Case Report

Primary pulmonary lymphoma-role of fluoro-deoxy-glucose positron emission tomography-computed tomography in the initial staging and evaluating response to treatment - case reports and review of literature

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ABSTRACT

Primary pulmonary lymphoma (PPL) is an uncommon entity of non-Hodgkin lymphoma, which accounts for < 1% of all cases of lymphoma. We present two rare cases of PPL of diffuse large B-cell lymphoma, which underwent ^{18}fluorine fluoro-deoxy-glucose positron emission tomography-computed tomography for initial staging and response evaluation after chemotherapy.

Keywords: Diffuse large B-cell lymphoma, fluoro-deoxy-glucose positron emission tomography-computed tomography, non-Hodgkin lymphoma, primary pulmonary lymphoma, treatment response evaluation

INTRODUCTION

Primary pulmonary lymphoma (PPL) is an uncommon entity of non-Hodgkin lymphoma (NHL), which accounts for <1% of all cases of lymphoma, 3–4% of all the extranodal manifestations of NHL, and only 0.5–1% of all primary pulmonary malignancies. PPL usually affects single lung but may involve both lungs also. Most of the cases of the primary lymphoma of the lung originate from the B-cell lineage. In 90% case, PPL is low-grade lymphoma; however, it can transform to high-grade lymphoma. Immunocompromised patients usually present with high-grade lymphoma. There have been only few case reports in the literatures reporting the usefulness of positron emission tomography-computed tomography (PET-CT) in the PPL. Here, we discuss two rare cases of PPL of diffuse large B-cell lymphoma.

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CASE REPORTS

Case 1

A 26-year-old male patient presented to our department for the initial staging of NHL. He had a history of smoking for the last 5-year. Patient initially had mild chest pain and fever for 1-year. Initial chest X-ray showed left lung hilar infiltration and left pleural effusion. Since pulmonary tuberculosis is highly prevalent in this part of the world, based on clinical and radiological investigations, he was put on antitubercular treatment (ATT). There was no clinical and or radiological improvement noted with 6 months of ATT treatment. Contrast-enhanced computed tomography (CECT) of the chest showed left lung upper lobe mass. CT guided fine needle aspiration cytology (FNAC) did not

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reveal any definite diagnosis, but findings were suspicious for malignancy. Based on FNAC finding, open chest thoracotomy biopsy was done which confirmed the diagnosis of diffuse large B-cell lymphoma. ^{18}Fluorine fluoro-deoxy-glucose (^{18}F-FDG) PET-CT performed to know the extent of the disease demonstrated increased FDG uptake (SUVmax- 10.7) in the left lung upper lobe mass measuring 5.5 cm × 6.5 cm × 7.0 cm with no extrapulmonary involvement [Figure 1]. Patient received 6 cycles of (rituximab, cyclophosphamide, cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy. A follow-up posttreatment, ^{18}F-FDG PET/CT scan done 6 weeks postchemotherapy showed complete resolution of left lung upper lobe mass [Figure 2].

Case 2

A 60-year-old female patient presented with a history of dry cough and easy fatigability for last 8 months. CECT revealed consolidation in the right lung middle lobe. ^{18}F-FDG PET/CT performed for initial staging to know the extent of the disease showed increased FDG uptake (SUVmax - 6.4) in the right lung middle lobe mass measuring 8.3 cm × 6.8 cm × 6.7 cm with no extrapulmonary involvement [Figure 3]. Biopsy was done from right lung mass which showed diffuse large B-cell lymphoma. Immunohistochemistry showed positive for CD20 and negative for cytokeratin, CD3, and CD10. Final diagnosis was primary pulmonary NHL. Patient was advised for chemotherapy.

DISCUSSION

Extranodal forms of lymphoma though common and represent 24–50% of cases of NHL, but primary extranodal lymphomas comprise only 3–5% of all lymphomas and are mostly reported in the stomach and gastrointestinal tract.[1] PPL is a rare entity encompassing <1% of all lymphomas.[2] Secondary involvement of the lung in patients with a history of lymphoma is much more frequent and has an incidence of 25–40%.[3] PPL defines as lymphoid proliferation affecting a single lung or both and that has not spread outside the lungs with no detectable extrapulmonary involvement at the time of diagnosis or does not spread in the following 3 months.[4]

