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Utility of Transbronchial Lung Cryobiopsy in Diagnosing Pulmonary Hodgkin's Lymphoma

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ABSTRACT

Lung involvement in Hodgkin's Lymphoma is relatively uncommon. Diagnosis is made by histopathological examination of lung tissue samples. The need for detailed immunohistochemical studies to establish the diagnosis necessitates obtaining tissue samples of adequate size and quality. We present a case of recurrent Hodgkin's Lymphoma in the lung, diagnosed from transbronchial lung cryobiopsy (TBLC).

Keywords: Pulmonary Lymphoma, Cryobiopsy, Bronchoscopy

Introduction

Hodgkin's Lymphoma mainly involves lymph nodes. Lung involvement in Hodgkin's Lymphoma frequently occurs in secondary or recurrent disease rather than in primary disease and accounts for 6-11% of cases (1-3). Definitive diagnosis is made via a complete immunohistochemical (IHC) examination of the lung tissue samples. Hence, obtaining tissue samples of good size and quality, i.e. large specimen chunks, less crushed artefacts and greater preserved architecture, is of paramount importance. This case highlights the importance of obtaining larger samples using cryo-probe in diagnosing parenchymal pulmonary lymphoma.

Case Report

This is a case of a 20-year-old female teacher with underlying Hodgkin's Lymphoma diagnosed two years prior to admission. At that time, she presented with fever and weight loss and was found to have mediastinal and abdominal lymphadenopathy on computed tomography (CT) imaging. Histopathological examination (HPE) from the lymph node biopsy confirmed the diagnosis of Hodgkin's Lymphoma. She subsequently received chemotherapy which consists of doxorubicin, bleomycin, vinblastine and dacarbazine, and was subsequently well after that. However, she presented again to the hospital with acute onset of fever and cough for a week during her current admission. Chest radiograph revealed consolidation in the middle zone of the left lung (Figure 1A). A diagnosis of community-acquired pneumonia was made and she was treated with antimicrobials. Her fever resolved after two courses of broad-spectrum antibiotics, however, her cough still persisted. She also had lost 2kg of body weight and had a poor appetite during the course of her current illness. She denied any history of contact with tuberculosis patients. A repeat chest radiograph revealed consolidation essentially unchanged from the previous radiographic study. A subsequent chest CT showed collapse-consolidation of the left upper lobe with nodular lung infiltrates (Figure 1B).

Flexible bronchoscopy revealed normal bronchoscopic findings. Bronchial washing was tested negative for tuberculosis, fungus and other pathogens. Given the high suspicion of tuberculosis and recurrent lymphoma, a TBLC guided by fluoroscopy was performed via rigid bronchoscopy under general anaesthesia in order to obtain a larger tissue sample. Two samples were obtained. The procedure was uneventful with minimal bleeding and she did not develop pneumothorax. The HPE revealed scattered mummified cells and atypical large

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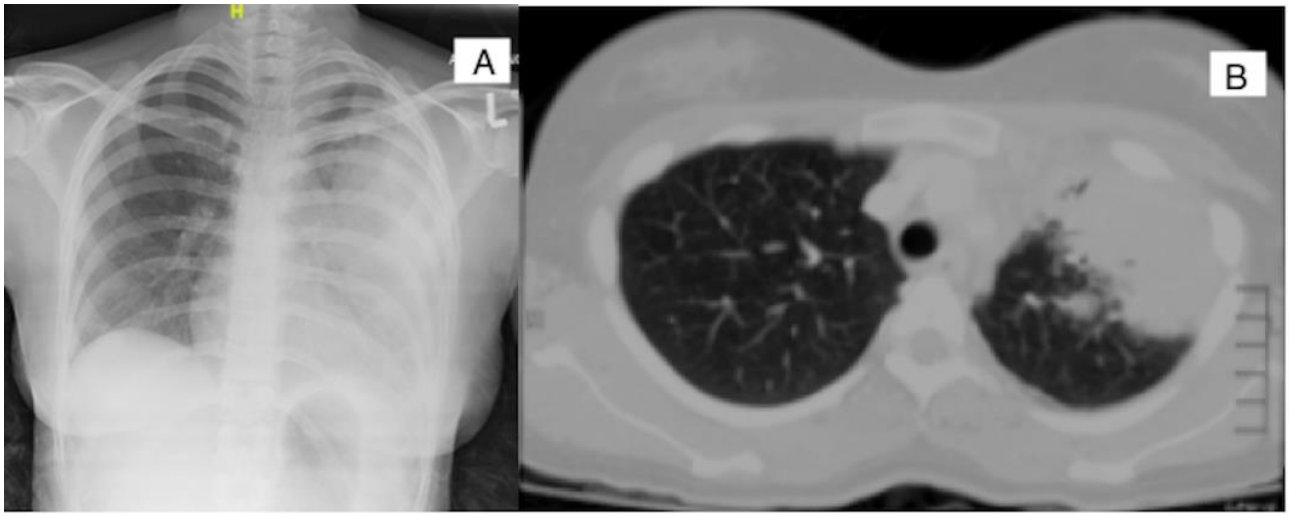

Figure 1. Panel A: Chest Radiograph Showing Consolidation in The Left Lung. Panel B: Chest CT Showing Collapse-Consolidation of The Left Upper Lobe with Nodular Lung Infiltrates

