F-18 Fluorodeoxyglucose Positron Emission Tomography Computed Tomography Findings in an Interesting Case of Primary Cauda Equina Lymphoma with Literature Review

Abstract

Primary lymphomatous involvement of spinal cord, nerve roots, and cauda equina is a rare entity and comprises only 0.1% of extra-nodal lymphoma spectrum. Here, we present a case of non-Hodgkin lymphoma involving cauda equina, initially suspected as ependymoma on magnetic resonance imaging that was later confirmed on nerve root biopsy as high B cell non-Hodgkin's lymphoma of L1-S1 nerve roots. F-18 fluorodeoxyglucose positron emission tomography-computed tomography was performed for staging workup which showed abnormal metabolic activity within the spinal canal from D10-S2 with no evidence of distant organ involvement.

Keywords: *Cauda equina lymphoma, F-18 fluorodeoxyglucose positron emission tomography-computed tomography, neurolymphomatosis, non-Hodgkin's lymphoma, spinal lymphoma*

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Introduction

Non-Hodgkin's lymphoma (NHL) is neoplastic transformation of B cell, T cell, and natural killer cells, frequently involving lymphohematopoietic systems. Extranodal presentation of NHL creates diagnostic difficulty. Renal infiltration of NHL is seen in 2%–14% of the cases, while primary lymphomatous involvement of the gastrointestinal system is seen in 5%, bone in <1%, subcutaneous panniculitis in <1% of patients.[1] Primary central nervous system (CNS) lymphoma accounts for 1% of NHL cases with predominant involvement of the brain, leptomeninges, and less frequently in the eyes and spinal cord.[2] Primary spinal lymphoma comprises only 0.1% of extranodal lymphoma spectrum, with cord compression being the common presentation.[3] Lymphomatous invasion of cranial nerves and peripheral nerve roots, plexus, or nerves by NHL is called neurolymphomatosis which is least common form of direct neurological manifestation of lymphoma.[4] Here, we report a case of F-18 fluorodeoxyglucose positron emission tomography-computed tomography (F-18 FDG PET CT) performed for the evaluation of neurolymphomatosis of cauda equina.

Case Report

A 43-year-old male patient presented with complaints of weakness of both lower limbs (LL) for 9 days with bilateral LL paresthesia and bowel and bladder incontinence after sustaining fall from bike 2 weeks before. The patient had no history to suggest meningitis or intracranial bleed. The patient had no comorbidities, not a smoker or alcoholic.

On examination, power of LL including hip, knee, ankle, and foot were 0/5 with absent abdominal reflex and extensor plantar response. Sensory system showed decrease of 30% below L1 dermatome for touch. There were no cerebellar signs or meningeal signs. Clinical examination suggests upper motor neuron type bilateral LL palsy with possible pathology above the level of L3 vertebrae.

Further evaluation with magnetic resonance imaging (MRI) lumbosacral (LS) spine raised a suspicion of ependymoma of filum terminale and cauda equina [Figure 1]. Viral markers for HIV, hepatitis C virus and HbsAg were negative. The patient underwent L1-S1 laminectomy and biopsy of the nerve root, suggestive of lymphomatous

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infiltration and further immunohistochemistry showed positive for leukocyte common antigen and CD20 with MIB-1 index of 30%, giving the impression of high-grade B cell NHL of L1-S1 nerve roots.

Patient came for whole-body F-18 FDG PET CT to rule out systemic involvement of lymphoma. It revealed soft tissue density lesion extending from D10-S2 vertebral level within the spinal canal over a length of 17.2 cm with no abnormality in adjacent bone and the lesion showed intense FDG concentration (standard uptake value maximum–16.7) [Figure 2]. There was no evidence of distant organ involvement, suggesting primary spinal lymphoma of cauda equina. The patient has been planned for R (Rituximab)-CHOP (Cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy.

Discussion

NHL can involve any organ system in the body. However, CNS involvement is rare with reported incidence of 2.2% to 6.9%.[4] F-18 FDG PET CT is well established in staging and treatment response assessment of lymphoma. After the availability of PET CT, there are few case reports documenting rare site of lymphoma in cauda equina.[5,6]

