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Case Report

Neurolymphomatosis – Rare presentation in non-Hodgkin's lymphoma: The role of ^{18}F-fluorodeoxyglucose positron-emission tomography and computerized tomography imaging

ABSTRACT

Neurolymphomatosis (NLS) is infiltration of lymphoma cells into the peripheral or cranial nervous system and is a rare manifestation of non-Hodgkin lymphoma (NHL). Nerve biopsy is considered as the gold standard for diagnosis but not a preferred choice, and magnetic resonance imaging has lower reported sensitivity. ^{18}F-Fluorodeoxyglucose (^{18}FDG) positron-emission tomography and computerized tomography (PET/CT) has a higher sensitivity for diagnosing and assessing the neurological and nonneurological metabolic tumor volume and response evaluation to therapy. We present the case of a lady, known to have NHL in remission. She presented with a short history of severe pain and weakness of the right lower limb. Baseline and interim ^{18}FDG PET/CT played a crucial role in diagnosing and assessing the extent of NLS and nonneurological disease burden and also in evaluation of response to treatment.

Keywords: ^{18}F-fluorodeoxyglucose positron-emission tomography and computerized tomography, magnetic resonance imaging, neurolymphomatosis, non-Hodgkin's lymphoma

INTRODUCTION

Neurolymphomatosis (NLS) is a rare manifestation of non-Hodgkin lymphoma (NHL) characterized by infiltration of lymphoma cells into the peripheral or cranial nervous system.[1] Patients may develop NLS at the initial presentation, during disease progression, or as relapse of disease. Due to nonspecific and variable symptoms, diagnosis is often a dilemma and challenging. Nerve biopsy is considered as the gold standard for diagnosis but less pragmatic due to invasiveness, possible irreversible neurological deficit, and scattered distribution of involved nerves. However, magnetic resonance imaging (MRI) findings that are suggestive of NLS (like enhancement of nerves or nerve roots beyond the root sleeve) are also seen in other inflammatory neuropathies.[2] ^{18}F-Fluorodeoxyglucose (^{18}FDG) positron-emission tomography and computerized tomography (PET/CT) imaging is considered as a highly sensitive tool for diagnosis and also for assessing response to treatment.[3] We present a case of NLS in which ^{18}FDG PET/CT was used for diagnosis and response evaluation to the treatment.

CASE REPORT

We present the case of a 53-year-old female, a known case of NHL (diffuse large B-cell lymphoma [DLBCL]) who had completed chemotherapy (8 × R-CHOPP) with a complete

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metabolic response in January 2018. In November 2018, she presented to the emergency room with a short history of progressively deteriorating pain and weakness in the right lower limb. On examination, she was well oriented and had normal vitals and a nontender mild swelling over the left maxillary region with few palpable nodes in bilateral upper cervical regions. Neurological examination revealed normal mental status and cranial nerve function. There was a significant lower motor weakness in the right lower limb (2/5), and sensory examination revealed mild appendicular acral numbness to light touch. There was also evidence of mild motor weakness in both the upper limbs (4/5) without significant abnormality on sensory examination. Biopsy of the left facial swelling revealed DLBCL (CD20 positive with Ki-67 index >90%). Her cerebrospinal fluid (CSF) and bone trephine did not reveal lymphomatous infiltration. A low-dose noncontrast ^{18}FDG PET/CT examination was performed (210 MBq ^{18}FDG and Celesteion, Cannon, Japan) which revealed hypermetabolic soft-tissue deposits involving the left maxillary, left buccogingival, left pterygoid, and left parotid regions and hypermetabolic lymph nodes in the left Level II, V, and celiac regions. There was also evidence of hypermetabolic uptake (predominantly linear pattern) over the bilateral brachial and right sacral plexuses and bilateral sciatic, right gluteal, and both femoral nerves [Figures 1a and 2a, c, e]. The patient refused a peripheral nerve biopsy. Based on the clinical, facial biopsy and ^{18}FDG PET/CT findings, a diagnosis of recurrent lymphoma with NLS was made. The second-line chemotherapy was started, and after four cycles, she became asymptomatic with a resolution of left facial swelling and normalization of sensory and motor deficits too. An interim ^{18}FDG PET/CT revealed a complete metabolic response too [Figures 1b and 2b, d, f].

