lung compression was further compounded by the presence of a large hiatal hernia containing portions of the stomach and colon. Notably, there was no radiographic evidence of invasion into the chest wall.

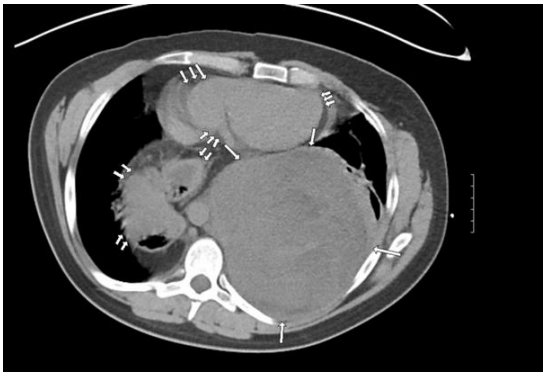

Figure 1: Axial non-contrast chest CT in a soft tissue window. A large intrathoracic, extrapulmonary mass is visualized compressing the heart anteriorly (single arrow). A hiatal hernia is incidentally noted within the right thoracic cavity, containing abdominal contents such as stomach and colon (double arrows). The heart is

displaced anteriorly and compressed against the chest wall by the mass (triple arrows). The lesion lacks areas of macroscopic fat density when compared to adjacent intra-abdominal fat. The measured attenuation of the mass ranges from 5 to 30 Hounsfield units (HU), with an average of approximately 25 HU.

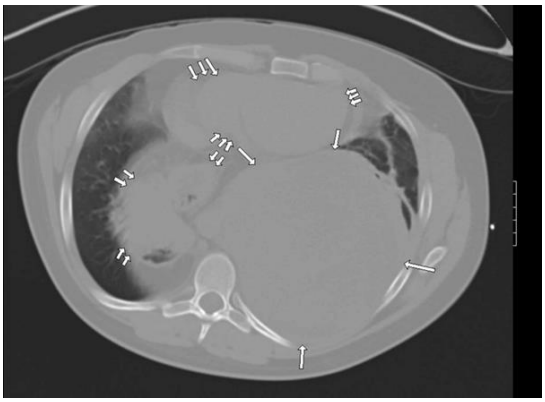

Figure 2: Axial non-contrast chest CT in a lung window. This image demonstrates the same findings as described in Figure 1, including a large extrapulmonary intrathoracic mass compressing the heart and displacing the left lung. The lung window provides improved visualization of the pulmonary parenchyma and air spaces, highlighting associated left lung atelectasis. The mass does not appear to invade the lung tissue.

The lesion's non-fatty, heterogeneous appearance and average attenuation of 25 Hounsfield units (HU) on CT imaging raised a differential that included hemothorax, empyema, and soft tissue neoplasm. In the absence of an air-fluid level and based on the density characteristics consistent with blood, hemothorax was initially considered the most likely diagnosis, prompting a plan for percutaneous drainage. Infectious Disease specialists also recommended empiric coverage with a seven-day course of piperacillin-tazobactam to address the possibility of empyema or a parapneumonic effusion.

A percutaneous thoracostomy was performed, yielding only a small amount of bloody effusion—presumed to be limited by clot formation and organization of the suspected hemothorax. Due to insufficient drainage and ongoing clinical concern, the patient subsequently underwent thoracotomy for pleural evacuation and decortication. Intraoperatively, a solid extrapulmonary mass was unexpectedly encountered in the posterior thoracic cavity. The mass caused near-complete compression of the left lower lobe and demonstrated adherence to the pleura of both the upper and lower lobes, raising concern for limited local invasion. A large volume of dark blood and necrotic debris oozed from the mass, with an estimated intraoperative blood loss of 3.8 liters. Partial resection of the tumor was performed, and tissue samples were submitted for histopathological analysis.

Histopathological evaluation revealed a high-grade liposarcoma characterized by extensive areas of necrosis, the presence of occasional multinucleated giant cells, pleomorphic lipoblasts, and numerous mitotic figures. Immunohistochemical staining showed strong positivity for vimentin and negativity for pancytokeratin, findings consistent with pleomorphic liposarcoma. However, the differential diagnosis initially included other high-grade dedifferentiated sarcomas.

The patient was initiated on a chemotherapy regimen consisting of adriamycin (doxorubicin), ifosfamide, and mesna (AIM), administered every 21 days for a total of five cycles. Pegfilgrastim was also given to reduce the risk of neutropenic complications. The patient subsequently transitioned care to an oncology center at another hospital and is currently completing the final cycle of the AIM regimen. Follow-up imaging will be performed upon completion of chemotherapy to assess the tumor's response to treatment.

Discussion

This case describes a rare instance of primary pleomorphic liposarcoma (PL) originating in the thoracic

cavity of a young adult, likely arising from the pleura, without chest wall involvement or evidence of widespread pulmonary metastasis. Such presentations are exceedingly uncommon—less than 1% of all primary liposarcomas occur in the thoracic cavity, and liposarcomas constitute under 1% of all mediastinal tumors[4,10]. Among the small subset of thoracic liposarcomas, most are associated with extensive metastatic disease, particularly to the lungs [2,10].

