Hong Kong J Radiol. 2012;15:187-91

CASE REPORT

Neurogenic Tumour Mimicker: Two Cases of Neurolymphomatosis

JWC Wai, MK Chan, KW Tang, SCH Chan

Department of Radiology and Imaging, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong

ABSTRACT

Infiltration of the peripheral nervous system by lymphoma is termed neurolymphomatosis. Prior to identification of the causative B lymphocyte, neurolymphomatosis was the least common clinical presentation of nervous system lymphoma. Neurolymphomatosis can easily be misdiagnosed as neurogenic tumour from imaging at the first presentation. This report describes two patients with neurolymphomatosis with characteristic sonographic, magnetic resonance imaging, and positron emission tomography features.

Key Words: *Lymphoma; Magnetic Resonance Imaging; Positron Emission Tomography; Ultrasonography*

中文摘要

擬似神經原性腫瘤的病症：神經淋巴瘤病兩個病例報告

衛穎莊、陳文光、鄧國穎、陳慈欽

淋巴瘤侵入周圍神經系統的情況被稱為神經淋巴瘤病。在未有分辨到誘發的B淋巴細胞前，神經淋巴瘤病被視為神經系統淋巴瘤的最罕見表現。在病發初期，單憑影像學很容易把神經淋巴瘤病誤診為神經源性腫瘤。本文報告兩宗神經淋巴瘤病的病例報告，它們均有超聲、磁共振影像及正子攝影影像的特徵。

INTRODUCTION

Non-Hodgkin's lymphoma involving the peripheral nervous system is a rare cause of peripheral neuropathy, and nerve-seeking lymphoma represents a unique subtype of extra-nodal lymphoma. Neurolymphomatosis denotes localised invasion of the cranial or peripheral nerve roots or nerves. This process is commonly outside the arachnoid investment of nerves.[1] Knowledge of lymphoma presenting as a solitary tumour of a peripheral nerve and dissemination of lymphoma extending along the peripheral nerves is limited to a few case reports.[2,3] The clinicopathological syndrome of neurolymphomatosis or lymphomatous infiltration of peripheral nerves is a relatively rare condition that usually develops in patients with widespread non-Hodgkin's lymphoma, and may be the first manifestation or the sole relapse site.[4] The differential diagnosis comprises herpes zoster infection, vinca alkaloid toxicity, compression or infiltration of nerve roots, lymphoma-associated vasculitis, and systemic amyloidosis.[5] Therefore, the causes of peripheral neuropathy may be difficult to distinguish during progressive disease and therapy for aggressive lymphoma. The combination of various modes of

Correspondence: *Dr Janet WC Wai, Room 115, Block K, Department of Radiology and Imaging, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong.*
Tel : (852) 2958 8888 ; Fax : (852) 2958 5653 ; Email : wwc053@ha.org.hk

Submitted: 3 Jan 2012; Accepted: 17 Feb 2012.

imaging and imaging-guided biopsy can enable prompt diagnosis and appropriate management.

CASE REPORTS

Case One

A 75-year-old man was diagnosed with stage IV diffuse large B cell lymphoma in 2008. He first presented with a right upper neck mass for the previous eight months, which was associated with dysphagia and foreign body sensation at the throat. Laryngoscopy showed a large tumour mass over the vallecula obstructing the oropharynx. Biopsy confirmed diffuse large B cell lymphoma (positive to CD20 immunostain). Eight cycles of chemotherapy with rituximab, cyclophosphamide, epirubicin, vincristine, and prednisolone (R-CEOP) were given. Complete response was noted on follow-up positron emission tomography–computed tomography (PET-CT).

The patient noted masses in the left upper epitrochlear, right groin, and right popliteal regions in September 2009. Hypermetabolism in various regions, including the left rectus femoris, left tensor fascia lata, right popliteal fossa, left upper arm, and liver, was noted by PET-CT (Figure 1). Localised sonography of the left arm showed an elongated hypoechoic mass measuring approximately 1.7 x 1.5 x 3.1 cm in the anteromedial aspect of the arm (Figure 2), surrounding a swollen