World Health Organization's classification system has divided PPL into B-cell primary pulmonary NHL and lymphomatoid granulomatosis.[5] The first group subdivides into low-grade B-cell PPLs (58–87%), high-grade B-cell PPLs (11–19%), primary pulmonary plasmacytoma, and intravascular pulmonary lymphomas. Ninety percent of low-grade B-cell PPLs are composed of marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue type (MALT lymphoma) or bronchus-associated lymphoid tissue (BALT).[5] Their development depends on MALT of the bronchus that is thought to be acquired as a result of chronic antigenic stimulation such as smoking, autoimmune disease (systemic lupus erythematosus, multiple sclerosis, Hashimoto's thyroiditis, and particularly Gougerot-Sjögren's syndrome), or infection.[6]

PPL usually pursue indolent courses, remaining localized to the lung for long periods before dissemination.[1] Treatment options are various, ranging from close observation to radiation, surgery, or combination chemotherapy.[5,6] In a retrospective study of 24 patients, who were treated with a variety of modalities such as observation, surgery, and single or combination chemotherapy, the overall survival rate at 3 years was 86% with a median follow-up of 32-months.[7] Aggressive PPL is less frequently detected and

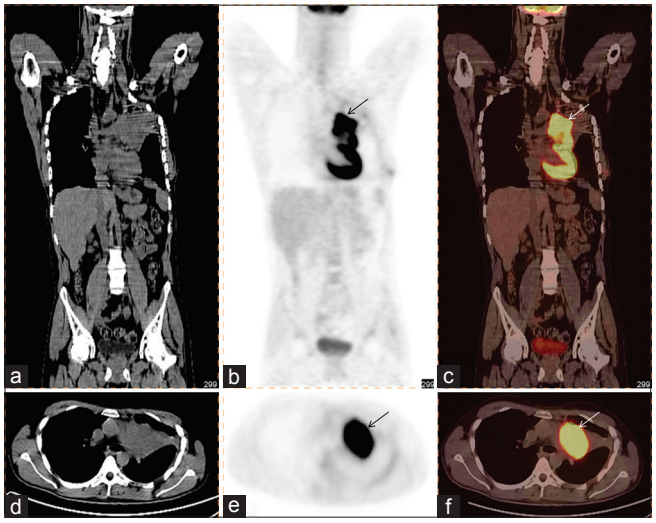

Figure 1: A 26-year-old male patient presented with a history of mild chest pain and fever for last 1 year. Whole body ^{18}fluorine fluoro-deoxy-glucose positron emission tomography-computed tomography baseline scan obtained for initial staging: Coronal and transaxial sections of computed tomography (a and d) showing left lung upper lobe mass with no extrapulmonary involvement. Coronal and transaxial sections of positron emission tomography (b and e, arrow) and positron emission tomography-computed tomography (c and f, arrow) shows left lung upper lobe mass with increased fluoro-deoxy-glucose uptake. The distribution of fluoro-deoxy-glucose in the rest of the body is within normal limits. The findings are suggestive of metabolically active disease involving left lung upper lobe

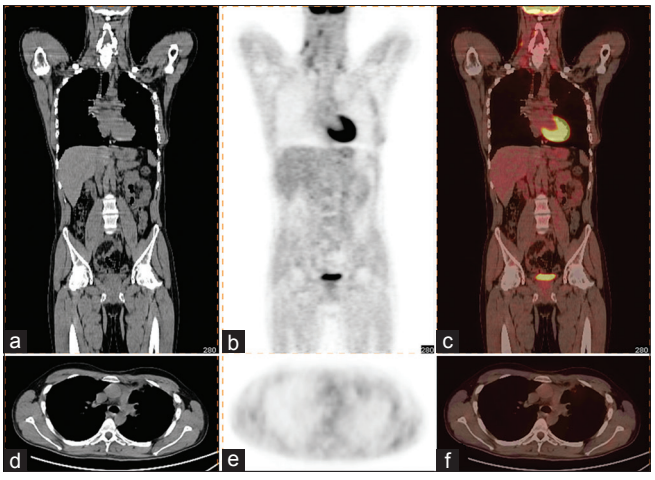

Figure 2: Whole body ^{18}fluorine fluoro-deoxy-glucose positron emission tomography-computed tomography follow-up posttherapy scan obtained for evaluation of treatment response: Coronal and axial sections of computed tomography (a and d), positron emission tomography (b and e), and positron emission tomography-computed tomography (c and f) showing no abnormal mass or tracer uptake noted in the left lung. The distribution of fluoro-deoxy-glucose in the entire body is within normal limits. The findings are suggestive of complete resolution of metabolically active disease involving left lung upper lobe seen in baseline whole body positron emission tomography-computed tomography

