

Secondary neurolymphomatosis of spinal nerve roots detected by ^{18}F -FDG PET/CT: a case report and differential diagnosis of the case

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Abstract

Objective: Neurolymphomatosis (NL) is a rare neurological manifestation of lymphoma. Clinical symptoms of NL differ greatly according to the sites involved and diagnosis with conventional imaging techniques may sometimes be difficult. We herein describe the case of a 58 years old man presenting as radiculopathy with a history of non-Hodgkin's lymphoma (NHL). Computed tomography was unrevealing and magnetic resonance imaging was contraindicated. Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG PET/CT) was performed and revealed multiple hypermetabolic lesions along the nerve roots, which corresponded to the patient's neurological symptoms. A differential diagnosis of patients with lymphomatous involvement of spinal nerve roots has been presented. **Conclusion:** Our case suggests that ^{18}F -FDG PET/CT successfully detected the infiltration of spinal nerve roots of NL due to lymphoma.

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Introduction

Neurolymphomatosis (NL) is a rare neurological manifestation of lymphoma defined as an infiltration of cranial or peripheral nerves, nerve roots or nervous plexuses by malignant lymphocytes. It is documented that NL accounts only for 0.2% of non-Hodgkin's lymphoma (NHL) [1]. The presenting symptoms of NL are diverse according to the sites involved and NL is occasionally difficult to diagnose using conventional imaging modalities [1].

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG PET/CT) is being increasingly used for the diagnosis, staging and assessment of the response to treatment in lymphoma, and it appears to be a highly sensitive tool. Here we describe a case of secondary NL of NHL presenting as radiculopathy that was successfully diagnosed by ^{18}F -FDG PET/CT.

Case Report

A 58 years old man was diagnosed with stage IV NHL 14 months before, with a liver mass identified as diffuse large B-cell lymphoma following hepatoma resection (Figure 1). The immunohistochemical staining of tumor tissues showed CD45 (+), CD20 (+), CD3 (-), CD5 (-), CD10 (-), bcl6 (+), mum1 (-), CD30 (-), MPO (-), PCK (-), CK7 (-), CK8 (-), Hepa (-), CgA (-), PLAP (-), S-10 (-), EBER1/2 (-).

Contrast enhanced computed tomography (CT) showed metastases in the cervical lymph nodes and the sternum. The patient completed six cycles of R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) followed by thoracic radiotherapy, which led to partial response. Radiotherapy was then performed due to brain metastases.

The patient was referred to our hospital, this time with progressive left upper limb pain and anterior thigh numbness which extended to the lower leg. This condition had been present for over 1 month before his admission. He reported that his pain in the left upper limb which scored as 7 to 8 on a numeric pain scale of 10, became worse in the morning and at night, not subsiding by relieving factors. The numbness was more in the left lower limb, especially the ankle, and his walking was impeded. In addition, the

the patient also experienced a weight loss of 5kg during the course of the disease. His overall health was good. Neurological examination showed normal muscles tone, strength, movements and coordination, but sensory deficit was found in the left lower limb. His vital signs including body temperature, blood pressure, pulse and breathing rate were within normal limits. General clinical examination was unremarkable.

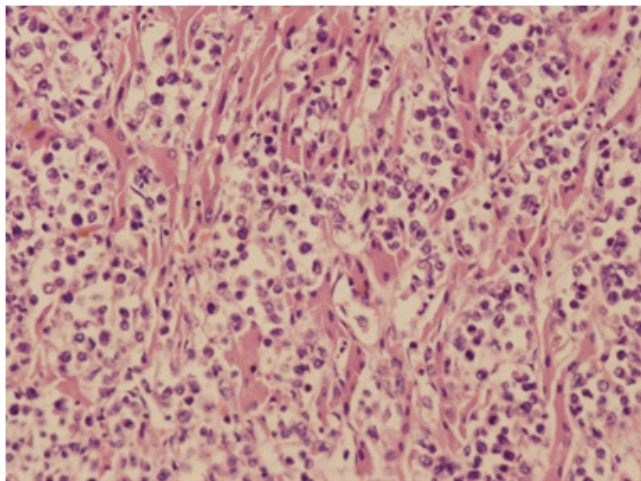


Figure 1. Hematoxylin and eosin staining ($\times 200$) of a liver lesion showed infiltrates of sheets of large lymphoid cells with prominent nucleoli.

