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Case Report
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Mediastinal T-Cell Lymphoblastic Lymphoma: A Rare Case in a Limited Resources Setting

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Abstract

Background: Lymphoblastic Lymphoma (LBL) is a rare neoplasm representing 1-2% of all non-Hodgkin's Lymphomas (NHLs).

Objectives: To present challenges in the diagnostic of a rare case in a limited resource setting

Case Presentation: A 36-year-old male came to Dr. Soetomo Hospital with shortness of breath, facial edema, and chest pain. Physical examination revealed a decreased breath sound and dull percussion in the right chest. CT scan showed a solid mass of 10.4 x 5.9 x 14.6 cm in the anterior - medius of the mediastinum. Fine needle aspiration biopsy guided by CT scan showed the spread of lymphoid cells, big in size, anaplastic, rounded, and hyperchromatic nuclei. Core biopsy showed a diffuse and monotonous pattern of pleomorphic cells, round to oval, and hyperchromatic nuclei. Immunostaining was positive for CD3 and Tdt, with a high Ki67 proliferation index of 98%, and negative for CD20.

Conclusion: T-LBL is a rare neoplasm that generally occurs in adolescents and young adults and is most common in males. It is an aggressive neoplasm, which can involve mediastinal mass and cause superior vena cava syndrome. Immunostaining would be positive for Tdt and would variably express CD1a, CD2, CD3, CD4, CD5, CD7, and CD8. The prognosis was poor due to the aggressiveness and the relapse.

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INTRODUCTION

Lymphoblastic Lymphoma is a rare and aggressive non-Hodgkin's Lymphoma accounting for 1-2% of all non-Hodgkin's Lymphoma[1,2]. It is a neoplasm of immature B cells committed to the B-cell or T-cell lineage. T-cell Lymphoblastic Lymphoma (T-LBL) is much more common than B-cell Lymphoblastic Lymphoma (B-LBL). It accounts for approximately 85-90% of all LBLs[3,4] and occurs most frequently in adolescents and young adults, with a male-to-female ratio 2:1[5].

The incidence rate for T-LBL in the United States is approximately 0.4 per 100,000 person-years, corresponding to approximately 1,000 cases per year in the United States[6]. In a Norwegian study for 1985-2004, restricted to patients 15 or older, the incidence of pre–T LBL was 0.2 per 100,000 people per year[6]. The incidence of T-LBL in Indonesia was not reported. In the database of Dr. Soetomo Hospital-Surabaya, there was only 1 case from 16 mediastinal lymphoma from 2016–2017.

T-LBL presents with widespread lymphadenopathy that is usually located above the diaphragm[6]. A common mediastinal mass, present in 60-70% of cases2, can cause superior vena cava syndrome, signaled by facial, neck, or hand edema[7]. Patients with T-LBL may complain of fatigue, shortness of breath, cough, dizziness, abdominal pain, easy bruising or bleeding[6]. T-LBL with mediastinal mass often exhibits rapid growth and presents as a respiratory emergency[8]. It frequently presents with pleural and pericardial effusion[3].

Although the new recommended treatment has improved, with complete remission up to 71%, the prognosis for T-LBL is poor, with a 5-year survival of 26-42% [9,10]. Here, we present the T-LBL case in Dr. Soetomo Hospital-Surabaya, an infrequent and aggressive case from which the patient died one month after being taken to the hospital because of the aggressiveness of the disease.

CASE PRESENTATION

A 36-yo man came to the emergency department of Dr. Soetomo Hospital with the chief complaint of dyspnea that gradually wor-sened in a week. The patient also complained of facial edema, cough, chest pain, and fever. During the interview, the patient said that he had epigastric pain and melena two days before being admitted to the hospital. Physical examination revealed a decrease in breath sound and dullness of percussion in the right hemithorax.

Computed Tomography (CT) examination showed a solid mass (54 HU) without a calcification component, indistinct border, and irregular edge, measuring 10.4x5.9x14.6 cm. The mass showed contrast enhancement (69 HU) in the anterior mediastinum to medius at vertebra Thoracal 2 – thoracal nine levels. It encased and narrowed the superior vena cava, aorta, truncus brachiocephalic, left common carotid artery, left subclavian artery, arcus aorta, right pulmonary artery, and vein, left and right subclavian vein. It pushed the trachea to the posterior and narrowed it at vertebra thoracal four levels. Pericardial effusion and pleural effusion on the right side were also found. There was an enlargement of multiple lymph nodes in the left axilla (the largest diameter: 0.9cm), the right axilla (the largest diameter: 0.5cm), and the left supra clavicle (the largest diameter: 1cm) (Figure 1). The radiologist

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suggested these findings were malignant Lymphoma.

