CASE REPORT

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Navigating diagnostic uncertainty in a giant anterior mediastinal mass: A case report of T-cell lymphoblastic lymphoma

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ABSTRACT

Introduction: Mediastinal masses account for about 3% of all thoracic tumors and include a range of pathologies in the anterior compartment, with thymoma, thymic carcinoma, teratoma, and lymphoma being the most common. Mediastinal T-cell lymphoblastic lymphoma (T-LBL) is rare and may mimic other mediastinal tumors, as demonstrated in this case. Anemia is frequently associated with malignancy, although severe anemia is rare. This case highlights the diagnostic limitations of imaging and tumor markers alone and emphasizes the crucial role of surgical biopsy and immunohistochemistry in establishing the definitive diagnosis of a large anterior mediastinal mass.

Case description: We report a 35-year-old man presenting with fatigue and palpitations after low-intensity exercise and a chronic progressive cough. Laboratory tests showed severe anemia, while bone marrow examination demonstrated reactive marrow. Fine-needle aspiration biopsy suggested chronic inflammation, with the possibility of a mature teratoma being considered. Chest radiography revealed multiple nodular and lobular opacities, raising suspicion of left lung malignancy, whereas contrast-enhanced computed tomography showed a large anterior mediastinal mass with lobulated, irregular, and dense calcification, measuring 14.6 x 7.2 x 6.8 cm, invading mediastinal structures. Tumor markers were normal. Surgical resection through a left hemiclamshell thoracotomy revealed a solid, elastic mass with partial cystic change and calcification, confirmed by immunohistochemistry as T-cell lymphoblastic lymphoma (T-LBL).

Conclusion: Accurate diagnosis remains challenging and may require surgical resection biopsy for confirmation. It also underscores the importance of surgical biopsy for large tumors invading mediastinal structures, particularly when non-invasive methods fail to provide sufficient information for a definitive diagnosis.

Keywords: anterior mediastinal mass, hemiclamshell thoracotomy, mediastinal T-cell lymphoblastic lymphoma, mediastinal teratoma.

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INTRODUCTION

Mediastinal tumors comprise approximately 3% of all thoracic tumors. Mediastinal mass includes several entities, presenting a wide variety of clinical and pathological features.[1,2] Mediastinal tumors are divided into anterior, middle, and posterior compartments, accounting for 50% of all mediastinal masses.[3] Anterior mediastinal masses (pre-vascular compartment) can represent a wide spectrum of diseases including thymoma, thymic carcinoma, teratoma, and lymphoma. Anterior mediastinal masses are relatively rare.[4] Large anterior mediastinal tumors may invade adjacent mediastinal structures and present diagnostic and therapeutic challenges because of the complex anatomy of the mediastinum.[5]

Lymphoblastic lymphoma (LBL) is rare and represents 1-2% of all non-Hodgkin lymphoma (NHL).[6,7] T-cell lymphoblastic lymphoma (T-LBL) represents approximately 90% of LBL cases and has a strong predilection for mediastinal involvement, often presenting as a large anterior mediastinal mass. Clinical manifestations are frequently nonspecific, including dyspnea, cough, chest pain, and symptoms related to mediastinal compression.[8,9] The radiological features of T-LBL may overlap with those of other anterior mediastinal tumors, particularly thymoma and germ cell tumors, making diagnosis based on imaging alone challenging.[10] Although fine needle aspiration biopsy (FNAB) and cytological examination may provide useful diagnostic information, definitive classification generally requires morphological and immunophenotypic assessment. T-LBL typically demonstrates an immature T-cell phenotype, including expression of terminal deoxynucleotidyl transferase (TdT) and cytoplasmic CD3.[9,10] Thus, T-LBL may be difficult to distinguish from other anterior mediastinal masses when clinical, radiological, and cytological findings are inconclusive.[11]

Surgical intervention plays an essential role and is required to obtain a definitive diagnosis and treatment

for large anterior mediastinal tumors, particularly when previous diagnostic workup is inconclusive.[11] Initial radiological, biochemical markers, and fine needle aspiration biopsy (FNAB) suggested a mediastinal teratoma. However, the definitive diagnosis of T-cell lymphoblastic lymphoma (T-LBL) was established only after surgical biopsy and immunohistochemistry. The novelty of this case lies in the rare presentation of T-cell lymphoblastic lymphoma (T-LBL) as a giant anterior mediastinal mass that mimicked a mediastinal teratoma on non-invasive evaluation. This case highlights the diagnostic limitations of imaging and tumor markers alone and emphasizes the crucial role of surgical biopsy and immunohistochemistry in establishing the definitive diagnosis of a large anterior mediastinal mass.