Blood routine examination was normal apart from a decrease of lymphocytes ($0.51 \times 10^9/L$, 9.9%). Serum biochemistry and renal tests were normal. Magnetic resonance imaging (MRI) was contraindicated due to the presence of an incompatible coronary stent.

Contrast enhanced CT scanning of the neck, thorax and upper abdomen performed 1 month after the onset of the symptoms showed no regrowth or no new lesions of lymphoma. Enhanced CT scan of the head showed that the lesion in the left temporoccipital lobe was smaller. Whole body ^{18}F -FDG PET/CT was accordingly performed which showed focal ^{18}F -FDG uptake in the region of the left spinal nerve roots of T1 and T9 and the right spinal nerve roots of L2, L3 and L5, without osseous deformities (Figure 2).

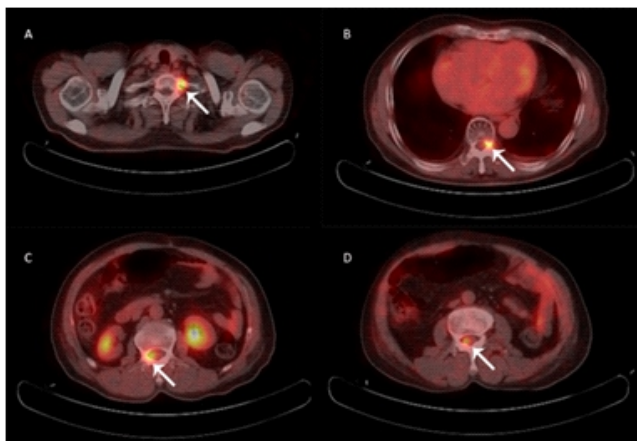


Figure 2. The ^{18}F -FDG PET/CT images showed increased ^{18}F -FDG uptake in (A) the left spinal T1 nerve roots, (B) the left spinal T9 nerve roots, (C) the right spinal L2/L3 nerve roots and (D) the right spinal L5 nerve roots (white arrows).

Chemotherapy (GDP+MTX scheme: gemcitabine, cisplatin, dexamethasone and methotrexate) was then administered. The patient experienced obvious relief of pain after the first cycle of treatment. No further evidence of disease has been noted during 5 months of follow-up.

Discussion

Extranodal presentation of lymphoma is documented in 15%-30% of all lymphoma cases [2]. Neurolymphomatosis is an uncommon entity with lymphocytic infiltration of peripheral and cranial nerves, nerve roots or nervous plexuses. It presents either as a primary disease or as a progression or relapse of the previously treated disease [1]. Most cases of NL are developed in patients with NHL (90%) [3]. However, the prevalence of NL only accounts for 0.2% of NHL [1]. Clinical symptoms of NL differ greatly according to the sites involved. Therefore, the diagnosis is often delayed. In brief, there are four clinical patterns of NL: painful polyneuropathy or polyradiculopathy, cranial neuropathy, painless polyneuropathy and peripheral mononeuropathy [1]. In clinical differential diagnosis when a patient with a history of hematologic malignancy complains of symptoms, as above, NL should be kept in mind. In the present case, the patient with a history of NHL experienced pain in the left upper limb and numbness in the leg. No systemic symptoms were identified except weight loss. Further examinations assessed the involvement of the nervous system and confirmed the diagnosis.

The diagnosis of NL is often very difficult and depends on histopathology.

The infiltration of malignant lymphocytes distinguishes NL from infectious diseases, paraneoplastic or inflammatory neuropathies, and/or complications of medical interventions [4]. Although biopsy remains the diagnostic gold standard, it is difficult to perform nerve or nerve root biopsy of the relevant parts, because it is possible to cause permanent nerve damage and false negative results [5]. More limited is the role of cerebrospinal fluid cytology, with reported sensitivity of 21% [1]. Alternatively, radiological evaluations are of great value.