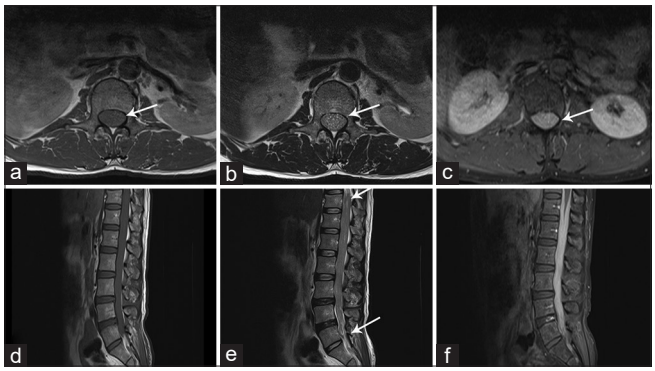

Figure 1: (a) Preoperative magnetic resonance imaging precontrast T1 axial, (b) T2 axial, (c) T1 postcontrast axial images, (d) Precontrast T1 sagittal, (e) T2 sagittal, (f) T1 postcontrast sagittal images. Nerve roots in the cauda equina show diffuse thickening with obliteration of intervening cerebrospinal fluid signal in T2-weighted images which appears isointense on T1-weighted image. Diffuse homogenous enhancement noted within the theca encircling the distal cord and conus and involving nerve roots

Lymphoma of extradural space was first described by Welch in 1910. Subsequently, similar case reports and series were documented, for which Rubenstein (1972) postulated the antigenic stimulation of lymphatic tissues in spinal epidural space or lymphoma of paraspinal lymph node with subsequent spinal infiltration as hypothesis.[5] Most of the documented cases of neurolymphomatosis are predominantly, NHL variety.[4] Baehring JM *et al*., (2003) suggested tissue-specific dissemination of lymphoma could be due to loose tethering, stable adhesion and migration by integrins, selectins, and cytokines.[6]

Primary CNS lymphoma (PCNSL) involves the brain, meninges, spinal cord, vitreoretinal regions and is most commonly seen in immune-compromised patients.[7] In our case study, the patient had normal blood profile, negative retroviral status, and no history of intake of drugs that cause immunosuppression. Primary spinal lymphoma usually presents with chronic back pain and later progressing with neurological signs and symptoms.

Baehring JM *et al*.,(2003) presented a study, in which patients presentation was classified into four different patterns, namely, painful involvement of nerve roots, cranial neuropathy, painless involvement of peripheral nerves, and painful/painless single peripheral nerve involvement. In his study of 72 patients, 31% had painful polyneuropathy, 28% presented with painless manifestation, 21% had cranial nerve involvement, and 15% had single nerve involvement.[6]

Neurolymphoma commonly presents with radiculopathy of involved nerve roots. The involvement of Cauda equina warrants evaluation with cerebrospinal fluid

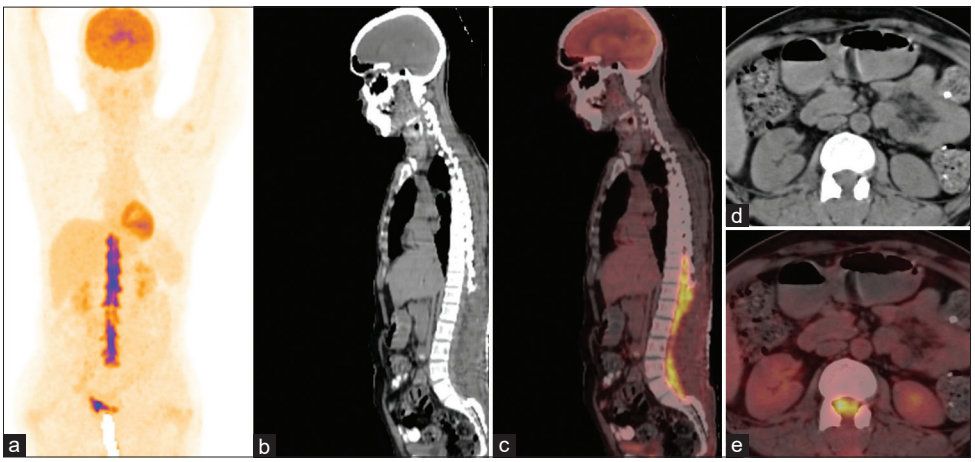

Figure 2: (a) F-18 fluorodeoxyglucose positron emission tomography-computed tomography - maximum intensity projection image, (c) positron emission tomography-computed tomography sagittal, (e) positron emission tomography-computed tomography axial images showing intense fluorodeoxyglucose uptake in the soft tissue density lesion in spinal canal extending from D10 to S2 vertebrae, (b) computed tomography sagittal image, (d) computed tomography axial images showing postlaminectomy changes from L1-L5 vertebrae

analysis, which has diagnostic utility to detect malignant cells in 20%–40% cases. Automated cell sorting and lymphocytic surface receptor gene rearrangement studies (immunoglobulin heavy-chain gene, T-cell receptor *F* subunit gene rearrangement) may increase the diagnostic yield in conjuction with cytopathology.[4] The presence and extent of lymphomatous involvement can be evaluated with the availability of several imaging techniques. MRI of the lymphomatous infiltration of nerve roots shows homogenous enhancement on contrast with diffuse or nodular nerve thickening.[8] Conventional radiography and CT are of lesser use unless bony infiltrations are present.