CASE DESCRIPTION

A 35-year-old male presented with 1-week of weakness and palpitations following low-intensity exercise, along with a tendency to get tired easily after physical activity. He also reported a progressively worsening cough over the past few years, increasing weakness and fatigue over the past year, and complaints of nausea and vomiting. He presented with recurrent episodes of severe anemia and had been hospitalized three times this year. He had been diagnosed with a left-sided lung cancer 10 years prior at another medical facility but declined further evaluation and treatment at that time. No medical records or detailed history from that prior visit were available. Physical examination revealed conjunctival pallor. Hepatomegaly was found. No peripheral lymphadenopathy was palpated.

An abdominal ultrasonography revealed mild hepatomegaly, thickening of the descending colon wall, and minimal free fluid in the Morrison pouch and pelvic cavity. Laboratory tests showed a severely reduced hemoglobin level of 3.5 g/dL. Further tumor marker investigations showed lactate dehydrogenase (LDH) levels of 161 U/L, β-human chorionic gonadotropin (β-HCG) levels of <1.2 mIU/mL, and alpha-fetoprotein (AFP) levels of 1.95 ng/mL. All values were within normal limits. Bone marrow

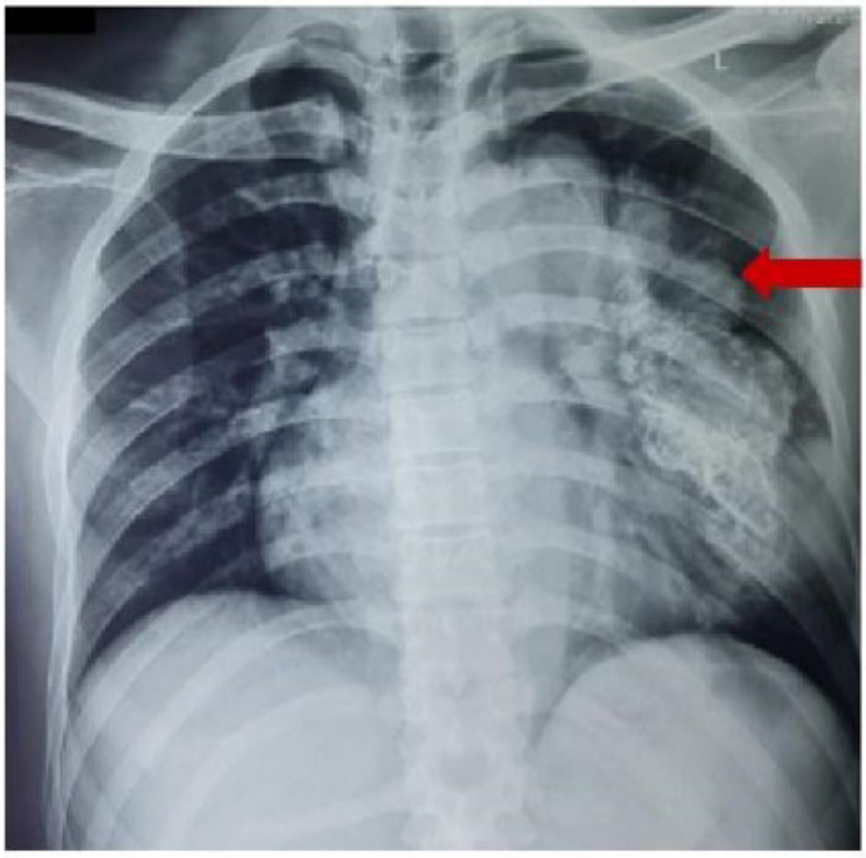


Figure 1. Preoperative chest X-ray demonstrating multiple nodular opacities in the left hilum and paracardial region (red arrow)

