Clinical note

Neurolymphomatosis as a late relapse of non-Hodgkin's lymphoma detected by 18F-FDG PET/CT: A case report

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A B S T R A C T

Neurolymphomatosis is a rare condition defined as an infiltration of nerves, nerve roots or nervous plexuses by haematomatological malignancy. Its diagnosis may sometimes be difficult with conventional imaging techniques. This paper aims to emphasize the importance of this entity and the role of 18F-FDG PET/CT in this indication. We present the case of a 53-year-old male who complained of sharp pain in his right hip and right leg paresthesia after 2 years of complete remission from Non-Hodgkin’s lymphoma. Physical examination and CT scan were negative and the lumbar MRI showed protrusion of L5-S1 disc. Physiotherapy, nonsteroid antiinflammatory drugs and steroids were inefficient. PET/CT was performed four months after the onset of the symptoms, revealing focal FDG uptake in the right S1 nerve root and linear FDG uptake along the right sacral plexus suggesting relapse. This was confirmed by histology.

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Neurolymphomatosis como recaída de un linfoma no Hodgkin detectada con 18F-FDG PET/TAC: a propósito de un caso

R E S U M E N

La neurolymphomatosis es una entidad rara definida por la infiltración de los nervios, raíces o plexos nerviosos por un proceso hematológico maligno, siendo en ocasiones difícil de diagnosticar mediante técnicas de imagen convencionales. La finalidad del caso es llamar la atención sobre su importancia y el papel de la 18F-FDG PET/TAC. Presentamos el caso de un varón de 53 años con dolor en la región de la cadera derecha y parestesias en la pierna derecha tras 2 años de remisión completa de un linfoma no Hodgkin. El examen físico y la TAC fueron negativos, mostrando la RM lumbar una protrusión discal en L5-S1. El tratamiento con fisioterapia y con antiinflamatorios no esteroideos y esteroideos fue ineficaz. La PET/TAC realizada a los 4 meses reveló una captación focal de FDG en la raíz del nervio S1 derecho y una captación lineal a lo largo del plexo sacro derecho sugestivo de recaída del linfoma, lo que fue confirmado por la histología.

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I n t r o d u c t i o n

Neurolymphomatosis (NL) is a rare entity which is defined as an infiltration of cranial or peripheral nerves, nerve roots or nervous plexuses by haematological malignancy and it is occasionally difficult to diagnose using conventional imaging modalities. 18F-fluoro-deoxy-glucose positron emission tomography alone and mainly combined with computed tomography (18F-FDG PET/CT) is increasingly being applied for the diagnosis, staging and assessing of the response to treatment in lymphoma. Recently, Ansell and Armitage published a review about the role of PET in lymphoma management based on a literature search of PubMed from 1999 to 2011. They found that 18F-FDG PET is definitely recommended for initial staging and restaging on completion of therapy in Hodgkin lymphoma (HL), diffuse large B-cell lymphoma (DLBCL), and follicular lymphoma (FL). It is probably indicated for initial staging and restaging on completion of therapy in peripheral T-cell lymphoma (PTLC) and mantle cell lymphoma (MCL). It is also suitable for interim response assessment in patients with HL and DLBCL and for detection of potential sites of transformation from indolent to aggressive lymphomas.1 Up to the present only few papers, mainly case reports, have been published in the literature demonstrating the utility of 18F-FDG PET and PET/CT in NL.2–5 A review was also published by the International Primary CNS Lymphoma Collaborative Group in 2010. They retrospectively analyzed 50 patients with the diagnosis of NL assembled over a 16-year period. NL was related to Non-Hodgkin’s lymphoma (NHL) in 90% and to acute leukaemia in 10% and it was the initial manifestation of malignancy in 26% of the cases. Peripheral nerves were the most involved site, whereas spinal nerve roots, cranial nerves and neural plexus infiltration occurred at a similar rate. Magnetic resonance imaging (MRI) and PET/CT yielded abnormal findings and facilitated
the diagnosis of NL in 77% and 84%, respectively. Cerebrospinal fluid cytology was positive in 40%, and nerve biopsy confirmed the diagnosis in 88%.2 In 2012, Salm et al. analyzed the importance of 18F-FDG PET/(CT) in the diagnosis of NL. In 36 patients 18F-FDG PET with or without CT was used as the diagnostic modality. In 91% of the patients PET showed uptake in various structures in the central or peripheral nervous system suggesting involvement by lymphoma. Brachial and lumbar plexuses, the course of peripheral nerves in the extremities and the trigeminal nerve root were primarily affected in these patients. MRI, cerebrospinal fluid test or bone marrow analysis were frequently negative.3 Since the NL is a rare entity, physicians often do not think about the opportunity of it being behind the complaints of the patient, therefore it remains often undiagnosed until becoming obvious. We would like to draw attention to the importance of this entity and role of PET/CT in this indication.

