

MRI and PET-CT in the diagnosis and follow-up of a lymphoma case with multifocal peripheral nerve involvement

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ABSTRACT

Lymphoma of the peripheral nerve, particularly of the T-cell variety, is an extremely rare subtype of extra nodal lymphoma that has a variable response to current therapeutic regimens. Here, we present a patient with natural killer (NK)/T-cell lymphoma in remission who presented with a two-month history of right forearm swelling and paresthesia in the ulnar nerve distribution. Magnetic resonance imaging (MRI) showed an ulnar nerve mass identified as a nerve sheath tumor. Frozen section and postresection biopsies showed an Epstein-Barr virus-positive NK/T-cell lymphoma, nasal type. Consequently, the patient received chemotherapy following resection. Four months later, the patient developed a proximal leg mass, which was diagnosed as tibial nerve lymphoma. The patient was then treated with chemotherapy and follow-up was done by positron emission tomography-computed tomography (PET-CT). In conclusion, lymphoma should be considered in the differential diagnosis of a peripheral nerve mass. MRI is a useful imaging tool together with PET-CT, which plays a beneficial role in the follow-up of these patients on therapy as well as diagnosis of new lesions.

Peripheral nerve lymphomas—both primary as well as those with known systemic involvement—are extremely rare (1, 2). The literature regarding peripheral nerve lymphoma is deficient, with most consisting of case reports (1, 3, 4). Peripheral nerve lymphoma can present as diffuse or nodular nerve thickening, or as a mass, with this latter variety of involvement being very rare. Here, we report a patient with right ulnar nerve involvement of extranodal nasal-type natural killer (NK)/T-cell lymphoma. The role of magnetic resonance imaging (MRI) and positron emission tomography-computed tomography (PET-CT) in the diagnosis and follow-up is discussed.

Case report

A 57-year-old woman with a 13-month history of NK/T-cell lymphoma was treated with SMILE (dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide) therapy and was in remission. In April 2011, she presented with right ulnar forearm swelling that had persisted for two months and paresthesia over the ulnar 1.5 fingers.

On examination, palpable swelling was noted over the mid-ulnar aspect of the right forearm. Wasting of the medial right forearm and numbness over the ulnar dermatome were observed. The remaining findings of general examination were unremarkable. Nerve conduction study showed right ulnar neuropathy with conduction block and slowing in the right forearm segment.

MRI of the right forearm demonstrated an oval-shaped, longitudinally oriented mass along the course of the ulnar nerve (Fig. 1a–e). The mass was eccentrically located along the nerve, which was shown to enter into the upper part of the mass. The mass was hypointense on T1-weighted images and hyperintense on T2-weighted and short tau inversion recovery (STIR) images. The morphology as well as magnetic resonance (MR) signal characteristics mimicked those of a neurogenic tumor. Post-gadolinium (contrast-enhanced) images showed predominantly peripheral enhancement. Most of the neurogenic tumors showed bright enhancement; predominantly peripheral enhancement was observed in cystic neurogenic tumors. The eccentric location of the mass and MR signal characteristics prompted an imaging diagnosis of cystic schwannoma (nerve sheath tumor).

Due to the progressive neurological deficit, the patient underwent surgery to remove the mass. Intraoperatively, the mass was seen to be attached to the nerve, and epineural dissection was performed to free the mass from the nerve.

Microscopic examination of the forearm mass showed sheets of monotonous medium- to large-sized lymphoid cells with markedly irregular nuclear membranes and distinct nucleoli. Some areas had a “starry-sky” appearance with scattered macrophages containing karyorrhectic debris

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(Fig. 1f). Mitotic figures were frequently observed, and large areas of tumor necrosis were present. No obvious angiocentric growth pattern was noted.

Immunohistochemistry and in situ hybridization were also performed. The neoplastic lymphoid cells showed positive staining for CD3, CD56, granzyme B, and EBER in situ hybridization. The cells were negative for CD4, CD8, and CD20. Ki-67 showed a high proliferative index of more than 90%. The phenotype was consistent with a diagnosis of Epstein-Barr virus-positive extranodal NK/T-cell lymphoma, nasal type.

