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Case Report

Primary Pulmonary Marginal Cell Lymphoma: Your Eyes See Only What Your Mind Knows

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Abstract

Lung cancer is the leading cause of cancer-associated mortality, with a 5-year survival of 19% for all types of lung cancer. Lymphoid malignancies of the lung have a significantly better prognosis, with 5-year survival approaching 90%, making it very important to identify these patients. As the signs and symptoms, laboratory investigations, and radiological features are non-specific and vague and the histological confirmation is invasive, they are usually either not diagnosed or diagnosed very late. We present a case of an elderly male who was treated for months with antituberculosis treatment (ATT) before being properly evaluated and diagnosed with primary pulmonary marginal cell lymphoma. This case was unique for having gross pleural effusion as a presenting feature and having been diagnosed with the help of radial endobronchial ultrasound (EBUS).

KEYWORDS: Lung cancer, marginal zone lymphoma, primary pulmonary lymphoma (ppl), tuberculosis, EBUS
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INTRODUCTION

Primary pulmonary lymphoma (PPL) is a rare entity with an incidence of 0.3% of all primary lung malignancies.[1] It comprises clonal lymphoid proliferation in the lungs with no extrapulmonary involvement at the time of diagnosis.[2] Histopathological examination of the lung specimen remains the only modality of its diagnosis as the clinical features, laboratory investigations, and radiological features can be diverse and very non-specific. We present a case of PPL who was empirically treated with ATT with clinical diagnosis of tuberculous pleural effusion for 3 months before being subjected to biopsy for tissue diagnosis and then diagnosed as PPL.

CASE PRESENTATION

A 64-year-old male, non-smoker, was initially evaluated outside our hospital for complaints of cough and shortness of breath. After being diagnosed with left pleural effusion, pleural fluid aspiration was done, and the analysis revealed a total leukocyte count (TLC) of 1600 cells/mm with 98% being lymphocytes, and adenosine deaminase (ADA) was 60.7 IU/L. The patient was labeled as "clinically diagnosed TB," and treated with ATT outside our institute. Chest X-ray obtained after pleurocentesis showed left upper lobe and lower lobe opacities (Figure 1A). There was not much symptomatic improvement with ATT. After 3 months, the patient was presented to our hospital and was admitted for evaluation. His baseline investigations revealed anemia with hemoglobin of 8.1 g% (normal range: 12-14 g%), TLC 6530/µL (normal range 4000-11 000/µL), differential leukocyte count (DLC) N_{78}, L_{17}, Mo_{02}, Eo_{03} (normal range $N_{55\text{-}70}$ $L_{20\text{-}40}$ $Mo_{2\text{-}8}$ $Eo_{1\text{-}4}$), and platelets 3.5 lacs/µL. He had hypoalbuminemia with serum albumin of 2.16 g/dL and hyponatremia with serum sodium of 129 mEq/L. The rest of the metabolic parameters were within normal limits. Contrast enhanced computed tomography (CECT) of the chest and abdomen revealed a mass lesion of approximately 6 cm in the largest dimension in the left parahilar region with gross left-sided pleural effusion (Figure 2A and 2B). No hilar lymph nodes were seen. CECT did not reveal any evidence of mediastinal or retroperitoneal lymphadenopathy or any abnormal finding in the abdomen. Thoracoscopy was done, which revealed unhealthy visceral pleura with few blackish nodules. Pleural biopsy was done and the fluid was sent for gram stain, but the results of the culture was inconclusive. Flexible video-bronchoscopy did not yield any intraluminal lesion initially. Thereafter, radial EBUS guided lung biopsy was done (EU-ME2:Olympus Ltd) equipped with R-EBUS probes measuring 2.0 mm (UM-S20-20R; Olympus Ltd) in diameter without a guide sheath through the working channel measuring 2.8 mm of a video bronchoscope (Olympus 1T-190). The radial EBUS showed a mixed blizzard pattern. Histopathological examination of the biopsy specimen revealed bronchial mucosa with subepithelial sheets of monomorphic small lymphoid cells with few scattered plasma cells. The lymphocytes were seen to infiltrate into the bronchial mucosa forming lymphoepithelial lesions. On immunohistochemistry (IHC), the lymphoid cells were positive for CD20 and negative for CD5, cyclin D1, BCL6, and CD23, suggestive of low-grade B-cell non-Hodgkin lymphoma