**Clinical case**

A 53-year-old male complaining about sharp pain in his right hip region and numbness in his right leg was examined by his treating physician. His right testis was removed 3 years earlier because of irritability and enlargement. Histological diagnosis confirmed NHL that was identified as diffuse large B cell phenotype. The first 18F-FDG PET/CT scan, which was performed after the removal of the testis, showed numerous lymph nodes with high FDG uptake on both sides of the diaphragm with the highest maximum standardized uptake value (SUVmax) of 32.2 observed in the head and neck region on the right side (Fig. 1). The second PET/CT scan was performed after 4 cycles and the third after 6 cycles rituximab, methotrexate, doxorubicin, bleomycin, cyclophosphamide, dexamethasone and vincristine (R-M-BACOD) treatment and they were both negative for lymphoma. First line treatment led to complete remission and in the following 24 months the patient did not have any clinical symptoms. However, 29 months after the initial diagnosis the above mentioned hip region pain and right leg paraesthesia were developed. Orthopaedic physical examination and CT did not provide a clue, lumbar MRI showed slight protrusion of L5–S1 disc. Physiotherapy and nonsteroid anti-inflammatory drugs and steroids were inefficient, the intensity of pain increased over time and walking difficulty appeared. The fourth whole body 18F-FDG PET/CT was performed 4 months after the onset of the symptoms. The patient fasted for 4 h because of diabetes prior to scanning and his fasting glucemia level was 6.4 mmol/l. A standard dose of FDG 3.7 MBq/kg (0.1 mCi/kg) was injected intravenously 70 min prior to scanning. The emission data were acquired with a TruePoint HD PET/CT scanner (Siemens, Knoxville, TN). 18F-FDG PET/CT revealed focal FDG uptake in the region of the right S1 nerve root and linear FDG uptake along the right sacral plexus with SUVmax of 11.6 and 5.2, respectively (Fig. 2a–d). It raised the suspicion of NL. The bone marrow was depicted with increased, diffuse FDG uptake without any focal character. Functional muscle activity and diffuse bowel activity were also noted. The second MRI which was recommended because of the suspicion of NL, showed thickening of right S1 nerve root and enlargement of the sacral plexus with inhomogeneous contrast enhancement. The symptoms were markedly relieved following the surgical removal of tumorous mass of S1 nerve root (Fig. 3a–d). The histological examination of the removed specimen confirmed the relapse of DLBCL. Bone marrow infiltration was excluded by biopsy that was performed because of its diffuse FDG uptake. There was not any pathological FDG uptake on the subsequent PET/CT scans performed after four cycles of rituximab, dexamethasone, cytarabine and cisplatin (R-DHAP) chemotherapy and after autologous bone marrow transplantation (ASCT) (Fig. 4). The patient is currently in complete remission for 13 months. Informed consent was obtained from the patient prior to all scans.

**Discussion**

NL is an uncommon entity that is defined as an infiltration of cranial or peripheral nerves, nerve roots or nervous plexuses in malignant haematologic diseases. Due to its nature, diagnosis is often delayed and its incidence remains unknown. Clinical signs of NL usually mimic non-neoplastic and paraneoplastic neuropathies. MRI may reveal nerve or nerve root enlargement with or without contrast enhancement and often the involvement of neural plexuses. However, these findings are not specific for NL and may also occur in acute or chronic inflammatory radiculoneuropathies or pseudotumor, in neurofibromatosis and in malignant tumours of the peripheral nerve sheath.2 18F-FDG PET/CT can support the diagnosis of NL showing elevated uptake in affected nervous structures and it may help the proper disease management by defining a target for biopsy and evaluating the response to therapy.2 However, similarly to MRI, 18F-FDG PET/CT also has certain well-known diagnostic limitations.9 According to a paper of Xu et al., the diagnosis of NL requires the integration of all the clinical information completed with 18F-FDG PET/CT.7

In our case the whole body 18F-FDG PET/CT suggested NL that was supported by the result of the subsequent MRI performed on the basis of the PET/CT findings. The medical team decided on the surgical removal of the tumorous mass of S1 nerve root followed by second-line chemotherapy and ASCT which have led to complete remission. Based on the literature data, therapy of
Fig. 2. Transaxial sections of the fourth $^{18}$F-FDG PET/CT examination demonstrating (red arrows) focal FDG uptake in the region of the right S1 nerve root (a) and linear FDG uptake along the right sacral plexus (b, c), both suspicious for relapse of DLBCL. The whole-body coronal section image is demonstrating the same (d).

NL usually consists of chemotherapy alone or chemotherapy with radiotherapy, but currently there is no known standard treatment for it. In our case surgery was performed for histological confirmation of the NL and the patient underwent ASCT later, because the clinicians, who had limited experience in NL tended to excess the therapy. Several studies have demonstrated the prognostic value of $^{18}$F-FDG PET/CT at midtreatment and after completion of chemotherapy in lymphoma. Some papers illustrated the

Fig. 3. Coronal T1-weighted (A), coronal (B) and axial fat-suppression (C) contrast–enhanced T1-weighted and axial T2-weighted images of MR examination (3 T). Red arrows show the thickening of right S1 nerve root (a) with pathological contrast enhancement (b, c), which has heterogeneous signal intensity on the T2-weighted image (d). Blue arrows show the normal left S1 nerve root which has contrast enhancement in the level of ganglion (c), but not elsewhere (b).
utility of $^{18}$F-FDG PET/CT in the assessment of response to therapy in NL. Based on the literature data the importance of $^{18}$F-FDG PET/CT in NL probably will increase in the future. Our opinion is that $^{18}$F-FDG PET/CT should be performed to evaluate the possibility of NL in lymphoma patients suffering from neurological symptoms.

Conflicts of interest

The authors have no conflicts of interest to declare.

References


Fig. 4. Maximum intensity projection (MIP) presentation of the last $^{18}$F-FDG PET/CT examination after ASCT demonstrating complete remission of DLBCL. Functional laryngeal uptake is noticeable.