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Case report

T-cell lymphoblastic lymphoma presenting with pleural effusion: A case report

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A B S T R A C T

Adult lymphoblastic lymphoma (LBL) is an aggressive form of non-Hodgkin lymphoma occurring in predominantly adolescent and young adult men, accounting for 1% to 2% of all non-Hodgkin's lymphomas. In contrast to B-LBL, T-cell LBL is much more common, accounting for up to 90% of disease in adults. Mediastinal mass, pleural and/or pericardial effusions are the major characteristics of T-LBL. We report an 18-year-old male with a pleural effusion, mediastinal mass, a light pericardial effusion, and a normal hemogram. The cytology of the pleural effusion initially suggested malignancy, but definitive diagnosis was unclear. After a medical thoracoscopy, the partial pleura was picked and immunophenotypic study revealed the following: $CD3^+$, TdT^+, $CD99^+$, $CD20^-$. The patient was finally diagnosed with T-LBL and died only 6 months after that. The case highlight the point that medical thoracoscopy is a safe and accurate diagnostic procedure for pleural diseases, and partial pleura biopsy with immunophenotyping was essential for achieving the correct diagnosis of LBL.

Introduction

Lymphoblastic lymphoma (LBL) is a rare malignancy accounting for less than 2% of non-Hodgkin's lymphoma (NHL). T-cell lymphoblastic lymphoma (T-LBL) comprises approximately 85–90% of all LBL and occurs most frequently in late childhood, adolescence, and young adulthood, with a male predominance of 2:1 [1]. Although pleural effusion and mediastinal adenopathy are common signs of T-LBL, the accurate diagnosis is often a challenge in clinic because of the low positive of malignancy cells by cytological examinations of PE, or as the malignant cells may be difficult to distinguish from reactive lymphoid cells [2]. In such situations, pleural biopsy using closed biopsy or thoracoscopy, especially the latter, becomes an important investigation so that the pleural surface can be visualized and the representative pleural can easily be picked, hence the diagnosis yield can be increased [3]. Nowadays, medical thoracoscopy (MT) is increasingly being utilized in the diagnosis of pleural diseases following undiagnosed pleural effusion cytology, especially for the malignant pleural effusion (MPE), because MT procedures have a 90% success rate for the diagnosis of MPE [4].

In this paper, we describe a case with pleural effusions, which was diagnosed as T-cell lymphoblastic lymphoma by pleural biopsy from medical thoracoscopy. Up to now, there are rare reports about a diagnosis of T-LBL by medical thoracoscopy.

Case report

An 18-year-young man was admitted to our department with cough and shortness of breath. One month before admission his referral, he presented with cough, shortness of breath and fever, and also experienced chest pain after rough cough. The highest temperature of the patient was 37.5 °C. He denied purulent sputum, hemoptysis and arthronalgia. Unfortunately, the cough and shortness of breath of the patient had progressively worsened over time. Chest examination revealed absent breath sounds on the lower two thirds of the left hemithorax and a dull percussion note. No detectable peripheral lymphadenopathy was found.

Laboratory results included normal creatinine, blood urea nitrogen, and serum electrolyte; lactate dehydrogenase (LDH), 179 U/L; alanine aminotransferase (ALT), 30U/L; aspartate aminotransferase (AST), 25 U/L; total protein (TP), 66.3 g/L; leukocyte count,

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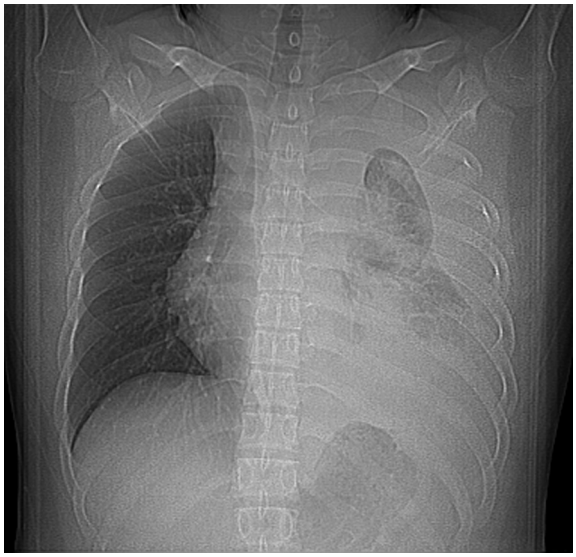

Fig. 1. Chest radiograph of an 18-year-old boy who presented with cough and tachypnea demonstrates a large anterior mediastinal mass and a left pleural effusion with a light contralateral shift of the trachea and mediastinum. Aspiration of the effusion and biopsy of the parietal pleura provided the diagnosis of lymphoblastic lymphoma.