Bone marrow biopsy showed no evidence of tumor. However, in late July 2011, the patient presented with complaints of weakness and numbness in the right foot. She was referred for PET-CT study (Fig. 2a, b), which showed a fluorodeoxyglucose (FDG)-avid lesion in the posterior compartment of the proximal right leg (maximum standardized uptake value [SUV_{max}], 18.4), with suspected lymphomatous

involvement. The mass probably involved the neurovascular bundle. The location of the mass suggested that it likely involved the tibial nerve.

The PET-CT study (Fig. 2a–c) also showed focal FDG-avid areas with adjacent fat stranding in the posterior medial aspect of the right elbow (SUV_{max} , 13.4). This finding was thought to be related to the recent surgical excision of the ulnar nerve lymphoma; however, the possibility of an underlying residual tumor was not excluded. No suspicious FDG-avid nodal or visceral disease was observed elsewhere.

The patient received chemotherapy, and a follow-up PET-CT study (Fig. 3) was performed two months later. The previously observed FDG-avid lesion in the posterior compartment of the proximal right leg (tibial nerve lymphoma) showed marked interval decrease in metabolic activity (current SUV_{max} , 3.8; previous SUV_{max} , 18.5). The PET-CT findings suggested a positive response to chemotherapy. The previously observed focal FDG activ-

ity in the posterior medial aspect of the right elbow also showed a marked decrease (current SUV_{max} , 2.4; previous SUV_{max} , 13.4), suggesting a positive response. No other/new suspicious FDG-avid lesion was noted.

The patient is currently well with no signs or symptoms of disease, i.e., she has achieved complete remission at the time of the writing of this manuscript.

Discussion

Lymphomatous involvement of a peripheral nerve presenting as a solitary fusiform mass is extremely rare (1, 2). Most such cases present as diffuse or solitary thickening of the nerves/nerve roots. They may present as mononeuropathy, plexopathy, or generalized neuropathy. These neuropathies may resemble an asymmetric mononeuropathy multiplex, a generalized disorder such as chronic inflammatory demyelinating polyradiculoneuropathy, or even Guillain-Barré syndrome (5, 6). A literature review indicated a paucity of previous reports regarding peripheral