The patient underwent a Fine Needle Aspiration Biopsy (FNAB) guided by a CT scan. The smear yielded the spread of lymphoid cells, anaplastic, with rounded nuclei, prominent in size, and hyperchromatic. These findings were concluded to be malignant round cell tumors appropriate for non-Hodgkin's Lymphoma (Figure 2A left side).

The pathologist suggested a core biopsy to make a definitive diagnosis. Core biopsy showed the proliferation of the tumor arranged in a diffuse and monotonous pattern. It consisted of the proliferation of cells with round-oval, pleomorphic, and hyperchromatic nuclei, with a mitotic count of 11/10 HPF. Some parts were indistinctly shaping a rosette. The pathologist concluded it to be a malignant round cell tumor, with differential diagnosis of non-Hodgkin's Lymphoma and small cell carcinoma (Figure 2A right side).

The core biopsy was followed by immunohistochemical staining. Immunostaining showed positive staining for CD45 and CD3, negative staining for CD20, and the Ki67 Proliferation index showed 98% (Figure 2B). The immunostaining corresponded to high-grade T-cell Non-Hodgkin's Lymphoma. Then, it was continued with terminal deoxynucleotidyl transferase (Tdt) marker staining, and positivity was observed in the nuclear section of the tumor (Figure 2C). The pathologist finally diagnosed it as T-cell Lymphoblastic Lymphoma.

Pleural effusion analysis showed high Lactate Dehydrogenase 2.235 u/L, with leucocyte within a standard limit. Blood test results showed high SGOT 155 and SGPT 235, LDH 2285 u/L, WBC 10.850 /ml, Hemoglobin 10,3 g/dl and thrombocyte 40.000. The patient received the following treatment: furosemide, dexamethasone, codeine, and paracetamol, while chemotherapy was planned for non-Hodgkin's Lymphoma regimen and radiotherapy. The patient's condition worsened with thrombocyte 18.000, and he was treated with tranexamic acid. The patient died as a result of internal bleeding.

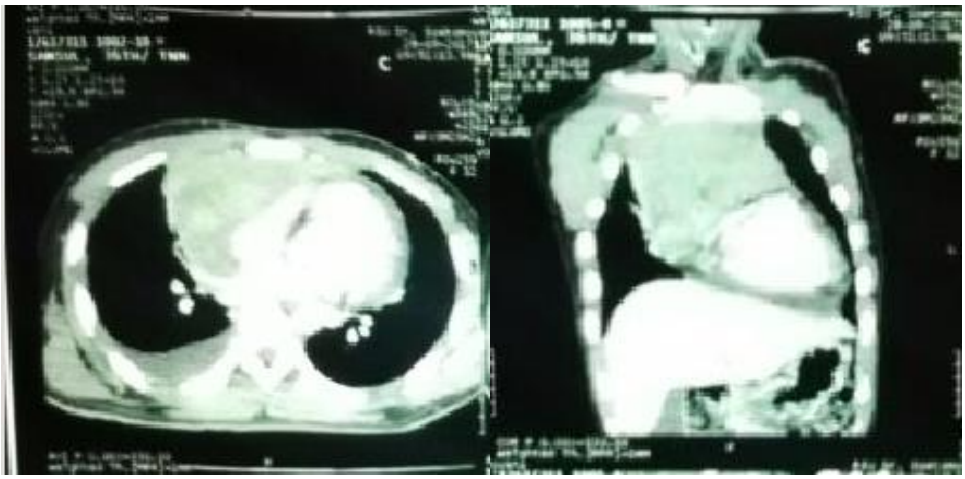

Figure 1. Computed Tomography showed a solid mass in the anterior mediastinum to medius at the Vertebra Thoracal 2 – 9 levels. Left: coronal view. Right: transversal view.