may arise from the transformation of an indolent lymphoma or occurs in individuals with an underlying disorder such as acquired immunodeficiency syndrome.[5,6] These patients generally require aggressive treatment with combination chemotherapy and prognosis seems to be worse than for low-grade MALT lymphoma.[6] In immunodeficient patients with high-grade PPL, the median survival is 4 months.[8] Therefore, it is very important to find out as soon as possible, if particular therapy is effective or not in these patients. Hence, that expensive, ineffective, and toxic chemotherapy can be discontinued, and more aggressive and effective therapy can be initiated as early as possible.

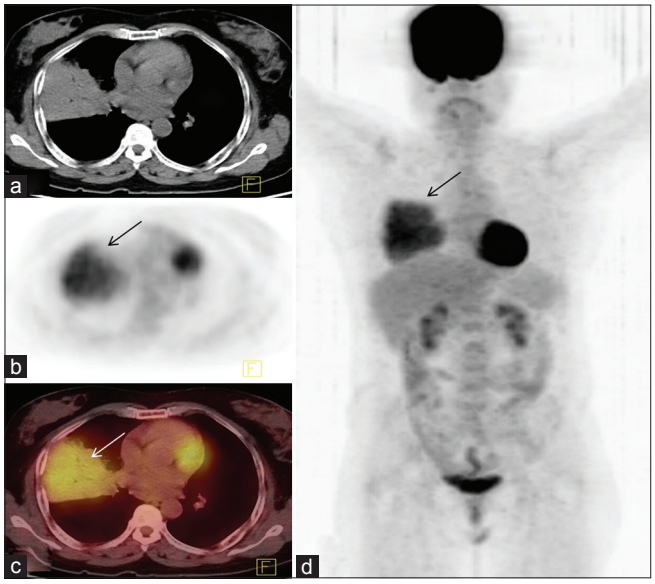

Figure 3: A 60-year-old female patient presented with a history of dry cough and easy fatigability for last 8 months. Whole body ^{18}fluorine fluoro-deoxy-glucose positron emission tomography-computed tomography scan obtained for staging: Transaxial computed tomography (a) showing right lung middle lobe mass with increased tracer uptake in positron emission tomography (b, arrow) and positron emission tomography-computed tomography (c, arrow) images. Maximum intensity projection (d, arrow) image shows fluoro-deoxy-glucose avid right lung middle lobe mass with no extrapulmonary involvement. The findings are suggestive of metabolically active disease involving right lung middle lobe

Radiological imaging techniques commonly used for evaluation of treatment response is chest radiography, CT, and magnetic resonance imaging (MRI). Currently, CT is the most commonly used technique for staging and evaluation of treatment response, owing to the short examination time and its wide availability. According to revised Response Evaluation Criteria in Solid Tumors criteria, a decrease in 30% the size of a tumor after completion of treatment as compared with the pretreatment scan is considered as a response.[9] Though CT/MRI is widely accepted for evaluation of treatment response in clinical practice, they have several limitations. These anatomical modalities cannot differentiate viable residual tissue from scar after the completion of treatment. Approximately, two-thirds of patients with Hodgkin's disease and half of patients with high-grade NHL present with fibrotic or recurrent mass lesions in the location of a previous tumor manifestation, but only one-quarter of these patients ultimately relapse.[10] ^{18}F-FDG PET is a functional modality targeting glucose metabolism, which is markedly increased in most malignant tumors including lymphomas. ^{18}F-FDG PET/CT can assess treatment response during (after one or two cycles) or after completion of therapy as changes in glucose metabolism are much earlier than structural changes. Recently, PET has been combined with CT, permitting combined anatomical and functional imaging information in one setting. ^{18}F-FDG PET is a well-established new modality in the evaluation of nodal and extranodal NHL.[11-13]

Few reports have been described in the past regarding the role of ^{18}F-FDG PET/CT in patients with PPL. Most of them represent isolated case reports and two articles concentrates on a small group of patients [Table 1].[14-20] PPL can be rarely presented as multiple cavitating pulmonary nodules; however, cavitation has been reported more frequently in the setting of HIV infection. In a report by Madan *et al.,* author showed intense FDG uptake in bilateral cavitary pulmonary nodules which histopathologically diagnosed as primary pulmonary diffuse large B-cell lymphoma.[15] Hence, pulmonary involvement by

