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Case report

Diagnostic utility of medical thoracoscopy in T cell lymphoblastic lymphoma presenting with pleural effusion

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ABSTRACT

Adult lymphoblastic lymphoma (LBL) is an aggressive form of non-Hodgkin lymphoma occurring among predominantly adolescent and young adult men, accounting for 1%–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 27-year-old male with a pleural effusion, mediastinal lymphadenitis, and a normal hemogram. The cytology of the pleural effusion initially was lymphocytic exudative and ADA was high. For definitive diagnosis a medical thoracoscopy was done. The partial pleura showed multiple irregular nodules and thickening in sheets. It was picked and immunophenotypic study revealed the following: CD3, TdTþ, CD7 with Ki 67 index of 70–80%. The patient was finally diagnosed with T-LBL. He was treated with chemotherapy and is on regular follow up with resolution of effusion. The case highlight the point that medical thoracoscopy is a safe and accurate diagnostic procedure for pleural diseases, and partial pleura biopsy yielded the correct diagnosis.

1. Background

Malignant pleural effusion (MPE) is presentation of many malignancies; however, the most frequent are lung and breast carcinomas, and lymphomas, followed by gastrointestinal and ovarian malignancy [1].

In ~10% of patients with undiagnosed pleural effusion, a lymphoma is finally detected [2]. MPE is observed in 10–30% of patients with Hodgkins lymphoma at presentation (3–5) up to 20% (7,8) of Non Hodgkin's lymphoma. Lymphoblastic lymphoma (LBL) is a rare malignancy accounting for less than 2% of non-Hodgkin's lymphoma (NHL) [2,3]. 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[4]. In such situations, medical thoracoscopy becomes an important investigation so that the pleural biopsies can be taken under direct visualization and it has a 90% success rate for the diagnosis of MPE[5]. 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 very few reports about a diagnosis of T-LBL by medical thoracoscopy.

2. Case presentation

A 27-year-young man presented to our department with dry cough and shortness of breath on exertion and intermittent fever and loss of weight and appetite for one month. He denied purulent sputum, hemoptysis and arthralgia. Chest examination revealed absent breath sounds on the lower two thirds of the right 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), 379 U/L; alanine aminotransferase (ALT), 23U/L; aspartate aminotransferase (AST), 19 U/L; leukocyte count, 8.32 $\times$ 10^3/L,; hemoglobin, 15.5 g/dl; platelet count, 379 $\times$ 10^3/L, and C-reactive protein (CRP), 43.6 mg/L. Sputum cultures were negative for bacteria, fungus, and *Mycobacterium*