10.3×10^9/L; hemoglobin, 16.7 g/dl; platelet count, 233×10^9/L. A peripheral blood smear examination revealed no abnormal lymphoid cells. Serum test results were negative for carcinoembryonic antigen (CEA), squamous cell carcinoma associated antigen (SCC), hepatitis B virus (HBV), human immunodeficiency virus (HIV), hepatitis C virus (HCV), Schaudinn's bacillus. We did not carry out human herpesvirus 8 (HHV8) test in our center. Also serum test showed erythrocyte sedimentation rate (ESR), 8 mm/h; and C-reactive protein (CRP), 43.6 mg/L. Sputum cultures were negative for bacteria, fungus, and *Mycobacterium tuberculosis*.

Chest X-ray demonstrates a large anterior mediastinal mass and a left pleural effusion with a light contralateral shift of the trachea and mediastinum (Fig. 1). Chest computed tomography (CT) showed an anterior and middle mediastinal mass with a light contralateral shift of the trachea, pleural thickening of the left hemithorax, and left-sided pleural effusion (Fig. 2). Chest ultrasonography revealed massive left pleural effusion. Echocardiography showed little pericardial effusion. And ultrasonography of superficial lymph node showed lymphadenopathy in bilateral axillary region (left 21.1×11.4 mm; right 15.4×4.4 mm), bilateral cervical region, (left, 18.7×17.1 mm; right 12×5.2 mm), and bilateral inguinal region (left 16×4.8 mm; right 11.3×9.3 mm), but not in retroperitoneal region. Thoracentesis were performed and revealed exudate with lactate dehydrogenase level of 721 U/L, ADA value of 25 U/L, and TP 15.3 g/L. Pleural fluid were grossly bloody and the routine examination of pleural fluid showed leukocytes 5×10^9/L (55% percent multinucleated cells, 54% percent mononuclear cells). The cytologic examination of the effusion smears revealed massive lymphocytes, a small amount of mesothelial cells, and partly abnormal cells (tumor cell?). Pleural fluid cultures were negative for *M. tuberculosis*.

Then the medical thoracoscopy was performed under local anesthesia, cardiovascular and respiratory monitoring, in the endoscopy suite by experienced operator. The inspection of the pleural by a direct vision optic revealed massive bloody pleural fluid in the pleural cavity, and widely membrane hyperemia with lots of small white apophysis involving the parietal pleura (Fig. 3).

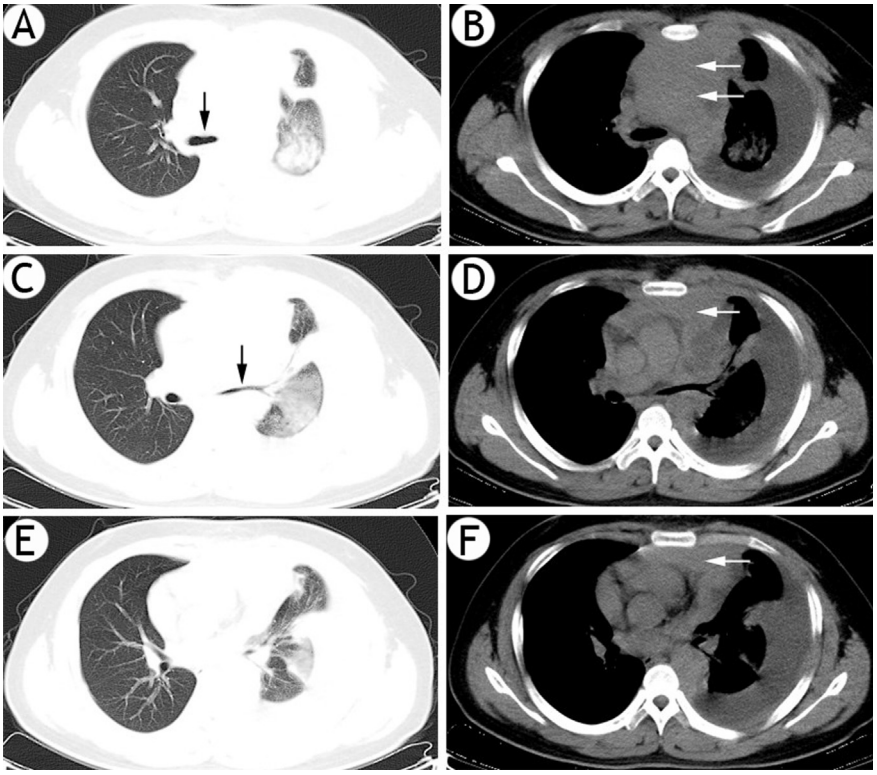

Fig. 2. Chest computed tomography view of the patient. Chest CT showed left-sided pleural effusion, an anterior and middle mediastinal mass (B, D, F, white arrow) which resulted in contralateral shift and stricture of the tracheal (A, black arrow) and left mainstem bronchus stricture (C, black arrow). Chest CT at the level of heart demonstrating pleural thickening of the left hemithorax, left-sided pleural effusion and a light pericardial effusion (E, F).