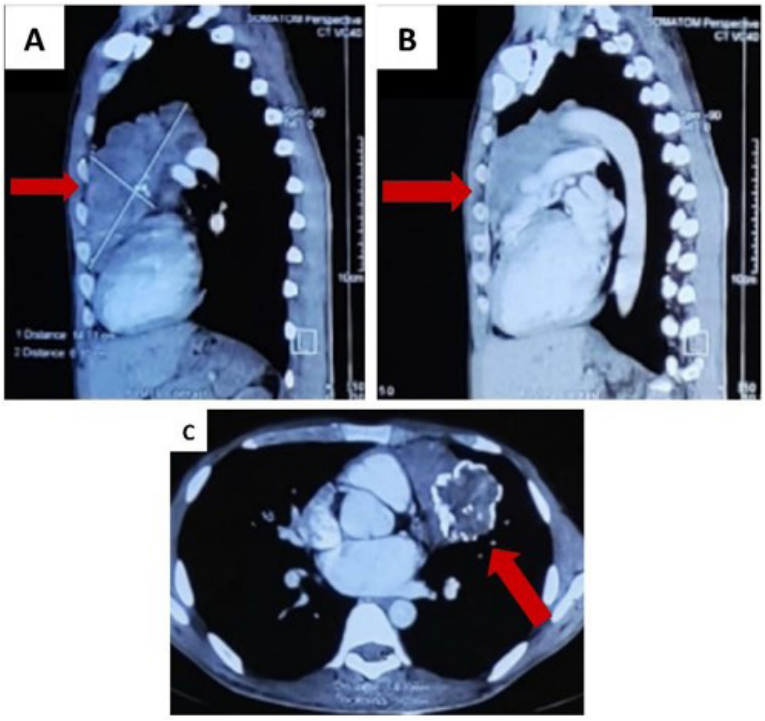


Figure 2. Pre-operative computed tomography scan revealed a lobulated, isodense soft tissue mass with irregular and dense calcifications in the left anterior mediastinum, extending to the left hilum. Sagittal view of the mass (red arrow) (A, B). Axial view of the mass (red arrow) (C).

examination was performed and revealed a reactive bone marrow, while fine-needle aspiration biopsy (FNAB) showed infiltration of chronic inflammatory cells, including neutrophils, lymphocytes, and macrophages, with no evidence of malignancy. However, the possibility of a mature teratoma should be considered.

A chest X-ray revealed multiple nodular opacities in the left hilum, along with lobular opacities in the left paracardial region with the "popcorn-like" calcification appearance (**Figure 1**). The radiological impression suggested a suspected left lung cancer, with differential diagnosis including lymphoma or pulmonary hamartoma.

A contrast-enhanced chest CT scan was subsequently performed, revealing a lobulated, isodense soft tissue mass with irregular and dense calcifications in the left anterior mediastinum, extending to the left hilum. The mass was found to be in contact with the left pericardium, ascending aorta, aortic arch, proximal descending aorta, and the anterior left pleura (**Figure 2**). It was also compressing the left pulmonary veins and artery. The size of the lesion measured approximately 14.6 x 7.2 x 6.8 cm and exhibited inhomogeneous enhancement with contrast. These imaging showed a suggestive of a large anterior mediastinal mass with extension to surrounding structures.

Patient then transferred to the Department of Thoracic, Cardiac, and Vascular Surgery. The patient declined intraoperative diagnosis of mediastinal tumor for a year. Hence, the patient agreed to undergo the surgery. Sternotomy and high-risk anterior mediastinal mass surgical resection were done. Surgical findings revealed a solid, elastic tumor with heterogeneous consistency located in the anterior mediastinum, with evidence of calcification and partial cystic (**Figure 3A**). Intraoperative findings revealed extensive tumor invasion involving the innominate vein, ascending aorta, aortic arch, proximal and descending aorta, left pulmonary artery and vein, left lung, and left phrenic nerve. The left phrenic nerve was sacrificed, and partial pericardiectomy was performed.

Postoperative histopathological examination revealed neoplastic cell proliferation, forming poly-multinodular areas separated by fibrous septa. The neoplastic cells were small to medium in size; nuclei were round to slightly irregular with coarse chromatin and conspicuous to prominent nucleoli, which were single or multiple. Mitotic activity was increased, with approximately 10 mitoses per 10 high-power fields. Tingible body macrophages producing a starry sky appearance were observed. This led to a differential diagnosis of lymphoma versus thymoma B1. Postoperative chest X-ray revealed no residual mediastinal mass and the presence of wire sternotomy (**Figure 3B**).