F-18 FDG PET CT is a useful aid in the diagnosis of neurolymphomatosis and in the identification of possible sites for biopsy. Quantitative analysis of F-18 FDG uptake with SUV max is considered to be a predictor of disease progression.[9] In our case study, F-18 FDG PET CT showed significant F-18 FDG uptake in cauda equina which corresponded to the MRI documented disease site.

In a study by Amin *et al*., sites of physiological F-18 FDG uptake in the spinal cord were documented at cervical, D11, D12, and L1 vertebral regions. The significant uptake at those sites was hypothesized, due to regional increase in transverse area and gray matter content.[10]

Imaging modalities are useful in staging and evaluation of disease extent. MRI findings of thickened nerve roots and postcontrast enhancement are not considered specific of neurolymphomatosis, as similar findings maybe seen in neurofibromatosis, malignant tumors of the peripheral nerve sheath. F-18 FDG PET/CT findings are considered highly sensitive and more specific for neurolymphomatosis.[8] However, abnormal spinal cord and cauda equina uptakes were also documented in intramedullary ependymoma, astrocytoma, leptomeningeal metastases.[11,12]

Ban *et al*., presented a case of secondary cauda equina lymphoma at the level of L3. F-18 FDG PET/CT showed high intrathecal uptake in the nodules at the level of L3 corresponding to the site of marked enhancement on MRI. However, MRI was able to identify more number of nodules (7 nodules) specifically in T2-weighted sequence compared to F-18 FDG PET CT (2 nodules). Patient underwent tumor resection followed by systemic chemotherapy.[13] F-18 FDG PET CT and MRI played complementary roles, while PET CT helped in exclusion of systemic involvement, with high-resolution MRI images, all the abnormal lesions were identified and surgically resected.

Hong CM *et al*., (2011) described a case of 74-year-old man on complete remission from diffuse large B-cell lymphoma, on follow-up F-18 FDG PET/CT revealed multiple linear hypermetabolic lesions in brachial plexus, left trigeminal, axillary, and bilateral sciatic nerves with varying SUV max correlating with clinical severity whereas MRI revealed diffuse thickening with enhancement in left brachial plexus and sciatic nerves with negative findings in other F-18 FDG avid sites. The patient could not survive despite the initiation of high-dose methotrexate treatment. F-18 FDG PET CT is able to detect additional F-18 FDG uptake in sites with early-stage neurolymphomatosis as in this case.[14]

Davidson T *et al*., (2018) presented a retrospective study of F-18 FDG PET/CT in 19 cases of neurolymphomatosis of various sites. Sixty-three percent of patients had multiple site involvement while remaining 37% of patients had single site involvement. Majority of the patients had advanced disease at the time of presentation (Stage III/IV). 77% of cases were confirmed on MRI, 84% on F-18 FDG PET CT, showing diagnostic ability of F-18 FDG PET CT to detect metabolic changes before structural changes. Median progression-free survival was 1.77 years. The study showed that correct diagnosis and early aggressive treatment could lengthen the patient's survival with longest survivor lived for 7.8 years.[15]

Nakashima *et al*., documented a case of 59-year-old immunocompetent man who presented with severe low backache and bilateral leg pain. F-18 FDG PET/CT revealed FDG accumulation involving spinal intradural area (T12 to S1) corresponding to the enhancing intradural space-occupying lesion on MRI. Surgical open biopsy from cauda equina revealed diffuse lymphomatous infiltration which is positive for CD 20. The patient's condition improved clinically after radiotherapy to LS region and methotrexate.[16]

The treatment of neurolymphomatosis is done in similar line as PCNSL, like systemic chemotherapy or combined systemic and intrathecal chemotherapy. Surgical decompression and nodule resection were also performed in few cases. Median overall survival from initial diagnosis based on the sparse case reports is 10 months. This poor outcome despite various polychemotherapy regimens could be due to blood-nerve barrier which prevents large molecule entry while better outcome seen with methotrexate-based treatment due to better barrier penetration.[8] Various retrospective studies and systematic reviews showed postchemotherapy response rate exceeding 50%. Patient with primary neurolymphomatosis found to have good prognosis than patients with secondary neurolymphomatosis who manifested nerve involvement on posttreatment relapse.[4]

Conclusion

Diagnosis of primary lymphoma of cauda equina is clinically challenging. Imaging modalities such as MRI and F-18 FDG PET CT helps in this regard, with histopathological evaluation being gold standard.

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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Conflicts of interest

There are no conflicts of interest.

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