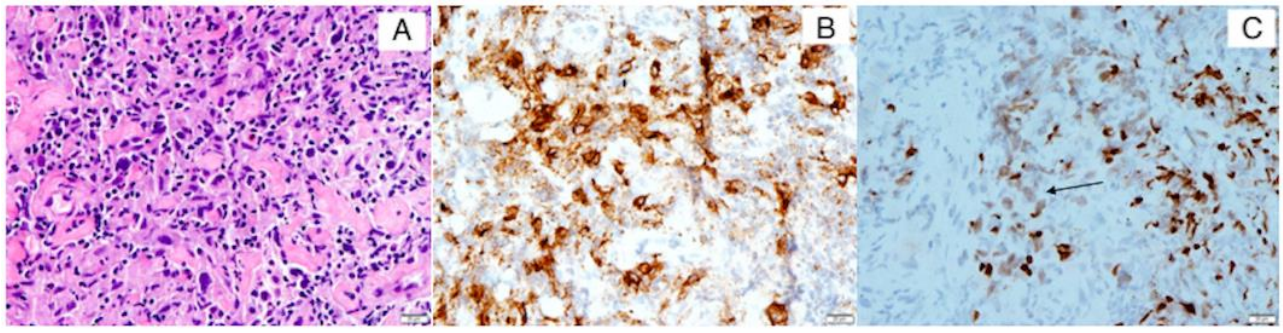

Figure 2. Panel A: H&E Stain Revealed Large Mononuclear Cells with Background Lymphocytes and Histiocytes. Panel A: CD30 Positive Immunohistochemical Studiespanel C: Arrow Showing Atypical Cells Weakly Positive for PAX5 Immunohistochemical Studies

mononuclear cells in a background of dense infiltration by lymphocytes, histiocytes and eosinophils, with foci of necrosis (Figure 2A). Immunohistochemical studies showed positive CD30 and PAX5 weakly positive atypical cells, while background small lymphocytes were positive for CD3 and CD20 (Figure 2B-C). Overall features were in keeping with Hodgkin's Lymphoma. She was then referred to a haematology centre for further management of her pulmonary Hodgkin's Lymphoma.

Discussion

Hodgkin's Lymphoma most commonly presents as centri-axial lymphadenopathy, with the majority in the supra-diaphragmatic region (4, 5). About 15-30% of Hodgkin's Lymphoma is an extra-nodal disease with or without lymphatic involvement (6). Spleen, lung, liver and bone marrow are the most common sites of extranodal Hodgkin's Lymphoma. (7). Lung involvement in Hodgkin's Lymphoma is most commonly seen as secondary involvement or relapse, occurring in 12-40% of the patients (8). The suspected diagnosis of pulmonary relapse must be established in patients with a background of Hodgkin's Lymphoma, who present with lobar/pulmonary atelectasis or infiltrates on chest radiograph or CT scan. This was clearly manifested in our case. Definitive diagnosis is based on recognition of Reed Sternberg cells in the background of reactive cellular infiltrate, with IHC studies demonstrating CD30, CD15 positivity, and negative for CD45 (9). However, in our case, the Reed Sternberg cells were not seen, hence the diagnosis was made based on the positivity of the IHC study.

The need for detailed IHC studies in the diagnosis of lymphoma requires obtaining tissue samples of sufficient size and quality. In this case, a total of two lung tissue biopsies were obtained using a cryoprobe. The diagnosis was then established from the samples obtained. Bleeding which occurred immediately following removal of the cryoprobe was observed, and we managed to secure haemostasis with the application of cold normal saline. A chest radiograph performed one hour later confirmed no pneumothorax.

The role of transbronchial lung cryobiopsy in diagnosing diffuse parenchymal lung diseases within the context of a multidisciplinary discussion is still being studied. The same goes for the comparison of its risks/benefits ratio with that of surgical lung biopsy. Diagnostic yields of TBLC have been reported to range between 50–100%, with observed complications such as pneumothorax to range between 0–30%, and these data vary widely among different institutions. (10)

In previous studies, Yap et al reported a case of successful TBLC as a diagnostic tool for pulmonary parenchymal lymphoma. (11) On the other hand, Schiavo et al. had also reported on the use of TBLC in diagnosing primary pulmonary lymphoma. (12) Pajares et al in an evaluation of cryoprobe versus conventional forceps transbronchial biopsy, reported on obtaining tissue samples of larger size and better quality using cryoprobe (13). Of late, Fabien et al. have come up with a consensus to suggest that TBLC is safer than surgical lung biopsy (SLB) and its diagnostic role in multidisciplinary discussion is non-inferior compared to SLB, albeit the histological diagnostic yield seems to be higher with SLB (14).

Ravaglia et al. suggested new sampling approaches for cryobiopsy after analyzing a large cohort of 699 patients. These strategies seem to be linked to a better diagnostic yield and a promising risk/benefit ratio. They advocate the provision of a good amount of sampling at least two samples in different sites, using either the 2.4 mm or the 1.9 mm probe, intubating the patients and using bronchial blockers/catheters (15). Further room for improvement and better improvisation of technology are anticipated in this dynamically growing field indeed.

This case highlights the diagnostic value of TBLC in diagnosing a rare occurrence of pulmonary lymphoma, especially in a case with normal bronchoscopic findings.

In conclusion, TBLC should be considered in a patient who presents with diffuse lung parenchymal abnormalities particularly when a rare disease such as pulmonary lymphoma is suspected. Normal bronchoscopic findings do not negate lung involvement in lymphoma and accurate diagnosis using TBLC can avoid unnecessary empirical anti-tuberculosis treatment in TB-endemic areas. TBLC is a less invasive diagnostic tool compared to surgical lung biopsy, and hence, more preferable for patients who are not fit for surgery. Further prospective studies are needed to establish the role of TBLC in diagnosing diffuse parenchymal lung disease, especially in a very rare disease such as pulmonary lymphoma.

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