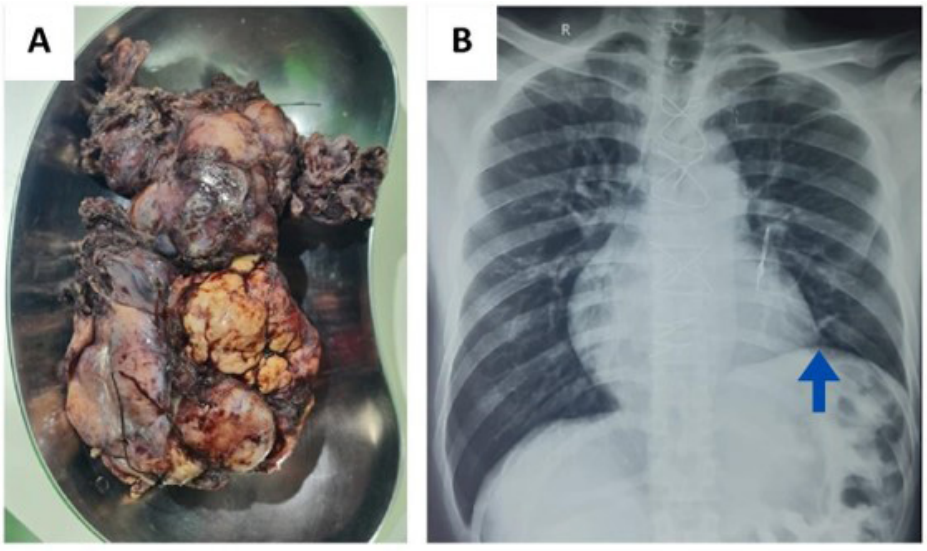


Figure 3. Gross examination of the mediastinal mass revealed a solid, elastic tumor with heterogeneous consistency located in the anterior mediastinum, with evidence of calcification and partial cystic (A). Postoperative chest X-ray revealed no residual mediastinal mass and the presence of a wired sternotomy. Postoperative left phrenic nerve paralysis (blue arrow) (B).

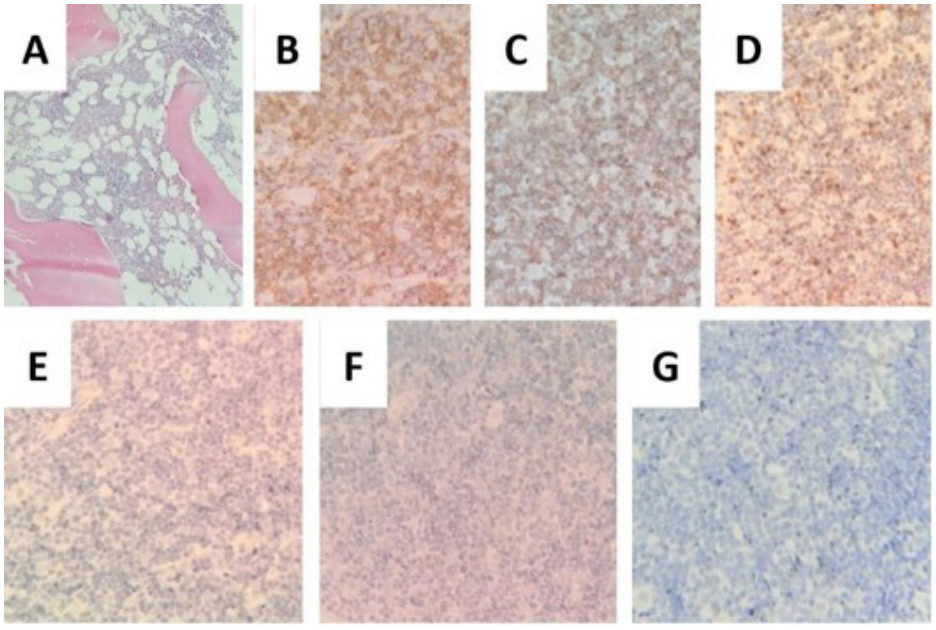


Figure 4. Histopathological examination revealed small to medium sized round cells with neoplastic cell proliferation, forming poly-multinodular areas separated by fibrous septa, and tingible body macrophages was observed (A), immunohistochemical revealed the lymphoid cells were positive for CD45 (B), CD3 (C), while Ki-67 showed proliferation index of over 40 (D), and negative for cytokeratin (E), CD30 (F), and CD20 (G)

Further immunohistochemical studies were performed (**Figure 4**). Immunohistochemical analysis revealed that the lymphoid cells were positive for CD45 and CD3, while Ki-67 showed a proliferation index of over 40 in tumor cell nuclei. Tumor cells were negative for cytokeratin, CD30, and CD20. These findings led to the diagnosis of high-grade non-Hodgkin lymphoma, T-cell type.