Contrast-enhanced CT is commonly used in the evaluation and follow-up of lymphoma patients. Nevertheless, it has limited sensitivity in the field of lymphomatous involvement of extranodal tissues [6]. In the diagnosis of NL MRI plays an important role. The high tissue contrast and multiplanar capability of MRI make it easy to identify masses involving nerves. Nerve or root enlargement are typical findings on the MRI scan [7-9] but can also be found in other diseases, such as inflammatory radiculopathy, neuro-fibromatosis and peripheral nerve sheath malignancy [10]. Currently, ^{18}F -FDG PET/CT is mainly used for staging and response assessment of systemic lymphomas. The fusion of PET and CT images has the advantage of providing more precise locations and details of lesions even if they are located in less commonly involved areas. A recent study has indicated that ^{18}F -FDG PET/CT is helpful in the diagnosis of malignant

involvement of the peripheral nerves, particularly when findings from MRI or CT are negative [11]. However, ^{18}F -FDG PET/CT has well-known diagnostic limitations similar to MRI. In addition, ^{18}F -FDG uptake may also be observed in sites where the rate of glycolysis increases, such as infection and neoplastic diseases.

Reviewing the English medical literature since 1990, MRI was performed in 14 out of 16 studies with lymphomatous infiltration of spinal nerve roots, whereas in only 5 studies ^{18}F -FDG PET/CT was used [12-27]. Although MRI has been the most commonly used modality in the diagnosis of lymphomatous infiltration of nerves, it failed to identify the infiltrating lesions in 4 of the 14 cases. On the contrary, ^{18}F -FDG PET/CT successfully detected the infiltration in all five cases in which was used.

Unfortunately in the present case, MRI was contraindicated. Contrast enhanced CT of the neck, thorax, upper abdomen and head performed on our patient was unrevealing, while ^{18}F -FDG PET/CT revealed the metastatic lesions in the related nerve roots. Symptoms were markedly relieved following chemotherapy and brain irradiation.

In conclusion, we reported a rare case of a large B lymphoma of the liver with secondary spinal nerve roots involvement. The diagnosis of NL should be kept in mind, especially in case of lymphoma patients suffering from neurological symptoms. Although the diagnosis of NL requires the integration of all clinical information, our case highlights the utility of ^{18}F -FDG PET/CT for early diagnosis when suspicion is high and contrast-enhanced CT unrevealing.

The authors declare that they have no conflicts of interest.