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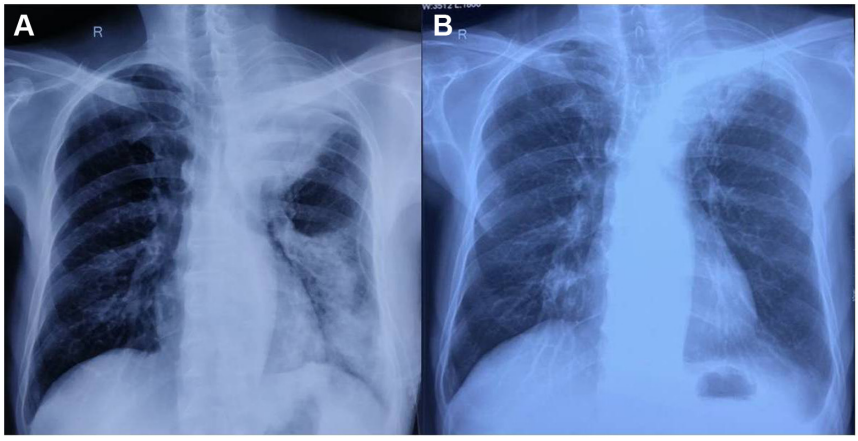

Figure 1. (A) Chest radiograph shows collapse-consolidation of the left upper lobe along with non-homogenous infiltrates in the lower zone. (B) Chest radiograph after the first cycle of chemotherapy shows significant resolution of left lung infiltrates.

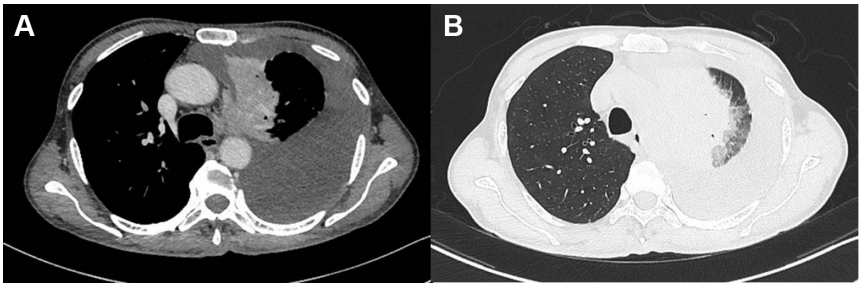

Figure 2. (A) Computed tomography scan of the thorax (mediastinal window) above the level of carina showing a mass lesion in the left parahilar region along with significant left pleural effusion. (B) CT scan of the thorax (parenchymal window) showing grossly normal right lung parenchyma and left lung findings as described above.

(marginal cell lymphoma) (Figure 3). CD3 highlighted some scattered T lymphocytes. The patient's bone marrow aspirate revealed normocellular marrow with normal hematopoiesis. The patient was started on chemotherapy (R-CHOP): rituximab, cyclophosphamide, vincristine, and prednisolone. The patient responded well clinically and radiologically (Figure 1B) after the first cycle of chemotherapy at the time of submission of this manuscript.

DISCUSSION

PPL constitutes <1% of pulmonary malignancies and also <1% of lymphomas.[3] Such rarity of the disease makes it worthy to be shared on an academic platform for early diagnosis and treatment. The incidence peaks in the sixth and seventh decades with no sex predilection.[4] These tumors originate from mucosa-associated lymphoid tissue (MALT).

Main Points

- PPL is an uncommon diagnosis and hence usually not considered in the differential diagnosis of lung lesions presenting with non-specific clinical features.
- The indolent nature of the radiological abnormalities should serve as a clue toward the suspicion of this condition.
- This case had gross ipsilateral pleural effusion, which has been rarely reported in the literature.
- A better 5-year survival rate as compared to bronchogenic carcinoma makes it worthy of early diagnosis and treatment.

MALT lymphoma is the most common pathological subtype of PPL, and diffuse large B-cell lymphoma is the most common variant of solitary pulmonary lymphoma. The most common types of PPL are marginal zone lymphoma arising from MALT, followed by other non-MALT low-grade lymphoma, and rarely high-grade B-cell PPL.[5] The tumor, in this case, was also low-grade marginal cell lymphoma. The other variant reported and kept in differential diagnosis was diffuse large cell lymphoma, which is relatively a higher grade tumor. Also, because of the lymphoma's small lymphoid cell nature, mantle cell lymphoma was a differential diagnosis. Clinical features are usually non-specific, which include cough, dyspnea, fever, and chest pain. Most authors advocate the absence of extra-thoracic disease, but mediastinal lymphadenopathy has been reported in up to 50% of patients with PPL.[6] The case reported here also was in the seventh decade with non-specific respiratory symptoms, and CT showed a left para hilar mass lesion with no mediastinal or hilar lymphadenopathy as reported previously in the literature. An unusual finding, in this case, was the presence of concomitant and ipsilateral gross pleural effusion, which has not been reported frequently in PPL except in cases of primary effusion lymphoma, which is a human herpesvirus 8 triggered disease but without a mass lesion.[7] Bronchoscopic examination has been less helpful to make a diagnosis. Occasionally, diagnosis has been made on transbronchial lung biopsies (TBLB), but they have a lower yield than surgical lung biopsies.[8,9] The case reported here showed normal findings via a flexible bronchoscope, and an eventual tissue sample was taken with the help of radial EBUS. We did not find any previous case of PPL diagnosed by radial EBUS in the literature. On histopathology, diffuse or

