Case Report

Paraneoplastic syndrome turned out to be non-Hodgkin's lymphoma on ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography

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ABSTRACT

Paraneoplastic neurological syndromes (PNSs) are commonly encountered with underlying malignant pathology. Though anti-neuronal antibodies play a major role in the diagnosis of the underlying malignant pathology but at many times it becomes inconclusive. As early detection of the primary cause and its treatment gives the best result in such situations, there arises an early and accurate diagnostic need. We present a 65-year-old patient presenting with rapidly progressive quadriparesis with both distal and proximal involvement. With all routine work-up tests within normal limits, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) was done which revealed multiple findings that suggested a diagnosis of lymphoma. In our case, PET/CT proved to be an important modality for finding the underlying malignant pathology in a suspected case of PNS.

Keywords: Fluorodeoxyglucose positron emission tomography/computed tomography, non-Hodgkin's lymphoma, paraneoplastic neurological syndrome

INTRODUCTION

The frequency of paraneoplastic neurological syndromes (PNSs) are very low which is approximately <1% of patients with solid tumors, particularly small-cell lung carcinoma, breast, and ovarian cancers. PNSs are rarely associated with Hodgkin lymphoma (HL) and non-HLs (NHLs).[1] In other studies, it has been demonstrated that they are mostly seen in small lung cancer followed by gynecological tumors (ovarian cancer), breast cancer, thymomas, and in a minority of cases in lymphomas mainly HLs.[2]

Accurate diagnosis of PNS is very important because an early recognition of a neurological syndrome as paraneoplastic often leads to the discovery and treatment of the underlying tumor.[3] Early diagnosis and prompt treatment of the underlying tumor can stabilize the patient and prevent further neurological deterioration.[4]

CASE REPORT

We present a 65-year-old patient presenting with rapidly progressive quadriparesis with both distal and proximal involvement. On examination, the patient was afebrile and deep tendon reflexes were completely absent. There was no palpable lymphadenopathy, or any other abnormality was observed. Routine complete blood count and electrolytes were within normal limits. Nerve conduction study was found to be slowed. Antibody titers for paraneoplastic

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work up were found to be normal. With a strong clinical suspicion of PNS, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) was done which revealed multiple enlarged lymph nodes with increased FDG uptake both sides of diaphragm. There were no signs of calcification and necrosis in the lymph nodes. Furthermore, there were focal sites of patchy FDG uptake noted in the bone marrow [Figure 1a-e]. These findings on PET/CT led to a diagnosis of lymphomatous involvement, and biopsy was advised. Biopsy from the right cervical node revealed diffuse infiltration of large atypical cells with prominent nucleoli and vesicular chromatin (H and E, ×400) which were positive for CD20 confirming it to be NHL [Figure 2].

DISCUSSION

Currently, it is thought that most or all paraneoplastic neurologic disorders are believed to have immune-mediated pathophysiology. The mechanism involves ectopic expression by a tumor of an antigen that is normally expressed exclusively in the nervous system, which is identical to the neural antigen, but for unknown reasons it is recognized as foreign antigens and an immune attack is initiated.[5] It has been described that several PNS are associated with onconeural antibodies. However, around 50% of patients with true PNS do not have any of the well-characterized onconeural antibodies.[6] In these patients, early diagnosis of the tumor becomes difficult, resulting in a significant delay in primary treatment.[7] An early diagnosis of a neurological syndrome as PNS is thus crucial for the management of patients. Detection of an onconeural antibody in a patient suspected to have a PNS is, at present, the most important diagnostic test.[6] In these patients where anti-neuronal antibody is negative, early diagnosis of the tumor is frequently difficult, resulting in a significant delay in tumor treatment.[7] Detection of an onconeural antibody in a patient suspected to have a PNS is, at present, the most valuable diagnostic test.[6]

HL is associated with a number of neurological complications that occur both as a direct consequence of HL (intraparenchymal brain metastases, epidural spinal cord compression, HL meningitis and dural metastases) and indirectly due to treatment or paraneoplastic disorders. The majority of nervous system complications of HL are due to metastatic lesions or due to treatment-related complications.[8]