Bibliography

- Baehring JM, Damek D, Martin EC et al. Neurolymphomatosis. *Neuro Oncol* 2003; 5: 104-15.
- Boddie AW Jr, Mullins JD, West G, Bouda D. Extranodal lymphoma: surgical and other therapeutic alternatives. *Curr Probl Cancer* 1982; 6: 1-64.
- Grisariu S, Avni B, Batchelor TT et al. Neurolymphomatosis: an International Primary CNS Lymphoma Collaborative Group report. *Blood* 2010; 115: 5005-11.
- Ceyssens S, Van den Wyngaert T, Blockx P et al. Lymphomatous meningitis diagnosed with [^{18}F]-fluorodeoxyglucose-positron-emission tomography/CT. *Am J Neuroradiol* 2009; 30: E150-1.
- van den Bent MJ, de Bruin HG, Bos GM et al. Negative sural nerve biopsy in neurolymphomatosis. *J Neurol* 1999; 246: 1159-63.
- Paes FM, Kalkanis DG, Sideras PA, Serafini AN. FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease. *Radiographics* 2010; 30: 269-91.
- Swarnkar A, Fukui MB, Fink DJ, Rao GR. MR imaging of brachial plexopathy in neurolymphomatosis. *Am J Roentgenol* 1997; 169: 1189-90.
- Moore KR, Blumenthal DT, Smith AG, Ward JH. Neurolymphomatosis of the lumbar plexus: high-resolution MR neurography findings. *Neurology* 2001; 57: 740-2.
- Hong CM, Lee SW, Lee HJ et al. Neurolymphomatosis on F-18 FDG PET/CT and MRI Findings: A Case Report. *Nucl Med Mol Imaging* 2011; 45: 76-8.
- Choi YJ, Shin JA, Kim YH et al. Neurolymphomatosis of Brachial Plexus in Patients with Non-Hodgkin's Lymphoma. *Case Rep Oncol Med* 2013; 2013: 492329.
- Bronstein Y, Tummala S, Rohren E. F-18 FDG PET/CT for detection of malignant involvement of peripheral nerves: case series and literature review. *Clin Nucl Med* 2011; 36: 96-100.
- Viswanathan R, Swamy NK, Vago J, Dunsker SB. Lymphoma of the lumbar nerve root: case report. *Neurosurgery* 1997; 41: 479-81; Discussion 481-2.
- Dong Q, Wong KK, Avram AM. Sacral nerve root neurolymphomatosis diagnosed on FDG-PET/CT and magnetic resonance imaging. *Clin Nucl Med* 2008; 33: 30-1.
- Perez-Martinez DA, Saiz-Diaz RA, de Toledo M et al. Cervical radiculopathy as a form of presentation of non-Hodgkin's lymphoma. *Rev Neurol* 1998; 27: 91-3.
- Reggars JW, French SD. A Case Of Leptomenigeal Disease Presenting As A Lumbar Nerve Root Radiculopathy: A Case Report. *Australas Chiropr* 1998; 7: 112-5.
- Al-Khayat H, Al-Khayat H, Al-Baker O et al. Cervical radiculopathy secondary to Hodgkin's lymphoma. *Surg Neurol* 2007; 67: 540-3.
- Guo H, Mosci C, Iagaru A. Demonstration of peripheral nerve root involvement by non-Hodgkin's lymphoma on ^{18}F -FDG PET/CT. *Eur J Nucl Med Mol Imaging* 2012; 39: 729-30.
- Suga K, Yasuhiko K, Matsunaga N et al. F-18 FDG PET/CT findings of a case of sacral nerve root neurolymphomatosis that occurred during chemotherapy. *Clin Nucl Med* 2011; 36: 73-6.
- Gialanella B, Prometti P, Ferlucchi C. Low back pain radiating to the leg: an atypical cause. *Clin Ther* 2013; 164: 417-20.
- Valencia J, Ayerbe J, Nieto J et al. Malignant non-Hodgkin lymphoma presenting as a nerve root tumour. *Acta Neurochir (Wien)* 1999; 141: 1355-7.
- Kajary K, Molnar Z, Miko I et al. Neurolymphomatosis as a late relapse of non-Hodgkin's lymphoma detected by ^{18}F -FDG PET/CT: a case report. *Rev Esp Med Nucl Imagen Mol* 2014; 33: 39-42.
- Tsai MC. Non-Hodgkin's B-cell lymphoma of a lumbar nerve root: a rare cause of lumbar radiculopathy. *J Clin Neurosci* 2013; 20: 1029-31.
- Herrlinger U, Weller M, Kuker W. Primary CNS lymphoma in the spinal cord: clinical manifestations may precede MRI detectability. *Neuroradiology* 2002; 44: 239-44.
- Galetta SL, Sergott RC, Wells GB et al. Spontaneous remission of a third-nerve palsy in meningeal lymphoma. *Ann Neurol* 1992; 32: 100-2.
- Baumgarten E, Fengler R, Brockmeier K et al. Syndrome of the posterior and anterior root in a late isolated CNS relapse of c-ALL. Case report. *Neurosurg Rev* 1990; 13: 73-5.
- Wachter D, Tschischka S, Huegens-Penzel M et al. T-cell lymphoma mimicking Schwannoma of a cervical nerve root. *Neurosurg Rev* 2009; 32: 117-21; discussion 121.
- Zhou WL, Wu HB, Weng CS et al. Usefulness of ^{18}F -FDG PET/CT in the detection of neurolymphomatosis. *Nucl Med Commun* 2014; 35: 1107-11.