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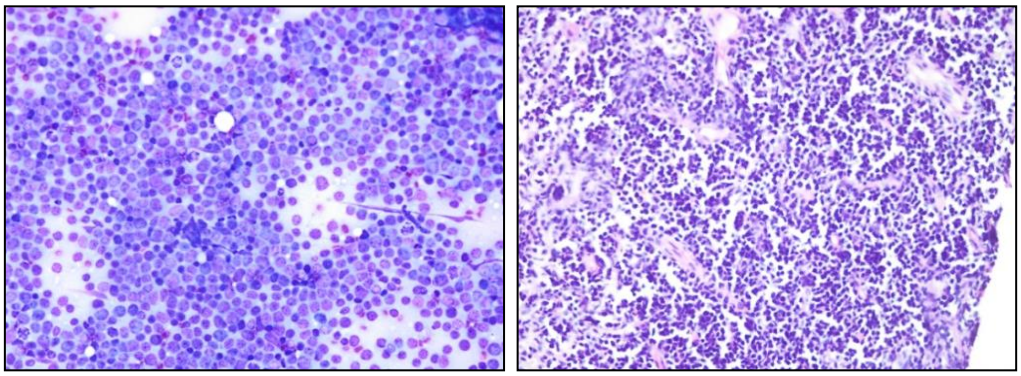

Figure 2 A. (Left side) Fine needle aspiration biopsy guided by CT scan showed the spread of lymphoid cells, anaplastic, with rounded nuclei, prominent in size, and hyperchromatic (100x). (Right side) Core biopsy showed the proliferation of the tumor arranged in a diffuse and monotonous pattern, with round-oval nuclei, pleomorphic, and hyperchromatic cells.

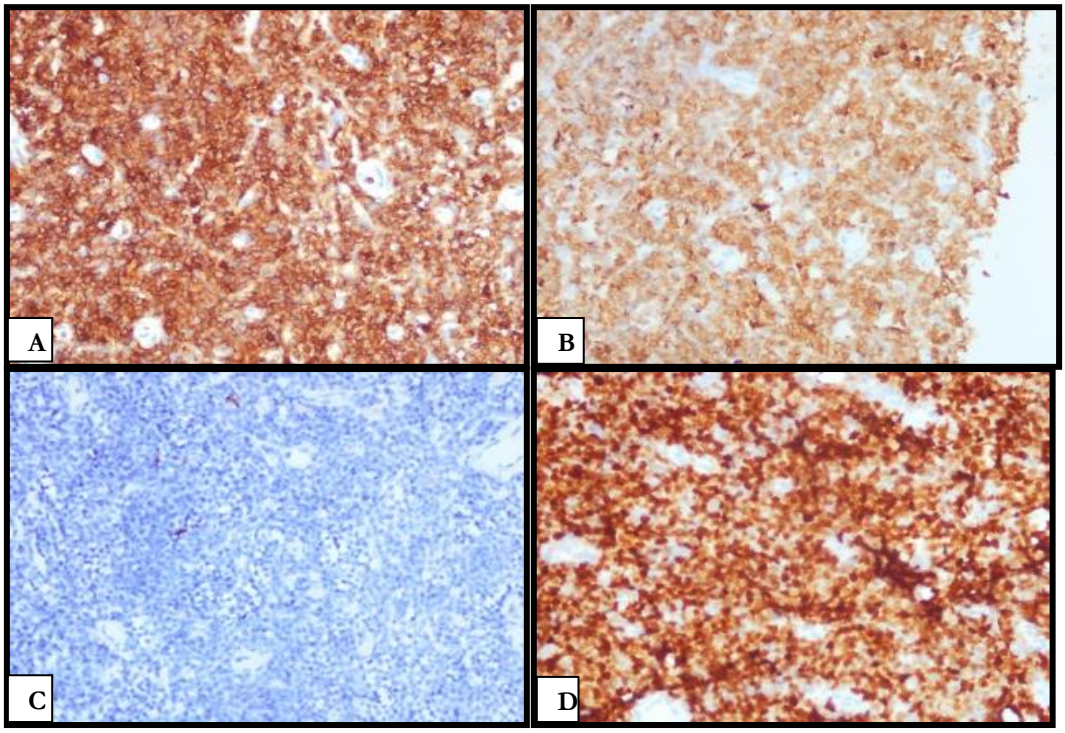

Figure 2B. Immunohistochemistry of T-LBL showed (a) positive staining with CD45, (b) positive staining with CD3, (c) negative staining with CD20, and (d) high Ki67 Proliferation index ± 98% (100x).