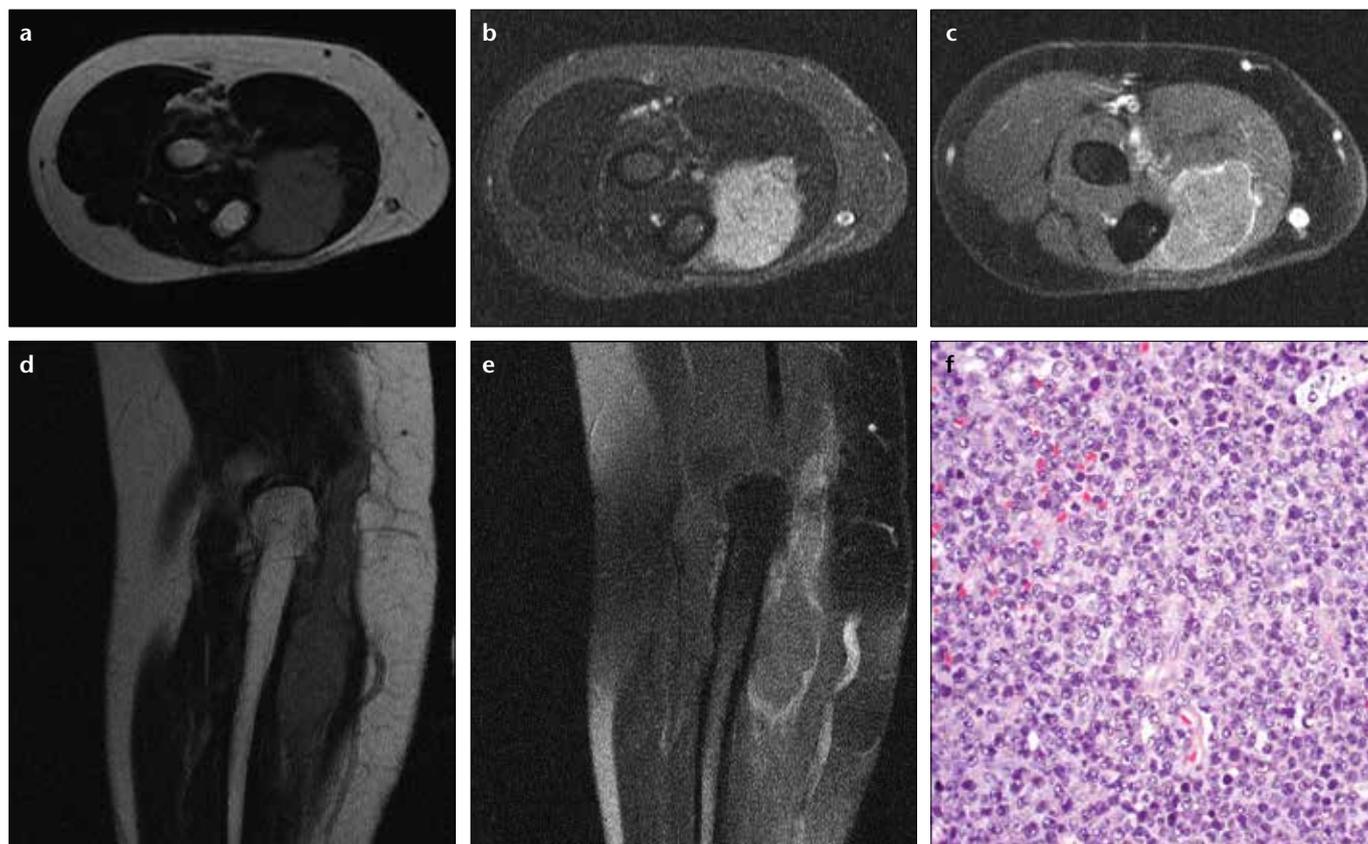


Figure 1. a–f. Axial T2 (a), axial STIR (b), axial postcontrast T1-weighted fat-saturated (c), coronal T2-weighted (d), and coronal postcontrast T1-weighted fat-saturated (e) images demonstrated an elongated oval-shaped mass along the course of the ulnar nerve, located eccentrically to the nerve. The lesion showed predominantly peripheral enhancement on postcontrast images (c, e). High-power view (f) showed sheets of large lymphoid cells with irregular vesicular nuclei and prominent nucleoli (hematoxylin-eosin, $\times 400$).