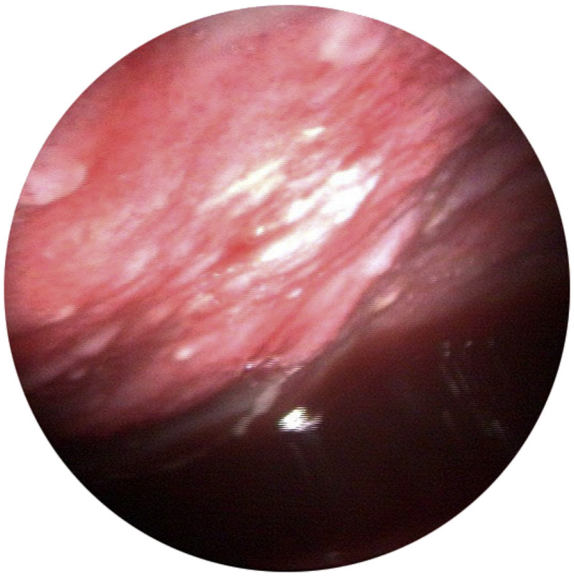

Fig. 3. Thoracoscopy view of patient. The inspection of the pleural by a direct vision optic revealed massive bloody pleural fluid in the pleural cavity, and widely irregular thickening with lots of small white apophysis involving the parietal pleura.

Specimens from the parietal pleural were picked ten times in different area by biopsy forceps. Pleural biopsies showed diffuse, partially nodular, infiltration by neoplastic lymphocytes. The immunohistochemical analysis of lymphoma cells showed CD20 (−), CD3 (+), CD21 (residual FDC+), Ki67 (30%+), terminal deoxynucleotidyl transferase (TdT, +), CD99(+), which was consistent with T-cell lymphoblastic lymphoma (Fig. 4). In addition, bone marrow aspirate showed no malignant involvement. Lymphadenopathy in the cervical and axillary regions was suspected to have relevance to nodal metastasis of lymphoblastic lymphoma.

Unfortunately, the patient gave up treatment and discharged due to the financial difficulties. He had a very aggressive course of disease and died only 6 months after diagnosis.

Discussion

T-LBL is a rare type of non-Hodgkin's lymphoma, with an overall incidence of ~0.1 per 100, 1000 inhabitants/y, and predominantly occur in male adolescents or young adults [5]. A mediastinal mass was present in ~80% of the patients with 60% having a pleural and/or pericardial effusion [6]. Here we reported an 18-year-old man with mediastinal mass and pleural effusion. The initial cytologic examination of pleural fluid revealed massive lymphocytes, and some abnormal cells (tumor cell?). MPE was suspected, but the definite diagnosis was unclear then. Forasmuch the MT was performed on the young man in our case by experienced operator, and pleural biopsies of partial pleura was picked. Dependent on the examination of the partial pleura by histological and immunohistochemical methods, T-lymphoblastic lymphoma was diagnosed finally. However, the patient gave up the treatment due to financial difficulties, and died miserably only six months after the diagnosis.

Although there are lots of researches about the prognosis of T-LBL, reliable prognostic factors have not been identified. Generally, a poor prognosis has been related to T-phenotype relative to B-cell lineage [7]. Mathilde et al. [8] reported that 7-year overall survival was 64%, and none of the following prognostic factors significantly affected survival with T-LBL: age, sex, presence or absence of fever or infection, splenomegaly, hepatomegaly, mediastinal mass, lymphadenopathy, initial platelet count ($>100 \times 10^9$), leukocyte count ($>30 \times 10^9$), LDH level, immunophenotypic subtype. However, Birgit et al. [9] found that 5-year overall survival was 14% for the patient with T-LBL which suffered from disease progression or relapse. The presence of pleural effusion and ≥ 2 of extranodal involvement were significantly associated with worse overall survival [7]. Meanwhile, Das et al. [10] also found that the presence of an effusion has been linked to a very poor outcome, and emphasized that lymphocyte-rich effusions frequently present diagnostic difficulty in clinical cytology, which was accordance with our case. Due to with both mediastinal mass and pleural effusion, the young man in our case suffered from disease progression and died six months later.