DISCUSSION

WHO stated that T-lymphoblastic leukemia/ lymphoma (T-ALL/LBL) is a neoplasm of lymphoblasts committed to the T-cell lineage. It comprises small to medium-sized blast cells with scant cytoplasm, moderately condensed to dispersed chromatin, and inconspicuous nucleoli [8]. T-ALL and T-LBL were distinguished to show whether they involve the bone marrow and blood (T-ALL) or present with primary involvement of the thymus or nodal or extranodal sites (T-LBL)[6]. If the patient has> 25 % blast in the bone marrow, it will be deemed T-ALL[9,11]. The etiology remains unknown. It is usually associated with human T-cell leukemia virus type-1[12].

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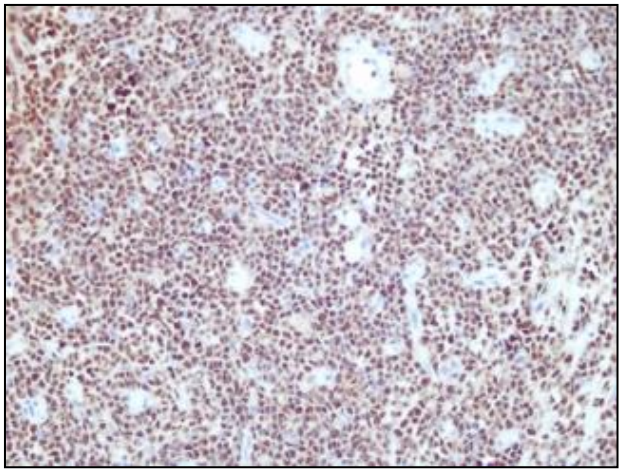

Figure 2C. Immunohistochemistry staining with the Tdt marker showed positivity in the nuclear area of the tumor (100x).

LBL is a rare disease comprising 1-2% of all NHL[2]. In a large adult series of 607 T-ALL/LBL cases from Germany, 101 had T-LBL (16.6%). Thus, the overall incidence of LBL is expected to be less than 10% out of a total ALL/LBL figure estimated at 1.3/100 000 annually[1]. T-cell LBL is typically seen in adolescents and young adults with a male predominance 2:1. T-cell LBL is much more common than BLBL in adults, accounting for up to 90% of the disease. T-cell LBL presents a mediastinal mass in 60% to 70% of cases, and 60% have a pleural and/or pericardial effusion[3]. It often presents shortness of breath due to superior vena cava compression or pericardial or pleural effusion[2]. T-LBL frequently shows mediastinal (thymic) involvement with lymph nodes or extranodal sites. The skin, tonsils, liver, spleen, CNS, and testes may be involved, although presentation at these sites without nodal or mediastinal involvement is uncommon[8]. Li Bo et al. have reported on primary T-LBL in the middle ear[13].

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The patient who came to Dr. Soetomo Hospital was a male, 36 years old, who presented with a mediastinal mass and complained of shortness of breath. The patient came with facial edema, which was a sign of superior vena cava (SVC) syndrome. SVC syndrome can be caused by the compression of the mediastinal mass or internal thrombus[14]. 12% of SVC syndrome is caused by Lymphoma, 50% by Non Small Cell Lung Cancer (NSCLC), and 22% by Small Cell Lung Cancer (SCLC). The symptoms of SVC syndrome are facial edema, arm edema, dyspnea, and cough [7,14,15].

From the radiology perspective, half of the mediastinal masses occurred in the anterior part of the mediastinum. In contrast, the remaining 25% occurred in the middle and 25% in the posterior of the mediastinum. The differential diagnoses were Thymic carcinoma, lymphoma, teratoma, and seminomatous or non-seminomatous germ cell tumors [16]. A solid mass in the mediastinum, with multiple enlargements of the lymph node combined with "B" symptoms such as fever, weight loss, and night sweats, suggested a diagnosis of lymphoma [16–18]. In this case, the patient had a

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solid mass that showed contrast enhancement in the anterior to the middle of the mediastinum, with multiple lymph node enlargements, and had a fever as a "B" symptom. Thus, the radiologist suspected it to be Lymphoma.

In smears, T-LBL showed the cells to be of medium size with a high N: C ratio. There may be a considerable range, from small lymphoblasts with very condensed nuclear chromatin and no evident nucleoli to more enormous blasts with finely dispersed chromatin and relatively prominent nucleoli. Nuclei range from round to irregular to convoluted. Cytoplasmic vacuoles may be present [6,8]. FNAB guided by CT and Core biopsy of this patient showed the proliferation of tumor arranged in a diffuse and monotonous pattern. It consisted of the proliferation of cells with round-oval, pleomorphic, and hyperchromatic nuclei with a mitotic count of 11/10 HPF.