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tuberculosis. Chest X-ray demonstrated a large right pleural effusion with a light contralateral shift of the trachea and mediastinum (Fig. 1). Chest computed tomography (CT) showed right sided moderate to massive pleural effusion with compressive collapse of underlying basal segments of right lower lobe and atelectatic consolidation of medial and lateral segments of right middle lobe. There were multiple enlarged conglomerate necrotic mediastinal lymphnodes in the prevascular, right hilar, subcarinal, paraortic, aortopulmonary and lower paratracheal stations. (Fig. 2). Chest ultrasonography revealed massive right pleural effusion with visceral pleural nodularity. (Fig. 3) Echocardiography showed minimal pericardial effusion in the right atrial region. Thoracentesis was performed and revealed exudate with lactate dehydrogenase level of 2023 U/L, ADA value of 110 U/L, and pleural fluid protein was 5.51 g/L. Pleural fluid cytology showed mesothelial cells and lymphocytes. There were no malignant cells. Pleural fluid culture was negative for *M. tuberculosis*. As pleural fluid ADA and LDH level was unusually high we decided to go ahead with pleural biopsy. The medical thoracoscopy was performed under local anesthesia, cardiovascular and respiratory monitoring, in the endoscopy suite by experienced operator. The inspection of the pleura by a direct vision revealed massive hemorrhagic pleural fluid in the pleural cavity. Parietal pleura showed linear nodularity along the rib margin with occasional large big nodules with smooth/irregular margins (Fig. 4). Specimens from the parietal pleura were picked multiple times from different areas by biopsy forceps. Pleural biopsies showed malignant round cell neoplasm favoring lymphoma. Immunohistochemistry revealed tumor cells were positive for terminal deoxynucleotidyl transferase (Tdt), CD 3, CD 7 with Ki 67 index of 70–80%. Tumor cells were negative for CK, LCA, CD 20, CD 30, ALK, PAX 5. Final diagnosis was malignant lymphoproliferative lesion, in keeping with T- Lymphoblastic lymphoma. (Fig. 5). In addition, bone marrow aspirate and biopsy showed normocellular marrow with trilineage maturation. Whole body positron emission tomography (PET) scan was taken which showed diffuse heterogeneous FDG uptake seen in right pleural effusion with minimal CT detected pleural nodularity (SUV Max 2.9). There was abnormal increased FDG uptake noted in following CT detected lymph nodes: a) right upper paratracheal (SUV max 5.2) b) Right lower paratracheal (SUV Max 2.3) c) right hilar (SUV Max 3.0) d) subcarinal (SUV Max 2.8) e) multiple juxtaphrenic (SUV max 2.3) f) celiac (SUV Max 3.2). There were not any distant metastasis or lymphnodes which were FDG avid.

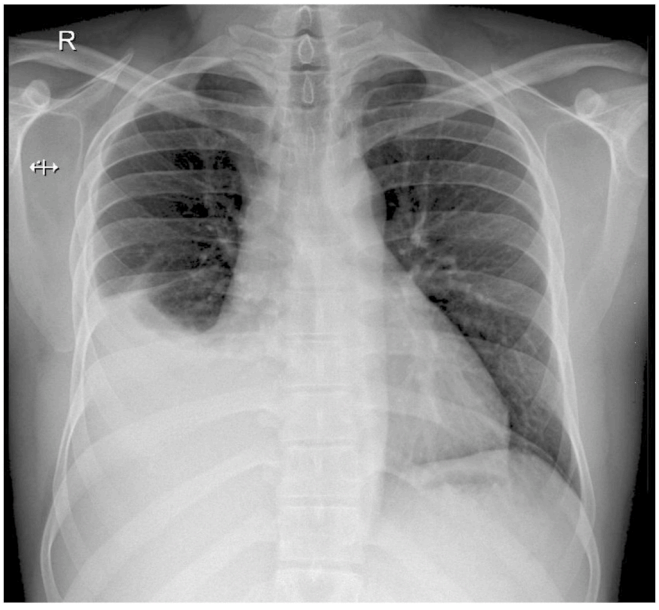

Fig. 1. Chest radiograph showing right pleural effusion with a light contralateral shift of the trachea and mediastinum.

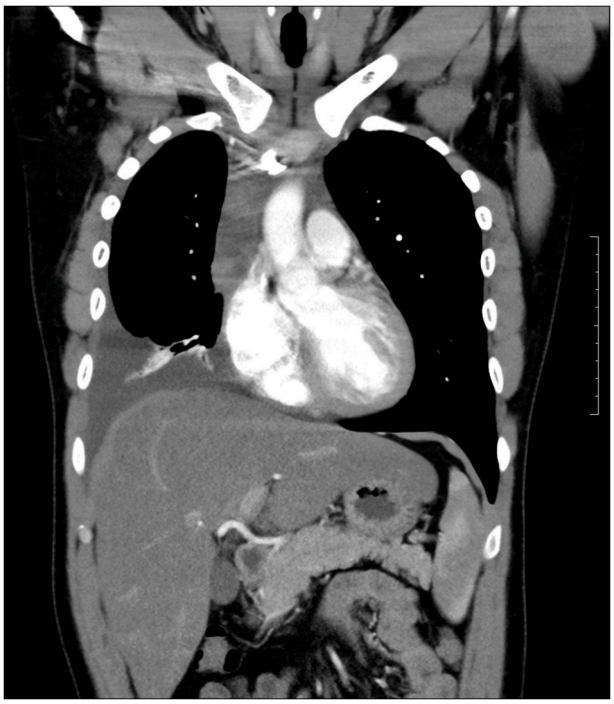

Fig. 2. CT chest showing right sided moderate pleural effusion with multiple enlarge mediastinal lymphnodes.