Table 1: Cases of primary pulmonary lymphoma reported in the literature using positron emission tomography-computed tomography

Author	Year	Number (sample size)	Age/gender	Clinical presentation	Pathology	SUVmax	Outcome
Xu *et al.*	2015	1	44/male	Cough, sputum, and intermittent chest pain	DLBCL	NA	NA
Madan *et al.*	2014	1	79/female	Cough, shortness of breath, and fever	DLBCL	NA	NA
Niu *et al.*	2014	10	15-84	Cough, chest pain	NHL	3.96-6.70	Surgery, chemotherapy
Chen *et al.*	2014	1	35/female	Cough, breathlessness, and fever	Primary intravascular large BCL	NA	Chemotherapy
Yoon *et al.*	2012	7	21-61, 6 female, 1 male	Cough, sputum, wheezing, and dyspnea	Marginal zone B-cell lymphoma of BALT	3.0, 2.3, 2.4, 5.7	Chemotherapy, RT, cryotherapy
Bural *et al.*	2012	1	64/female	History of Sjogren's syndrome	Marginal zone B-cell NHL	10.2	Chemotherapy
Shin *et al.*	2010	1	52/male	Cough, fever, and sweating	Primary pulmonary T-cell lymphoma	8.9	Chemotherapy

DLBCL: Diffuse large B-cell lymphoma, NA: Not available, BALT: Bronchi-associated lymphoid tissue, NHL: Non-Hodgkin lymphoma, RT: Radiotherapy, SUVmax: Maximum standardized uptake values

lymphoma should be considered in the differential diagnosis of multiple cavitating pulmonary nodules. Niu *et al.* showed differences in radiological features between primary (PPL) and secondary pulmonary lymphoma (SPL).[16] Radiologically, PPL were mainly manifested with lung masses, while those of SPL were mainly pleural involvement and mediastinal and hilar lymph node enlargement. PET/CT study may be helpful for the initial diagnosis and staging of pulmonary lymphoma; however, misdiagnosis rate of pulmonary lymphoma was high, and diagnosis must rely on lung tissue biopsy and immunohistochemistry. Chen *et al.* reported a rare case of primary intravascular large B-cell lymphoma which manifests as diffuse ground glass shadow, or nodular consolidations in the lung.[17] FDG PET/CT is an important and significant diagnostic modality in its early diagnosis. Primary endobronchial marginal zone B-cell lymphoma also called BALT presented as solitary intraluminal nodule which shows homogeneous and mild FDG uptake on PET. Yoon *et al.* studied in seven patients with primary endobronchial marginal zone B-Cell lymphoma, in which six patients showed nodular lesion in trachea or bronchus, and one patient with diffuse wall thickening of distal trachea. On ^{18}F-FDG PET/CT ($n = 5$), four lesions showed homogeneous uptake with maximum standardized uptake values (SUVmax), ranging 2.3–5.7 (mean SUVmax: 3.3) and one lesion showed no significant hypermetabolic activity.[18] Bural *et al.* studied response assessment with FDG PET/CT in a rare case of marginal zone B-cell NHL in a patient with Sjogren's syndrome.[19] FDG PET has been shown to be considerably more accurate than anatomical imaging in response assessment because of its ability to distinguish between viable tumor and nonviable posttreatment findings and can identify individuals with treatment resistance to certain forms of chemotherapy, early in the course which provides the clinician, a sufficient time window to change the therapeutic strategy. Shin *et al.* reported a rare case of primary pulmonary peripheral T-cell lymphoma.[20] On PET/CT study, it was presented with multiple hypermetabolic masses with photopenic defects in correlates well with central necrosis on CT in both lungs which showed progression despite that the patient had undergone chemotherapy. Tumor necrosis is uncommon finding in lymphoma; however, it generally correlates with hypoxia and is a predictor of a poor prognosis for patients with malignant tumor.

In the first case, patient presented with diffuse large B-cell lymphoma and disease activity was seen localized to lungs on baseline PET/CT scan. Follow-up posttherapy PET/CT scan findings were consistent with clinical and radiological response with no FDG uptake. In the second case, PET/CT was done for initial staging and to know extent of disease, which showed disease localized to lung with no extrapulmonary involvement. In conclusion, we feel PET/CT is a good modality in the management (initial staging and evaluation of therapy response) in patients with PPL, especially with DLBCL type.

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Conflicts of interest

There are no conflicts of interest.

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