The patient was discharged a week postoperative and was scheduled for follow-up with the Department of Oncology. Chemotherapy was delayed for one year after surgical treatment due to the patient's refusal. One year later, the first chemotherapy regimen, consisting of cyclophosphamide, doxorubicin, vincristine, and prednisone, was administered. For a more detailed chronological case, we add a timeline figure below (**Figure 5**).

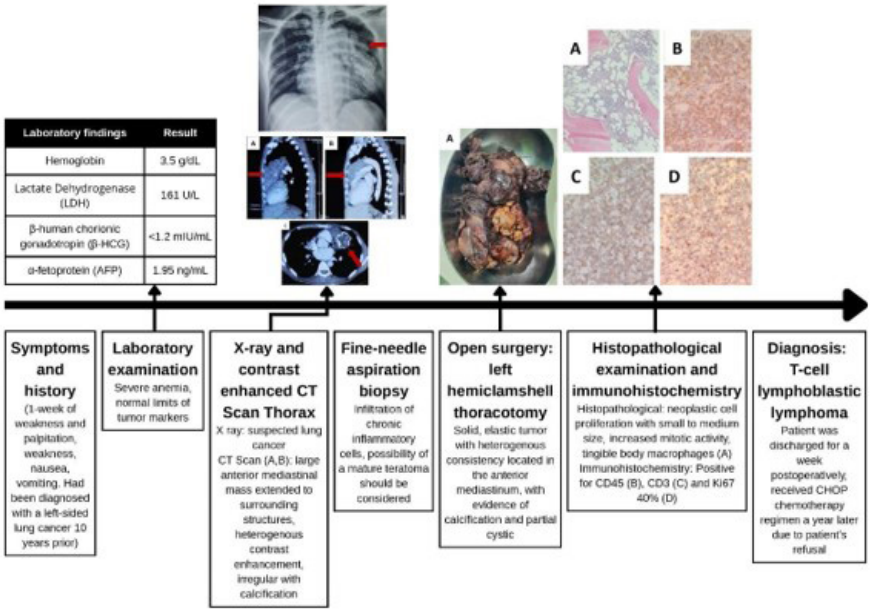


Figure 5. Timeline of patient's clinical course

DISCUSSION

Primary mediastinal lymphoma is a rare entity, accounting for approximately 10% of all mediastinal lymphomas. It typically arises in the anterior mediastinum and is often associated with more extensive disease. Hodgkin lymphoma (HL) represents approximately 50-70% of mediastinal lymphomas, while non-Hodgkin lymphoma (NHL) accounts for 15-25%. The most common anterior mediastinal NHLs are primary mediastinal large B-cell lymphoma and primary mediastinal T-cell lymphoblastic lymphoma (T-LBL).[12,13]

Lymphoblastic lymphoma (LBL) is rare and represents 1-2% of all non-Hodgkin lymphoma (NHL). Among these, T-cell lymphoblastic lymphoma (T-LBL) accounts for about 85-90% of cases of all lymphomas arising in the anterior mediastinum and predominantly affects males. It is typically diagnosed during late childhood (15-20%), adolescence, and young adulthood (25%).[6,7]

In this case, the chief complaints associated with weakness and a tendency to get tired easily may indicate a significant decreased of hemoglobin, as presented by severe anemia. Anemia is a common finding among cancer patients, occurring in up to 40% of those with solid tumors. Hence, only 1% have severe anemia (6.5-7.9 g/dL). Negative prognostic factors in malignancy include anemia, bulky mediastinal disease, superior vena cava syndrome, bone marrow and/or central nervous system involvement, and effusions. Among these, anemia alone has been identified as an important predictor of prognosis of mediastinal tumors. The presence of anemia has been associated with poorer survival outcomes and increased mortality risk.[12,14]