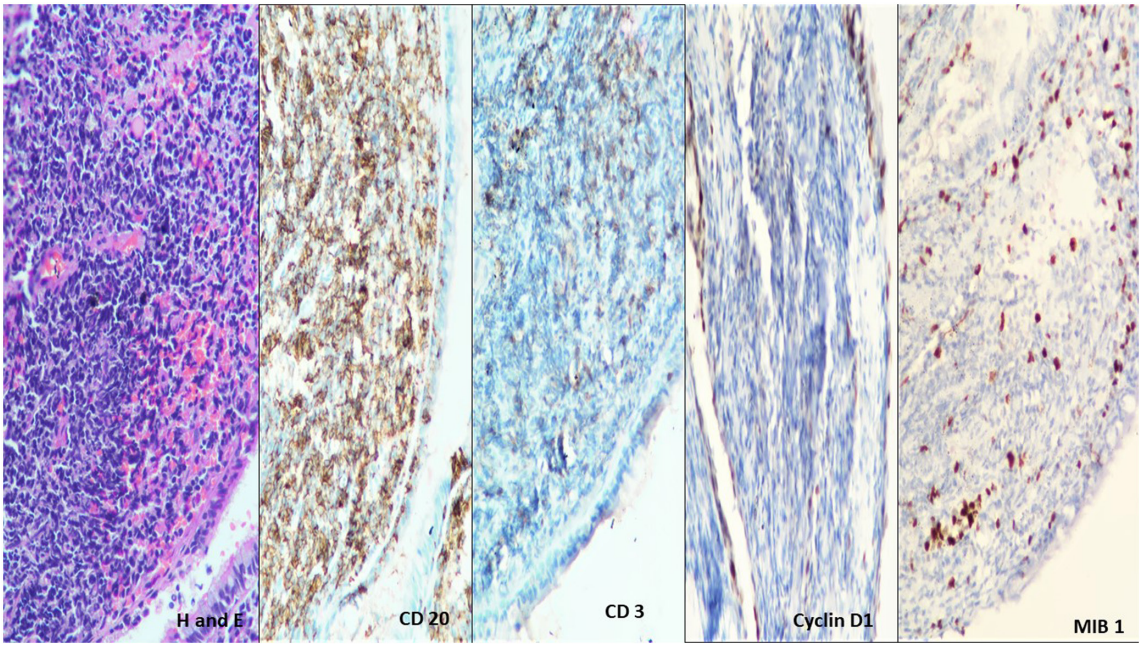

Figure 3. Photomicrograph of a section of radial EBUS guided biopsy shows a respiratory mucosa lined tissue piece. The subepithelium shows sheets of monomorphic small lymphoid cells with interspersed plasma cell; occasional Russell body is also seen. Intraepithelial lymphocytes are also seen (H&E; ×400). On IHC, these lymphoid cells are CD20 positive (CD20; ×400), CD3 negative (CD3; ×400), and cyclin D1 negative (cyclin D1; ×400). MIB-1 labeling index is 5% (MIB; ×400).

nodular tumor infiltration and lympho-epithelial lesions have been described previously, as was also seen in this patient. Morphologically, infiltration was heterogenous and consisted of lymphocytes, monocytoid cells, and plasma cells. On IHC, positivity for CD20 and negative results for CD5, cyclin D1, BCL6, and CD23 helped to make the diagnosis of low-grade B-cell non-Hodgkin lymphoma (marginal cell lymphoma). Mantle cell lymphoma, another small B-cell lymphoma which showed in differential diagnosis, was ruled out as the lymphoma was CD5 and cyclin D1 negative. Alternatively, a larger cell morphology, a positive bcl-2, CD10, and high MIB 1 index would have led to the diagnosis of diffuse large B-cell lymphoma. Considering the difficulty in obtaining a tissue specimen and bronchogenic carcinoma being a differential diagnosis, surgery was used as a diagnostic cum therapeutic option in the past. However, chemotherapy with R-CHOP/CHOP regime has been used successfully in most of the cases reported in the last decade with a good 5-year survival rate of above 75%, and radiotherapy is reserved for small lesions only.[10] Our patient has responded very well both clinically and radiologically (Figure 1B) even after the first cycle of chemotherapy and is doing well under follow-up.

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer Review: Externally peer-reviewed.

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