Neurolymphomatosis: role of positron emission tomography in diagnosis

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Dear Editor,

A 49-year-old woman presented with stage IA diffuse large B cell lymphoma (DLBCL) of the uterine cervix. She received four courses of R-CHOP (rituximab, cyclophosphamide, adriamycin, vincristine, and prednisolone) and two cycles of R-ICE (rituximab, ifosfamide, carboplatin, and etoposide), followed by local tomotherapy. A complete remission was achieved, as shown by 18F-fluorodeoxyglucose positron emission tomography–computed tomography (PET/CT).

However, she developed gradually numbness over her right thoracic 10 dermatome. A magnetic resonance imaging (MRI) scan performed 4 months later showed abnormal signal intensity in the anterior and posterior wall of the lower thoracic cord, at the origin of cauda equina and at the anterior and posterior nerve roots of right thoracic

10 and thoracic 11 roots, suggestive of leptomeningeal deposits. Lumbar puncture showed normal cerebrospinal fluid, and although a dose of intrathecal methotrexate and cytarabine was given there was no symptomatic improvement.

On referred 6 months after the onset of neurologic symptoms, another MRI focusing on the thoracic spine showed abnormal signal intensity in the anterior and posterior wall of the lower thoracic cord at the origin of cauda equina and at the anterior and posterior right thoracic 10 and thoracic 11 nerve roots (Fig. 1a, arrow). To resolve the nature of the lesion, a PET/CT scan was performed. It showed a hypermetabolic soft tissue nodule (standardized uptake value maximum, 4.2) extending across the right thoracic 10/11 neural foramen (Fig. 1b, arrow), suggesting a lymphomatous lesion.

The surgical resection specimen showed the presence of atypical lymphoid cells among the neuroganglion tissue, which were CD20+, CD3–, and BCL-2+ (Fig. 2a–d). The overall features were consistent with DLBCL relapsing as neurolymphomatosis.

Neurolymphomatosis refers to direct lymphomatous infiltration of the cranial and peripheral nerve and roots [1–3]. It is a very rare condition, with a recent study identifying merely 50 patients from 12 centers in 5 countries over a 16-year period [3]. Four different clinical presentations have been described: painful infiltration of nerves or roots; cranial neuropathy with or without pain; painless involvement of peripheral nerves; and painful or painless involvement of a single peripheral nerve [1]. Aggressive B cell lymphoma is the predominant underlying pathology [1–3]. Owing to the nonspecific presentation, the diagnosis is often delayed. Furthermore, biopsies are not feasible when deep-seated roots or cranial nerves are involved. Hence, when neurologic

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Fig. 1 Imaging studies in neurolymphomatosis. **a** MRI scan showing a lesion (*arrow*) at the anterior and posterior right thoracic 10 and thoracic 11 nerve roots. **b** Positron emission tomography/computed tomography, showing an isolated hypermetabolic lesion in the right thoracic tenth foramen (*arrow*)

Fig. 2 Histopathology of neurolymphomatosis. **a** Surgical specimen showing neuroganglion tissue diffusely infiltrated by abnormal lymphoid cells (hematoxylin–eosin). **b** Lymphoid cells were positive for CD20 (immunoperoxidase stain). **c** Lymphoid cells were negative for CD3. **d** Lymphoid cells were positive for BCL-2

symptoms are the initial manifestation, the diagnosis of neurolymphomatosis may not be made until at post-mortem [1–3]. In a patient with a history of lymphoma, the diagnostic challenge is to distinguish neurolymphomatosis from other pathologies not due to direct nerve invasion, including leptomeningeal lymphoma, nerve compression from adjacent lymphoma masses, neuropathy related to chemotherapy and radiotherapy, lymphoma-associated vasculitis, and paraneoplastic syndromes [2]. Imaging studies are therefore very helpful in these differential diagnoses. Earlier studies have relied on MRI, which might not be able to distinguish between lymphomatous or a primary nervous tissue lesion. As shown in the present study, PET/CT allows the lesion to be accurately localized and gives an indication of the metabolic activity of the lesion [4], which provides useful information on the differential diagnosis of the nature of the pathology.

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