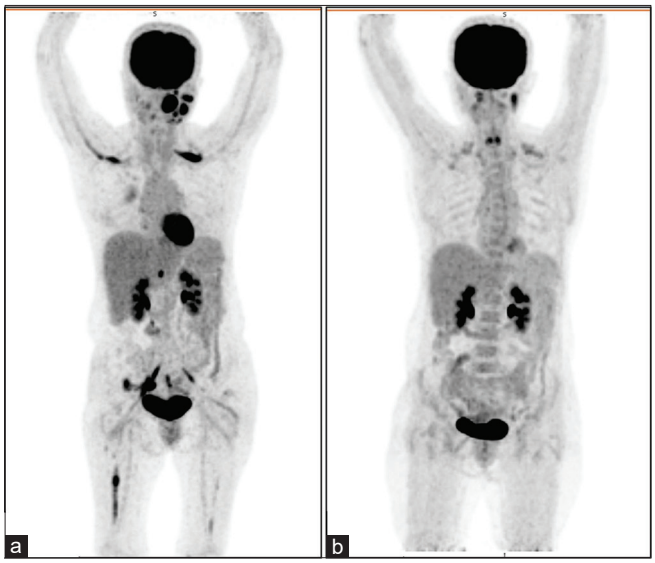

Figure 1: ^{18}F-fluorodeoxyglucose positron-emission tomography and computerized tomography MIP images. (a) Baseline MIP shows linear-shaped hypermetabolic uptake over bilateral brachial and right sacral plexuses and bilateral sciatic, right gluteal, and both femoral nerves. In addition, soft-tissue deposits are seen over the left side of the face and celiac regions. (b) Interim MIP shows complete metabolic response with moderate brown adipose tissue in both the supraclavicular regions. MIP: Maximum intensity projection

DISCUSSION

NLS is the diffuse infiltration of peripheral or cranial nerves by lymphomatous cells in patients with NHL (90%) or acute leukemia (10%).[4] It is a rare entity and estimated to occur in about 0.2% of all NHL patients.[5] However, an autopsy series of 145 patients who died of NHL, 40% demonstrated evidence of peripheral nerve involvement, suggesting an infrequent clinical recognition of NLS.[6] It may be the first manifestation of NHL (10%), present concurrently (25%), or as a pattern of disease recurrence (40%).[7]

Clinical presentation of NLS is variable and may be associated with or without pain. Painful limb syndrome with relatively rapid but asymmetric progression in all four limbs is the most characteristic manifestation. In the literature, four clinical patterns of presentation have been described in patients with NLS: (a) painful involvement of multiple nerves or roots (30% of all cases); (b) painful or painless cranial neuropathy (25%); (c) painless peripheral neuropathy (30%); and (d) painful or painless mononeuropathy (15%).[5] Concomitant leptomeningeal metastasis with NLS is not uncommon and has been reported in 20%–25% of cases.[7]