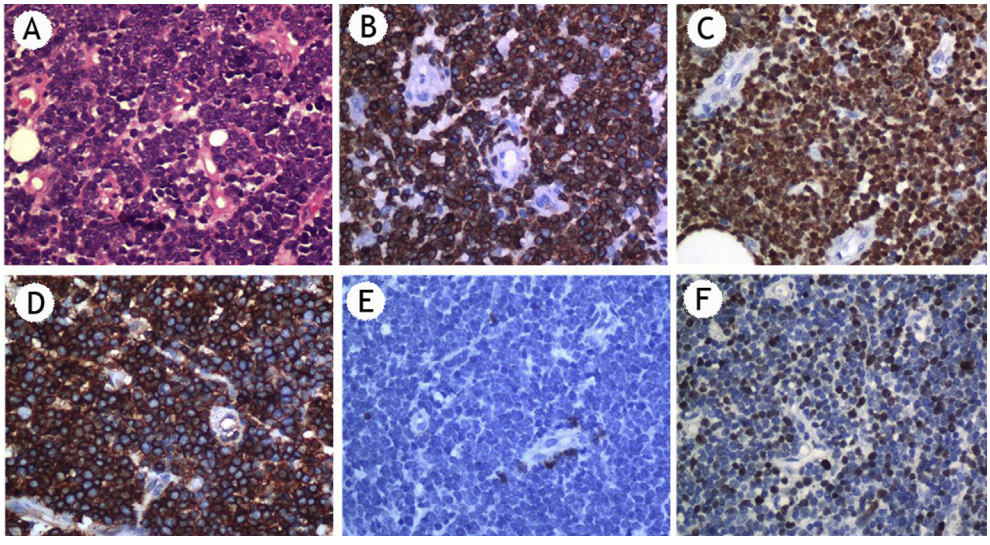

Fig. 4. Hispathological examination of the parietal pleural biopsies after medical thoracoscopy. (A) Parietal pleural infiltrated by monotonous small lymphoid cells with scantly cytoplasm and slightly irregular, round oval nuclei, and dense chromatin (hematoxylin and eosin staining, original magnification ×400). (B) CD3 immunoreactivity in parietal pleura infiltrates (original magnification ×400). (C) TdT immunoreactivity in parietal pleura infiltrates (original magnification ×400). (D) CD99 immunoreactivity in parietal pleura infiltrates (original magnification ×400). (E) staining shows negative reaction for B-cell marker in parietal pleural infiltrates (original magnification ×400). (F) Ki67 immunoreactivity in parietal pleura infiltrates (original magnification ×400).

It was reported that pleural effusion in lymphoma can emerge from the results of variety of mechanisms, such as impaired lymphatic drainage owing to mediastinal lymph nodes or thoracic duct obstruction, pleural or pulmonary infiltration by tumor, venous obstruction, pulmonary infection, or radiation therapy [11]. In which, lymphatic obstruction is the most frequent factor for pleural effusion [12]. Serous effusions are a common complication of lymphoma. According to Santos et al. [13] reported 256 serous effusions associated with lymphoma, which included 197 pleural. Das et al. [3] reported that the effusion caused by lymphoma was single-sided in 15 cases, and bilateral in 6 cases. Our patient had left-sided pleural effusion that was serous effusion.

Medical thoracoscopy has become a core diagnostic and therapeutic tool in pleural disease care, because despite the fact that thoracentesis and pleural biopsy were widely used, there were still approximately 15–20% pleural effusions remain undiagnosed [14]. During the procedure guided biopsies are performed and the extension of the disease in the pleural cavity is assessed, so the biopsy provides a valuable opportunity to achieve the earlier diagnosis [14]. Moreover, medical thoracoscopy under local anesthesia has the same diagnostic accuracy and safety, while it is less expensive than the video-assisted thoracic surgery, since it is performed in the endoscopy suite. Therefore, MT should be performed on these undiagnosed patients, owing to its high sensitivity in malignant and tuberculous pleural effusion [15]. As technology has become more available and confidence in the use of equipment has grown, MT has become less invasive, safer, better tolerated and therefore preferable, which is usually done with single entry ports, and local anesthesia in an endoscopy suite [16]. In this case, MT was performed in our endoscopy room, and only mild chest pain was present in the patient after examination.

In conclusion, we reported a case with pleural effusions, which was diagnosed as T-cell lymphoblastic lymphoma by pleural biopsy from MT. Our case point out the importance of early utilization of a minimally invasive method, the medical thoracoscopy, for the undiagnosed pleural effusion, which provides an ancillary option for physician to make diagnosis of pleural diseases.

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Authors' contributions

QZ and XLH designed the study and drafted the manuscript. XLH, FY were responsible for clinical data collecting. TG performed hispathological examination. FX, XNT and JCZ performed medical thoracoscopy. All authors read, critically revised, and approved the final manuscript.

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