The initial diagnosis of mature teratoma was primarily based on contrast-enhanced chest CT findings demonstrating heterogeneous contrast enhancement and irregular and calcified components, a finding that contributed to the presumptive diagnosis of mediastinal teratoma. Imaging findings include calcification in 20-40% of cases, which may manifest as calcified tumor walls, mature bones, or residual dental elements in mediastinal teratoma. Attenuation is heterogeneous, with varying combinations of soft tissue, fluid, fat, and calcification. CT scan typically demonstrates a well-demarcated lesion with both cystic and calcified components.[15,16]

Teratoma is a type of germ cell tumor that commonly presents as a large anterior mediastinal mass. Patients may experience symptoms such as chest pain, chronic cough, or dyspnea, which are typically caused by compression or obstruction of adjacent mediastinal structures. These clinical manifestations are generally related to the tumor size and extent of compression of surrounding structures. Systemic symptoms are uncommon.[15,16]

This case may also be presented with inconclusive results of various diagnostic workups. Aida et al. reported a similar case in which the initial diagnostic workup was inconclusive. However, it was confirmed through histopathological examination of a surgical biopsy specimen as mediastinal tuberculosis.[11] This may highlight the importance of establishing an accurate differential diagnosis, as lymphoma requires chemotherapy as definitive treatment.[12,17]

In this case, normal LDH was observed, and it correlates with tumor burden, growth rate, cellular proliferation, and invasive potential. LDH is a metabolic enzyme widely expressed in different tissues and detectable in serum. It catalyzes the conversion of lactate to pyruvic acid and has been recognized as a prognostic tumor marker in various solid tumors.[18]

FNAB was performed in this case but was unable to establish a definitive diagnosis. FNAB is a minimally invasive technique for obtaining cytological specimens and is often used as an initial diagnostic approach for mediastinal masses. However, false-negative results may occur due to inadequate tissue sampling

is always possible. In particular, the diagnostic sensitivity and diagnostic yield of FNAB in anterior mediastinal masses are reported to be low. Therefore, to obtain sufficient tissue for histopathological examination and immunohistochemical analysis, open surgery was performed to obtain a definitive diagnosis.[19]

Open surgery is indicated for radical resection of large mediastinal tumors that involve mediastinal vascular structures, lungs, and chest wall. In this case, the tumor was found to be extended to the innominate vein, ascending aorta, aortic arch, proximal and descending aorta, left pulmonary artery and vein, left lung, and left phrenic nerve. We aimed to achieve complete surgical resection as much as possible due to the invasion into surrounding mediastinal structures. A left hemiclamshell thoracotomy was selected because the large tumor extended laterally into the left hemithorax, providing adequate exposure for resection.[5] Intraoperatively, the left phrenic nerve was sacrificed because it was inseparable from the tumor, resulting in postoperative left phrenic nerve paralysis (**Figure 3B**).

The hemiclamshell incision combines a partial median sternotomy and anterolateral thoracotomy, providing excellent exposure of the mediastinum, one pleural cavity, and cervical structures. While median sternotomy offers adequate access to the mediastinum and neck, it provides limited visualization of the thoracic cavity, which may be necessary for the resection of large thoracic tumors, lung resection, and preservation of critical structures such as the phrenic nerves, jugulo-subclavian venous confluence, aortic arch, supra-aortic vessels, and superior vena cava. In contrast, an anterolateral thoracotomy provides an excellent view of the thoracic cavity, but limited exposure of the entire mediastinum. By combining the advantages of both approaches, the hemiclamshell thoracotomy offers wide exposure of the cervical structures, mediastinum, and one pleural cavity, making it particularly useful for the resection of large mediastinal tumors extending into the left hemithorax, as observed in our case.[20,21] However, no suitable alternative surgical approach was identified for this case based on the tumor's size, location, and involvement of adjacent structures. The lateral decubitus position used in conventional thoracotomy may be less suitable for large thoracic tumors, as tumor-related compression of the heart and great vessels can further decrease venous return and compromise hemodynamics.[21]

Surgical biopsy with histopathological and immunohistochemical analysis remains the gold standard when non-invasive methods are inconclusive, or when tumors are irregular, lobulated, large, or invading mediastinal structures. In this case, despite multiple diagnostic modalities, a definitive diagnosis was achieved only after open biopsy via thoracotomy, confirming high-grade T-cell non-Hodgkin lymphoma.[14,15]

Microscopically, T-LBL is characterized by small to medium-sized lymphoblasts, with round, irregular, clefted, or convoluted nuclei; moderately condensed or fine chromatin, and frequent mitotic figures. Tingible-body macrophages may be present. These findings were observed in our case, concluded lymphoma or thymoma.[16] However, immunohistochemistry (IHC) analysis was subsequently performed to establish the definitive diagnosis.