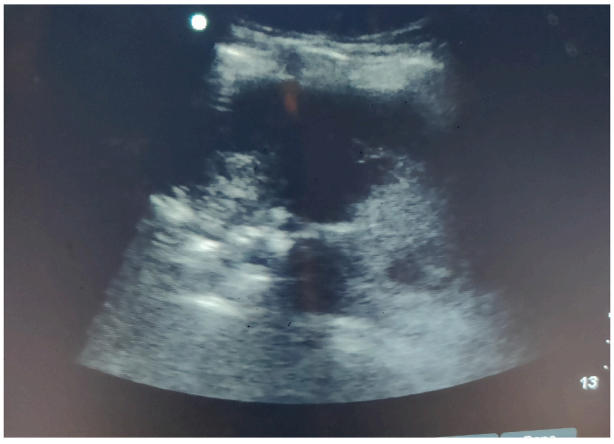

Fig. 3. Ultrasonography image showing effusion with underlying collapsed lung with airbronchogram and visceral pleural nodule.

2.1. Treatment

The patient was transferred under Hematology and Oncology unit for further treatment. He was initiated on chemotherapy as per MCP 842 protocol. Intercostal tube was removed as the patient was started on chemotherapy.

2.2. Outcome and follow up

The follow up PET CT after 4 cycles showed complete resolution of effusion and mediastinal and abdominal lymphnodes, suggesting good response to treatment.

3. Discussion

T-LBL is a rare type of non-Hodgkin's lymphoma, with an overall

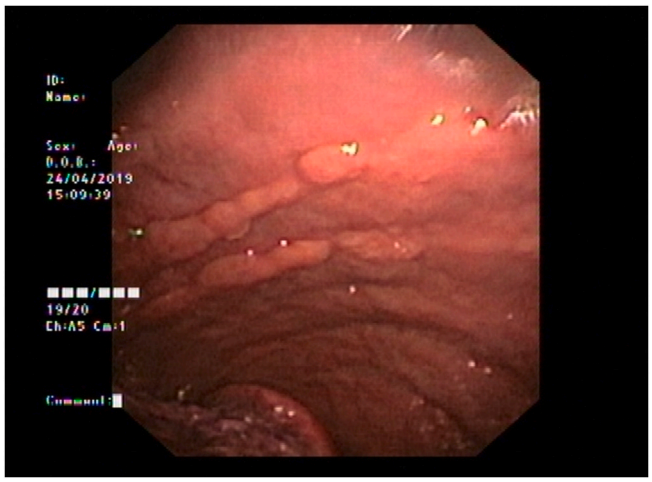

Fig. 4. Thoracoscopy image showing linear thickening of parietal pleura along with the rib margin.

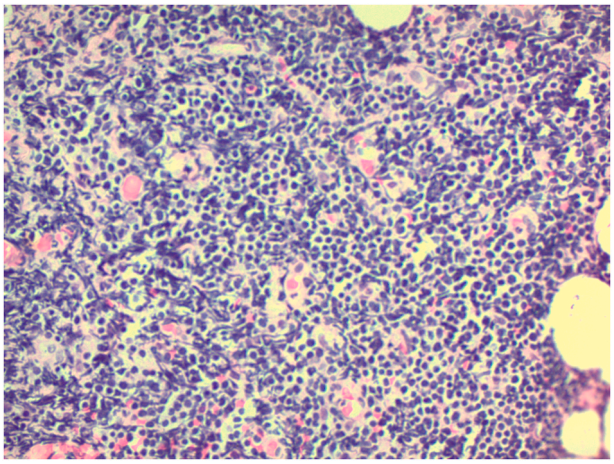

Fig. 5. Hispathological examination of the arietal pleural biopsies after medical Thoracoscopy showing parietal pleura infiltrated by monotonous small lymphoid cells with scanty cytoplasm and slightly irregular, round oval nuclei, and dense chromatin (hematoxylin and eosin staining, original magnification ×400).