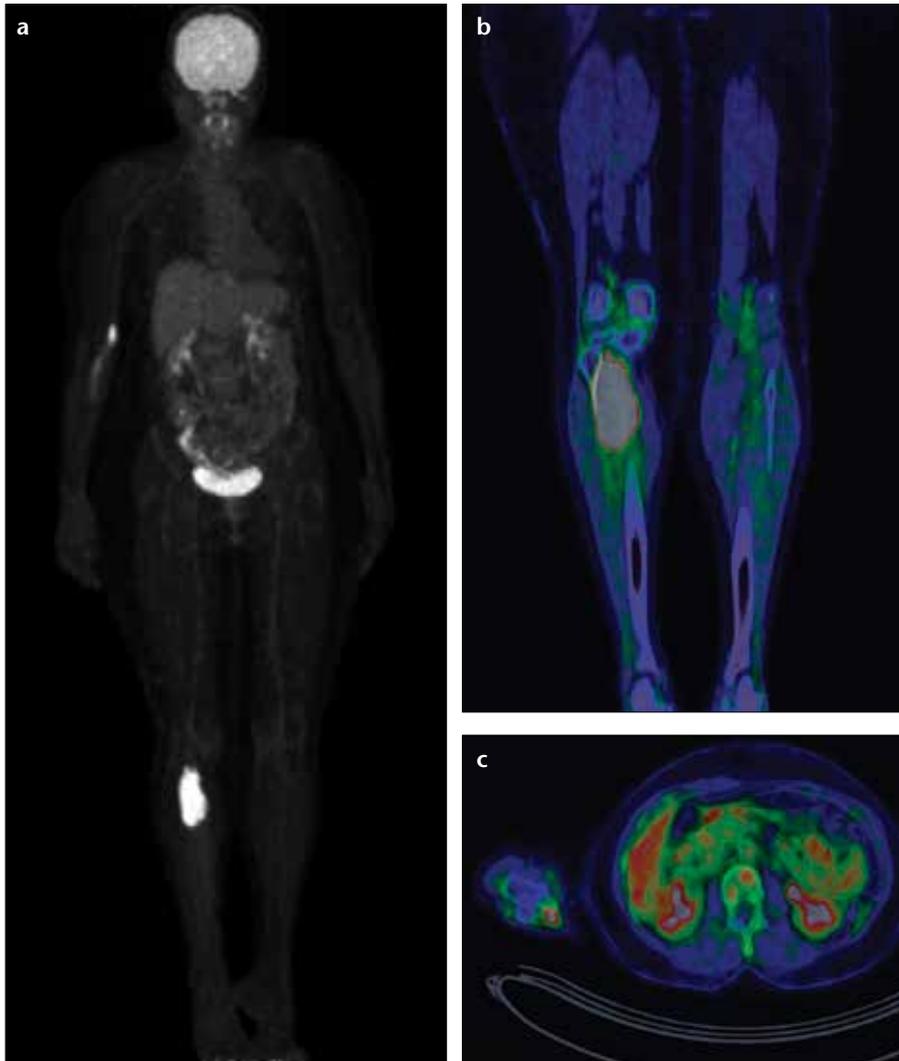


Figure 2. a–c. PET of whole body (a) and coronal PET-CT of lower limb (b) images demonstrated an FDG-avid lesion in the posterior compartment of the proximal right leg (SUV_{max} 18.4), suggestive of lymphomatous involvement. PET of whole body (a) and axial PET-CT (c) images also showed a focal FDG-avid area in the posterior medial aspect of the right elbow (SUV_{max} 13.4), suggestive of either a postoperative change or residual tumor following surgery.

multiplanar capability can accurately identify a mass involving a nerve. Demonstration of the relationship with the mass is important to exclude the possibility of other soft-tissue tumors. Tumor dimensions as well as the extent and relationship of the tumor with surrounding structures are accurately depicted, providing invaluable information to the surgeon in cases where surgery is planned (12). However, despite its high sensitivity and excellent anatomical depiction, MRI lacks specificity. The MRI features of a peripheral nerve lymphoma can be mimicked by those of a neurogenic tumor (1). In our case, the mass was typically eccentric in location, mimicking a nerve sheath tumor. Its T1-weighted, T2-weighted, and STIR signal intensities were also similar to those of a neurogenic tumor. The postcontrast images showed predominantly peripheral enhancement. Most solid neurogenic tumors have bright postcontrast enhancement; however, peripheral enhancement could be observed in a cystic schwannoma. Thus, a peripheral nerve lymphoma should always be considered in the differential diagnosis of peripheral nerve tumor together with the much more common neurogenic tumors. The postresection specimen indicated that the mass was neither cystic nor necrotic; therefore, the discussion also encourages a more detailed study to determine if most peripheral nerve lymphomas or any particular cell type have predominant peripheral enhancement.

PET-CT plays an important role in the follow-up of these patients on therapy (3). This method can determine the response to treatment by a decrease in activity and lesion size. PET-CT can also determine recurrence, and in cases of known systemic lymphomas can diagnose development of new masses. The fusion of PET and CT has the advantage of a higher confidence level of lesion localization; therefore, an FDG-avid lesion may be determined to be arising from a peripheral nerve.

In conclusion, we reported a rare case of an extranodal lymphoma presenting as a peripheral nerve tumor. MRI is helpful in lesion localization and surgical planning. MRI features may mimic a neurogenic tumor; therefore, peripheral nerve lymphoma should be included in the differential diagnosis of a peripheral nerve tumor, particularly

nervous system lymphoma, and there have been very few reported cases of solitary peripheral nerve lymphoma presenting as a fusiform mass (1, 3, 4). Most of the peripheral nerve lymphomas described in the literature have involved the sciatic nerve (4). Only one case of lymphoma involving the ulnar nerve has been reported in the English literature (7). The natural history of these lymphomas is variable. Most of the reported cases of primary peripheral nerve lymphomas have heralded the onset of systemic lymphoma, whereas there have been few cases found in patients with known systemic disease. In either case, it may be a harbinger of a more disseminated disease involving the peripheral and cen-

tral nervous systems (1, 4, 8, 9). The B-cell type of non-Hodgkin lymphoma is the predominant type involving the peripheral nerves, with the NK/T-cell subtype being extremely rare (2, 4, 8). Our case was an NK/T-cell subtype of lymphoma. The response of these lymphomas to treatment is variable (10). Various treatment approaches have been applied, including chemotherapy, radiotherapy, and surgery, alone and in various combinations (11). Prophylactic and therapeutic intrathecal methotrexate therapy is also commonly used because these patients have an increased risk of central nervous system relapse (1, 4, 8, 9).