Immunohistochemistry (IHC) played a crucial role in confirming the diagnosis of T-cell lymphoblastic lymphoma, as demonstrated in this case. IHC is a highly specific and sensitive diagnostic method for diagnosing neoplastic disease and relies on monoclonal and polyclonal antibodies to detect specific antigens or proteins within a tissue sample. Neoplastic cells variably express T-cell-associated markers such as CD1a, CD2, CD3, CD5, CD7, CD10, CD34, and CD45.[16,22] In this case, lymphoid cells were positive for CD45 and CD3. Ki-67 showed a proliferation index of approximately 40%. CD3 is a pan-T-cell marker widely used to establish T-cell lineage, whereas CD45 is expressed on nearly all hematopoietic cells and plays an essential role in T and B cell antigen receptor-mediated activation. T-LBL is typically characterized by a high proliferation index, with Ki-67 exceeding 90%, reflecting its highly aggressive biological behavior. In our case, the Ki-67 index was lower than typically reported for T-LBL.[16,23,24]

However, the patient's progression of disease (over ten years) is inconsistent with the typical behavior of T-LBL, which is known for its aggressive nature, rapid tumor growth, and swift clinical progression, thereby contributing to the diagnostic challenge. The progression of ten years, with slow-growing CT scan characteristics, biochemical markers, and FNAB, showed a preoperative diagnosis of mediastinal teratoma.[25] Apter et al. reported two patients with calcified T-LBL, in which calcifications were located centrally within the tumor and surrounded by hypodense areas. Although calcification can occur in various tumors, calcification before treatment is uncommon in lymphoma and more often associated with prior chemotherapy or radiotherapy. In mediastinal NHL, calcification before treatment has been linked to more aggressive disease and poorer prognosis. In our case, the presence of calcification contributed to the initial misdiagnosis of mature teratoma.[26]

After the surgery, the patient was discharged a week postoperatively with clinical improvement and referred to the Oncology Department for chemotherapy. However, chemotherapy was delayed for one year due to the patient's refusal, after which the first regimen of cyclophosphamide, doxorubicin, vincristine, and prednisone was administered.

This case report describes a single case and therefore has limited generalizability. The clinical presentation, imaging findings, and diagnostic challenges observed in this patient may not represent in all patients with mediastinal T-LBL. Also, long-term follow-up data were unavailable because lost to follow-up due to socioeconomic constraints and limited access to our hospital resulting from the patient's remote residence. Despite all these limitations, this case provides valuable insight into the rare presentation of T-LBL mimicking a mediastinal teratoma and highlights the importance of surgical biopsy with immunohistochemical analysis when non-invasive methods failed to achieve definitive diagnosis.

CONCLUSION

This case highlights the diagnostic challenges of T-LBL, a rare and aggressive subtype of NHL with a poor prognosis that may mimic other mediastinal masses. It also underscores the importance of considering surgical biopsy, particularly after repeated non-invasive methods fail to establish a definitive diagnosis, as timely histopathological and immunohistochemical confirmation following surgical biopsy is essential for guiding appropriate treatment.

DISCLOSURES

ETHICAL APPROVAL

The patient consented to the publication of this case for research purposes or in a journal.

CONFLICT OF INTEREST

The authors declare that they do not have any conflict of interest, and this case is currently not submitted to any journal or under any consideration for publication in any journal.

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The authors declare that no funding was received for the preparation of this case report

AUTHOR CONTRIBUTION

ES, HH, and AAS contributed to the conception, design, and supervision of this case report. All authors participated in the preparation, drafting, and revision of the manuscript and approved the final revision for submission.

GENERATIVE AI DISCLOSURE

The authors confirm that generative AI tools were used solely for grammar correction and language editing. No generative AI was used to generate or modify the scientific content, data, analysis, figures, or conclusions of this manuscript.

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