In contrast, this patient's tumor showed no significant metastatic spread, and the pulmonary symptoms were attributed primarily to the compressive effects of the mass rather than parenchymal invasion. The anterior displacement and compression of the heart, along with localized pleural irritation, likely accounted for the patient's dyspnea and thoracic pain. These findings are consistent with the characteristic clinical progression of liposarcomas, which often remain asymptomatic until the tumor grows large enough to cause mechanical compression and organ displacement [10]. In this case, the gradual onset of symptoms evolving into acute respiratory compromise underscores the slow-growing yet space-occupying nature of these tumors.

The unusual nature of this case is underscored not only by the tumor's thoracic location but also by the patient's age and histological subtype. Liposarcomas are typically diagnosed in older adults, making this young adult presentation particularly uncommon[8]. While the patient's demographic profile aligns with the known epidemiology—white males having a higher incidence of LPS[11]—the tumor's histological subtype further distinguishes this case. Among pediatric and young adult populations, myxoid liposarcoma (ML) is by far the most prevalent subtype, whereas pleomorphic liposarcoma (PL), as seen in this patient, is exceedingly rare in this age group[12].

Additionally, the pathology report raised the possibility of dedifferentiated liposarcoma (DDL) variants, citing the expanding morphological spectrum of DDL to include less typical presentations. This distinction is clinically relevant, as ruling out DDL through further histological sampling would reinforce the PL diagnosis and help guide management[7]. Accurate subtype classification remains critical due to differences in prognosis, recurrence risk, and response to therapy.

Few cases of liposarcoma have presented in the thoracic cavity with minimal pulmonary metastasis and no identifiable risk factors, as observed in this patient. He lacked a family history of genetic syndromes commonly linked to soft tissue sarcomas, such as Li-Fraumeni syndrome, retinoblastoma, or neurofibromatosis type 1—conditions most frequently associated with liposarcoma development[2]. Additionally, he had no history of smoking, toxic chemical exposure, industrial solvent contact, or prior radiation—environmental factors often implicated in sarcomagenesis. In the absence of these typical risk factors, the pathophysiological basis for this patient's pleomorphic liposarcoma remains unclear. Further genetic testing for germline and somatic mutations may provide insights into predisposing molecular mechanisms.

Pleomorphic liposarcoma (PL) accounts for only 5–10% of all liposarcomas, yet it is considered the most aggressive, with a high propensity for early and widespread metastasis, particularly to the lungs—reported in over 50% of cases[9,13]. Notably, in this case, the tumor originated within the thoracic cavity but showed no significant infiltration of the lung parenchyma, a rare feature that underscores the unusual nature of this presentation.

Standard management of PL involves early and aggressive surgical resection, often followed by adjuvant

chemoradiation to reduce recurrence risk. Despite these measures, PL has a local recurrence rate of approximately 45%[13]. Given this high risk, radical surgeries involving resection of adjacent organs (such as kidneys or sections of the colon) are frequently necessary[14], contributing to increased morbidity and diminished quality of life. Thus, there is a critical need for improved strategies that reduce tumor recurrence while minimizing the invasiveness of surgical intervention.

Current treatment approaches for unresectable or advanced liposarcomas focus on systemic chemotherapy to delay disease progression and metastasis. However, the efficacy of chemotherapy in PL remains limited, partly due to its genetic and morphological heterogeneity [14]. The patient was treated with the AIM regimen (adriamycin, ifosfamide, mesna), a commonly used combination for soft tissue sarcomas[15]. Although this regimen is widely used, it is not specifically tailored to pleomorphic subtypes due to the scarcity of subtype-specific clinical data [16].

Emerging alternatives, such as pegylated liposomal doxorubicin combined with ifosfamide, have demonstrated comparable efficacy with reduced toxicity when compared to traditional AIM regimens[17]. Moreover, newer agents like eribulin and trabectedin have shown promise in improving outcomes in advanced or treatment-resistant liposarcomas, with some studies suggesting superiority over doxorubicin monotherapy[15]. Continued research into molecular profiling and targeted therapies remains essential to improving survival outcomes and quality of life in patients with PL.

Conclusions

This case illustrates an exceptionally rare presentation of pleomorphic liposarcoma (PL) in a young adult, originating intrathoracically from the pleura with minimal pulmonary involvement. The unusual combination of patient age, tumor location, and histological subtype underscores the diagnostic and therapeutic challenges associated with PL. The absence of identifiable genetic, environmental, or familial risk factors further highlights existing gaps in our understanding of the disease's etiology and progression in atypical patient populations.

While multi-agent chemotherapy regimens such as AIM (adriamycin/doxorubicin, ifosfamide, and mesna) offer some efficacy in managing soft tissue sarcomas, the lack of subtype-specific, targeted therapies limits the ability to achieve durable responses in PL. Given its aggressive behavior, high recurrence rate, and resistance to conventional treatment, PL requires further investigation into its molecular drivers and therapeutic vulnerabilities. This case reinforces the need for ongoing research into personalized treatment strategies that can improve clinical outcomes and quality of life for patients facing this rare and aggressive malignancy.

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