incidence of 0.1 per 100,000 inhabitants/y, and predominantly occur in male adolescents or young adults[6]. Medical thoracoscopy has been reported to be successful in diagnosing pleural lymphomas[5]. In the present case, the definite diagnosis of T-LBL was established through MT. The patient did not have any other indications of lymphoma based on medical history, physical examination, routine blood work and CT scans of the chest. Bedside thoracic ultrasound showed moderate anechoic effusion with underlying collapsed lung and few nodules in visceral pleura. As shown in previous study by Shkolnik et al. [7] anechoic effusion are commonly exudative effusion. We also found the effusion to be exudative lymphocytic with high ADA. Thoracentesis results were also non contributory. Thoracocentesis with pleural fluid cytology is usually an early step in diagnosing MPE. Pleural effusion in lymphoma can be due to 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.

In pleural effusion caused by lymphoma, to make a definitive diagnosis of lymphoma is not easy, as either lymphomatous cells in pleural fluid are sparse or cells in pleural fluid looks similar to lymphocytes in other tissues involved, such as lymph nodes[8]. Then it is difficult to distinguish lymphomatous cells from reactive lymphocytes, or whenever a mixed population of lymphomatous and reactive lymphoctyes exists [9]. Although cytological investigation with immunophenotyping of pleural fluid cells can be diagnostic of malignancy and of the lymphoma subtype and cytogenetic analysis may further support the diagnosis and define other specific types of lymphomas[10]. MT has been a routine method for patients with exudative pleural effusion that remain undiagnosed by clinical, radiologic, laboratory or cytological investigation [11].

It was found in one study that extensive infiltration of pleura indicates that the major mechanism for the development of PE is the direct involvement of the pleura by lymphoma[12], rather than obstruction to lymphatic flow as seen in present case.

Here we reported a 27-year-old man with mediastinal mass and pleural effusion. The initial cytologic examination of pleural fluid revealed massive lymphocytes, and mesothelial cells. In view of high ADA and fever with loss of weight and appetite with normal hemogram even possibility of tuberculosis was also considered. In a study published by us in 2014, we found that the median ADA for TB effusion was 51.8 IU/ml [13] while in the current case it was 110U/L. The study showed that pleural fluid ADA of 40 U/L yielded 89.5% negative predictive value and 75% positive predictive value[13]. Previous studies have found that pleural fluid ADA can be elevated in parapneumonic effusion and other conditions in which there is increase in lymphocytes such as lymphoma, rheumatoid pleuritis, Q fever, brucellosis and legionnaire's diesease[14].

In present case we did MT for confirming the diagnosis and it turned out to be T-LBL by histological and immunohistochemical methods. The patient has been started on chemotherapy and is under follow up thereafter. The presence of pleural effusion and >2 of extranodal involvement were significantly associated with worse overall survival [15] Medical thoracoscopy has become a core diagnostic and therapeutic tool in pleural disease care[11]. It is done 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. 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 [5].

4. Conclusion

- T Cell lymphoma can present as Pleural effusion
- Pleural fluid ADA can be high in lymphoma too.
- Medical thoracoscopy can yield the diagnosis in such cases

Patient consent

The patient gave his consent for the publication of this case.

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Contributor statement

Planning: TMS, AAM, Conduct: KP, Reporting: AN, conception and design: AM, Acquisition of data: TMS.

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