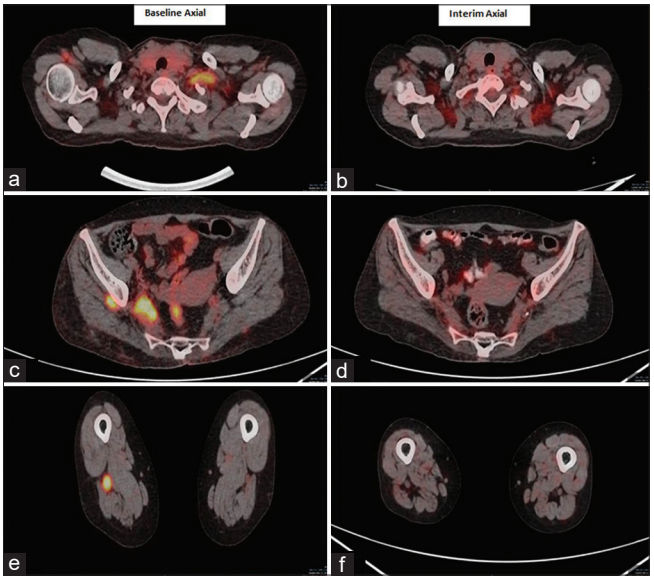

Figure 2: Axial fused ^{18}F-fluorodeoxyglucose positron-emission tomography and computerized tomography images. (a, c, e): Baseline images showing hypermetabolism involving bilateral brachial and right sacral plexuses and right femoral nerve. (b, d, f): Interim images showing interval normalization of size and metabolic activity of nerves and interval appearance of moderate brown adipose tissue in both the supraclavicular regions

Diagnosis of NLS is very challenging despite a large number of techniques that can lead to this diagnosis, such as CSF cytology, nerve biopsy, MRI, and ^{18}F-FDG/PET scan. Nerve biopsy (sural or peroneal nerves are the commonly used sites) due to its invasiveness and possible postprocedural neurological deficit is not a preferred choice. When it is performed, the main difficulty resides in their small size and distinguishing reactive cell infiltrates from neoplastic lymphoproliferation on histological examination.[8] The reported diagnostic yield of nerve biopsy for NLS is 84%.[4] CSF cytology shows malignant cells in patients with NLS with a positive yield of only 40%.[4] MRI and ^{18}FDG PET/CT are the two major imaging tools for the diagnosis of NLS. MRI shows characteristic features of NLs as enlarged involved cranial nerves, nerve roots, plexus, and trunks of peripheral nerves. These are isointense on T1-weighted images, hyperintense on short tau inversion recovery, and T2-weighted MR images with contrast enhancement as nodular or linear lesions.[9] However, the sensitivity of MRI is often limited (40%) because of the patchy distribution or small lesion(s) size, resulting in a false-negative assessment of the affected neural structures.[3]

In the current era, ^{18}FDG PET/CT has become a standard of care in staging and treatment monitoring of lymphoma. ^{18}FDG-PET/CT shows hypermetabolism over involved peripheral nerves and other tissues in patients with NL. Contrary to its reduced sensitivity for central nervous system lymphoma, the reported sensitivity of ^{18}FDG-PET/CT for NLS is 87.5%–100%.[10] In the current case, PET/CT demonstrated a characteristic pattern of hypermetabolism over involved nerves and nerve plexuses consistent with NLS. In addition, it also revealed recurrent disease over nodal and nonnodal sites with invaluable information about viable metabolic tumor burden to the treating team. Furthermore, follow-up (interim) ^{18}FDG PET/CT also helped in assessing the response of NLS and nodal and nonnodal soft-tissue disease to the second-line chemotherapy. Prognosis of patients with NLS remains poor despite treatment with chemotherapy and rituximab.[11] However, by the time of writing this manuscript, our patient is alive and clinically asymptomatic. Future studies must be performed to assess the negative predictive value of ^{18}FDG PET/CT for disease-free survival in patients with NLS.

CONCLUSION

We conclude that NLS must be considered in patients with NHL presented with neurological symptoms. MRI and ^{18}FDG PET/CT are effective diagnostic tools although the former has lower sensitivity. ^{18}FDG PET/CT plays a crucial role in diagnosing and assessing the extent of NLS and nonneurological disease burden and also in the evaluation of response to treatment. Furthermore, the negative predictive value of interim/end-of-treatment ^{18}FDG PET/CT may be explored for disease-free survival in patients with NLS.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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