In NHL, the mechanisms of direct involvement are similar to HL. It can form nodular lesions in brain parenchyma due infiltration from subarachnoid space. Other manifestations include chronic inflammatory demyelinating polyneuropathy, acute inflammatory polyradiculopathy, multifocal motor neuropathy with conduction block and chronic axonal-demyelinating polyradiculoneuropathy. Nerve conduction velocity is slowed in demyelinating diseases. Paraneoplastic demyelinating sensorimotor neuropathy due to antibodies to IgM antibodies against disialosyl residues have been reported in NHL. Opsoclonus-myoclonus syndrome, paraneoplastic stiff-person and related syndromes, paraneoplastic myelopathy, and paraneoplastic neuronopathy are also seen to be associated with NHL.[1]

Apart from anti-neuronal antibodies, many conventional tests such as ultrasonogram, CT of various body parts may lead to a diagnosis of underlying pathology. Study have found that performance of ^{18}F-FDG PET/CT, a single imaging study, for diagnosing occult malignant disease in patients with myositis was comparable to that of broad conventional screening, which includes multiple tests.[9] ^{18}F-FDG PET/CT has been proved to be a useful screening tool for patients with clinically suspected PNS, who do not exhibit well-characterized paraneoplastic antibodies.[10,11]

In our patient with presentation of PNS, all routine blood examinations, and other routine tests could not give any confirmatory diagnosis. Furthermore, the antibody test was found to be negative. ^{18}F-FDG PET/CT provisionally diagnosed the case to be NHL, which was confirmed with histopathological examinations. No evidence of any other comorbid benign disorder was found after through clinical and laboratory evaluation. The patient was treated with

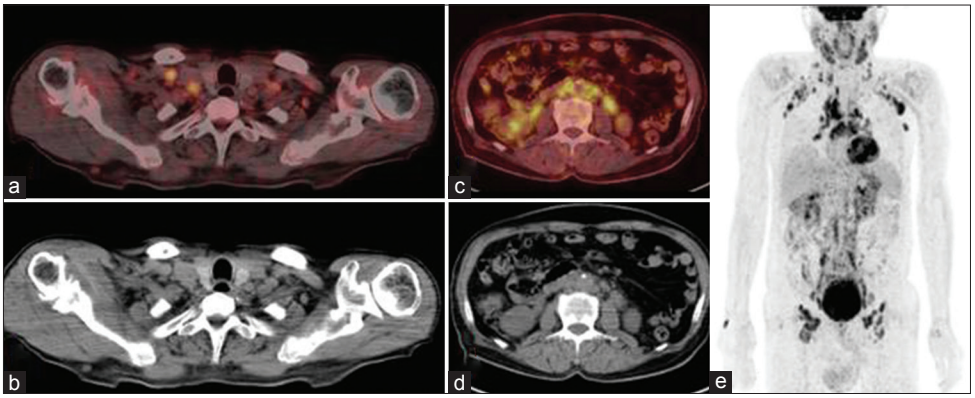

Figure 1: Multiple enlarged bilateral supraclavicular lymph nodes with increased fluorodeoxyglucose uptake (a and b). Multiple enlarged retroperitoneal lymph nodes with increased fluorodeoxyglucose uptake (c and d). Maximum intensity projection image showing increased fluorodeoxyglucose uptake involving both sides of diaphragm along with focal sites of patchy fluorodeoxyglucose uptake noted in the bone marrow (e)

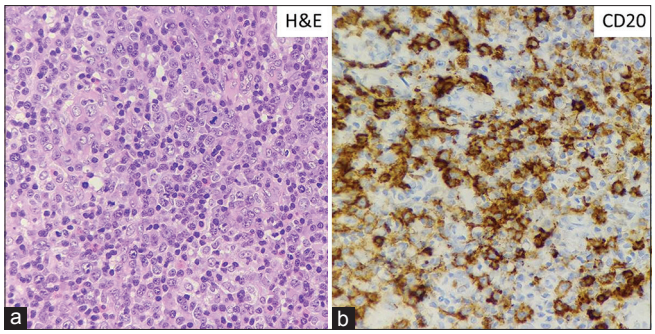

Figure 2: Lymph node biopsy showing diffuse infi ltration of large atypical cells with prominent nucleoli and vesicular chromatin (H and E, ×400) (a) which were positive for CD20 (b)

chemotherapy, and there was general sense of well-being as well as significant improvement in neurological symptoms in the early posttreatment period. ^{18}F-FDG PET/CT proved to be an important modality for finding the underlying malignant pathology in a suspected case of paraneoplastic syndrome in the setting of negative antibody titer.

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Conflicts of interest

There are no conflicts of interest.

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