Table 1. Differential diagnosis of T-cell Lymphoblastic Lymphoma

Differential diagnosis of T-Cell Lymphoblastic Lymphoma	Note
Blastic NK-cell Lymphoma	Patients with NK cell lymphomas are usually elderly and rarely have a mediastinal mass. TdT is generally expressed by only a subset of cells in NK-cell lymphoma and is often variable or with weak intensity.
Peripheral T-cell lymphoma (PTCL)	PTCL is composed of larger cells and is associated with a much greater variety of reactive cells than those seen in T-LBL. PTCL do not possess blastic-chromatin and are negative for TdT.
Mediastinal (thymic) large B-cell Lymphoma (MLBCL)	MLBCL patients have a median age similar to patients with T-LBL who present with a large mediastinal mass. Histologically, MLBCL cells are large and commonly associated with sclerosis. Immunophenotypic studies show that MLBCL is a neoplasm of mature B-cell lineage.
Burkitt lymphoma (BL)	BL occurs in children, adolescents, and usually younger adults. Histologically, BL has a diffuse pattern with a high proliferation index. BL patients generally present with an abdominal mass rarely involving the mediastinum. BL usually has a more prominent "starry-sky" pattern than T-LBL, and BL cells are more prominent than lymphoblasts. On smears, BL cells usually have numerous cytoplasmic vacuoles. Immunophenotypic and cytogenetic studies are also distinctive. BL cells are of mature B-cell lineage. They are positive for pan–B-cell antigens and germinal center cell-associated antigens (e.g., CD10 and BCL-6) and negative for T-cell antigens and TdT.
Ewing sarcoma/ Primitive Neuroectodermal Tumor (ES/PNET)	ES/PNET and T-LBL can be positive for the CD99 marker. T-LBL can also be negative for CD45. Thus, the combination of CD99+/CD45– might lead to misdiagnosis if only a small panel of markers is assessed. A larger panel of immunophenotypic markers resolves this issue. Most cases of ES/PNET express keratin, and all lack T-cell antigens.

Source: Ioachim, H. L. and Medeiros LJ, 2009

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T-LBL lymphoblasts are usually TdT-positive and variably express CD1a, CD2, CD3, CD4, CD5, CD7, and CD8. Of these markers, CD7 and CD3 (cytoplasmic) are most often positive, but only CD3 is considered lineage-specific[8,19]. Differential diagnoses of the diffuse and monotonous lymphoid cells were varied, as shown in Table 1. [6]

In this case, because of the financial limitation and small specimen of biopsy, the immunohistochemical staining was performed only for CD45(+), CD3 (+), CD20 (-), Ki67 (proliferation index 98%), and Tdt (+).

Standard therapeutics for LBL patients are based on intensive multidrug leukemia chemotherapy. The regimens contain 7–10 drugs, such as cyclophosphamide, methotrexate, prednisone, vincristine, cytarabine, thioguanine, l-asparaginase, nitrosoureas, etoposide, and anthracyclines, including intensive intrathecal chemotherapy for Central Nerve System (CNS) prophylaxis. It is also combined with mediastinal radiotherapy 30-39 Gy[5,10,20]. Unfortunately, the patient had not yet been given chemotherapy due to the general condition of the patient.

LBL is highly aggressive but frequently curable with current therapy. The prognosis in all age groups has improved with intensive chemotherapy. Disease-free survival has reached 73-90 % in children and 62-66 % in adults, with complete remission in up to 71% of cases[5,20]. There are many factors which affect the prognosis of the patient. Age over 40, bone marrow and CNS involvement, and Ann Arbor stage III and IV are associated with poor survival [20,21]. In some studies, higher serum LDH levels were associated with lower complete remission and poorer survival[20]. The patient, in this case, was 36 years old with a high level of LDH. His condition was getting worse because of thrombocytopenia, which led the condition to occult internal bleeding.

CONCLUSION

T-cell Lymphoblastic Lymphoma in the mediastinum is a rare and aggressive neoplasm. Based on the histomorphology of a diffuse and monotonous pattern, which consists of a proliferation of cells with round-oval nuclei, pleomorphic and hyperchromatic, and positive immunostaining for CD3 and Tdt, we conclude this case to have been T-cell Lymphoblastic lymphoma. Immunohistochemical staining has an essential role in the diagnosis of mediastinal mass.

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