MRI plays an important role in the diagnosis. The high tissue contrast and

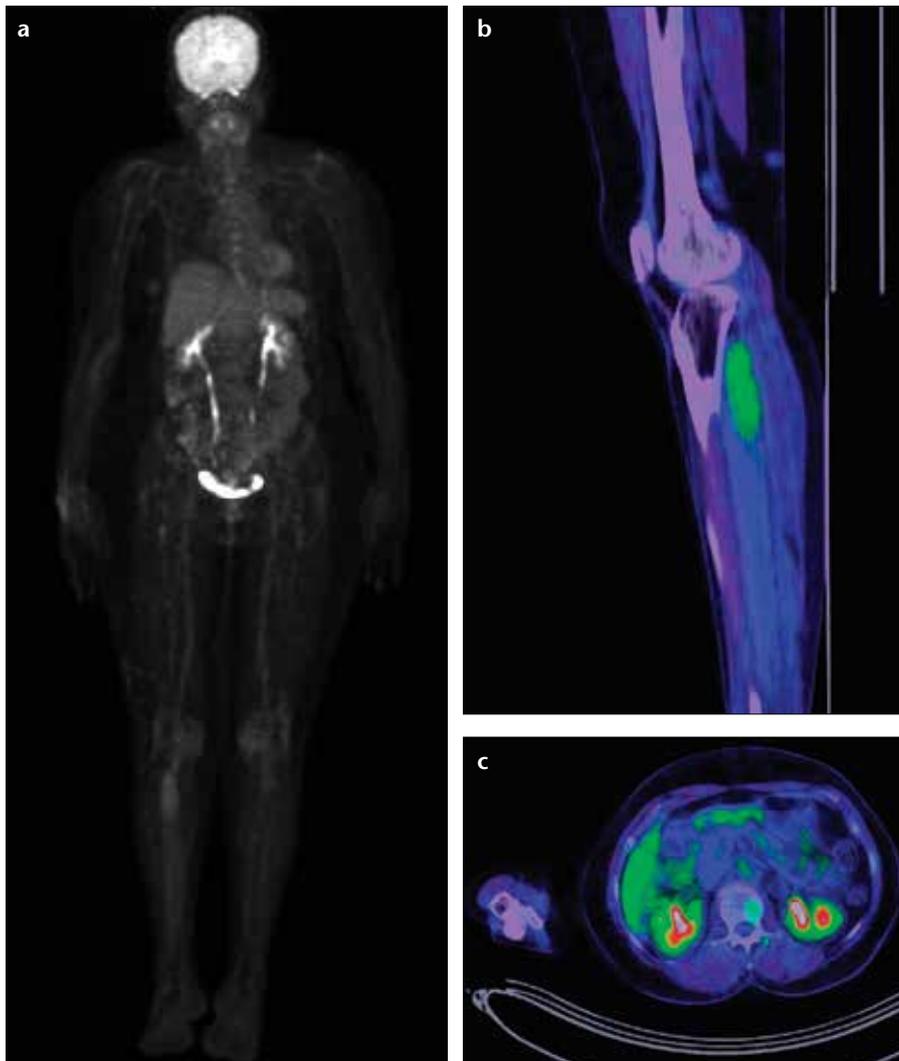


Figure 3. a–c. Follow-up PET-CT study after chemotherapy. PET of whole body (a), sagittal PET-CT of lower limbs (b), and axial PET-CT (c) images demonstrated a marked interval decrease in FDG activity in the previously seen FDG-avid lesions in the posterior compartment (a, b) of the proximal right leg (current SUV_{max} 3.8; previous SUV_{max} 18.5) and in the posterior medial aspect (a, c) of the right elbow (current SUV_{max} 2.4; previous SUV_{max} 13.4), suggesting a positive response to chemotherapy.

in the setting of an already established lymphoma. PET-CT represents a novel tool for imaging in relapse of peripheral nerve lymphoma and prompt thera-

peutic implications without the risk of invasive procedures.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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