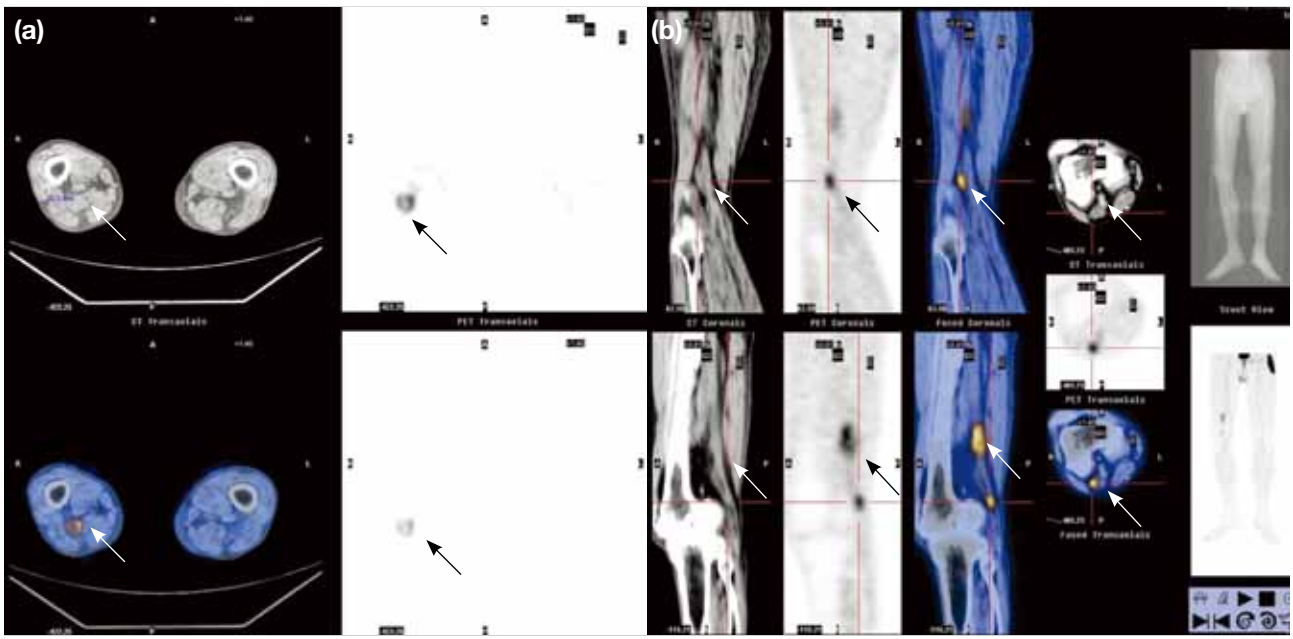

Figure 1. Positron emission tomography–computed tomography images of the right popliteal fossa of case 1. (a) Axial images show increased 18F-fluorodeoxyglucose uptake (arrows) corresponding to the lesion detected by ultrasonography and magnetic resonance imaging. (b) Sagittal and axial images show increased 18F-fluorodeoxyglucose uptake (arrows) corresponding to the lesion detected by ultrasonography and magnetic resonance imaging.

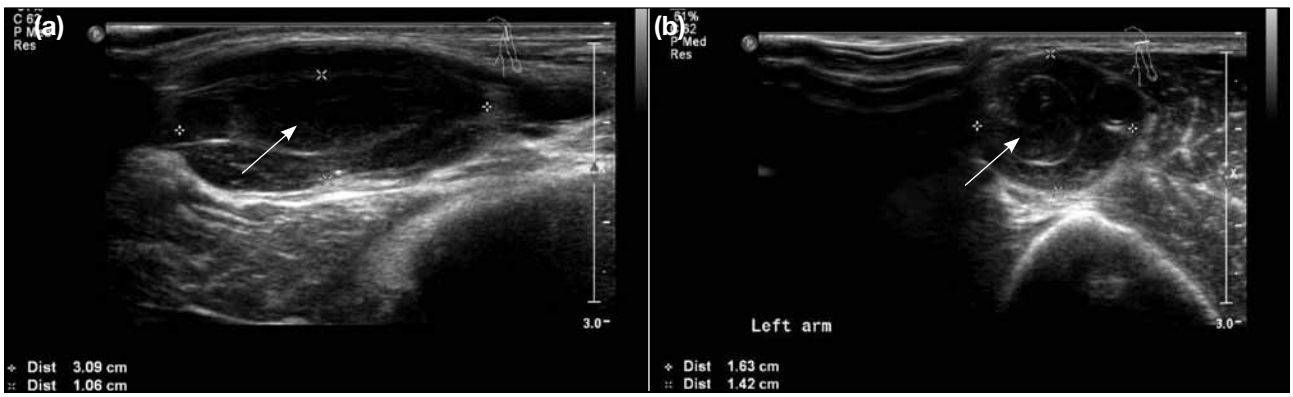

Figure 2. (a) Longitudinal and (b) transverse ultrasonographic scans of the anteromedial aspect of the left upper arm of case 1 show an elongated hypoechoic mass surrounding the swollen median nerve (arrows). The thin layer of normal echogenic connective tissue around the median nerve is absent.

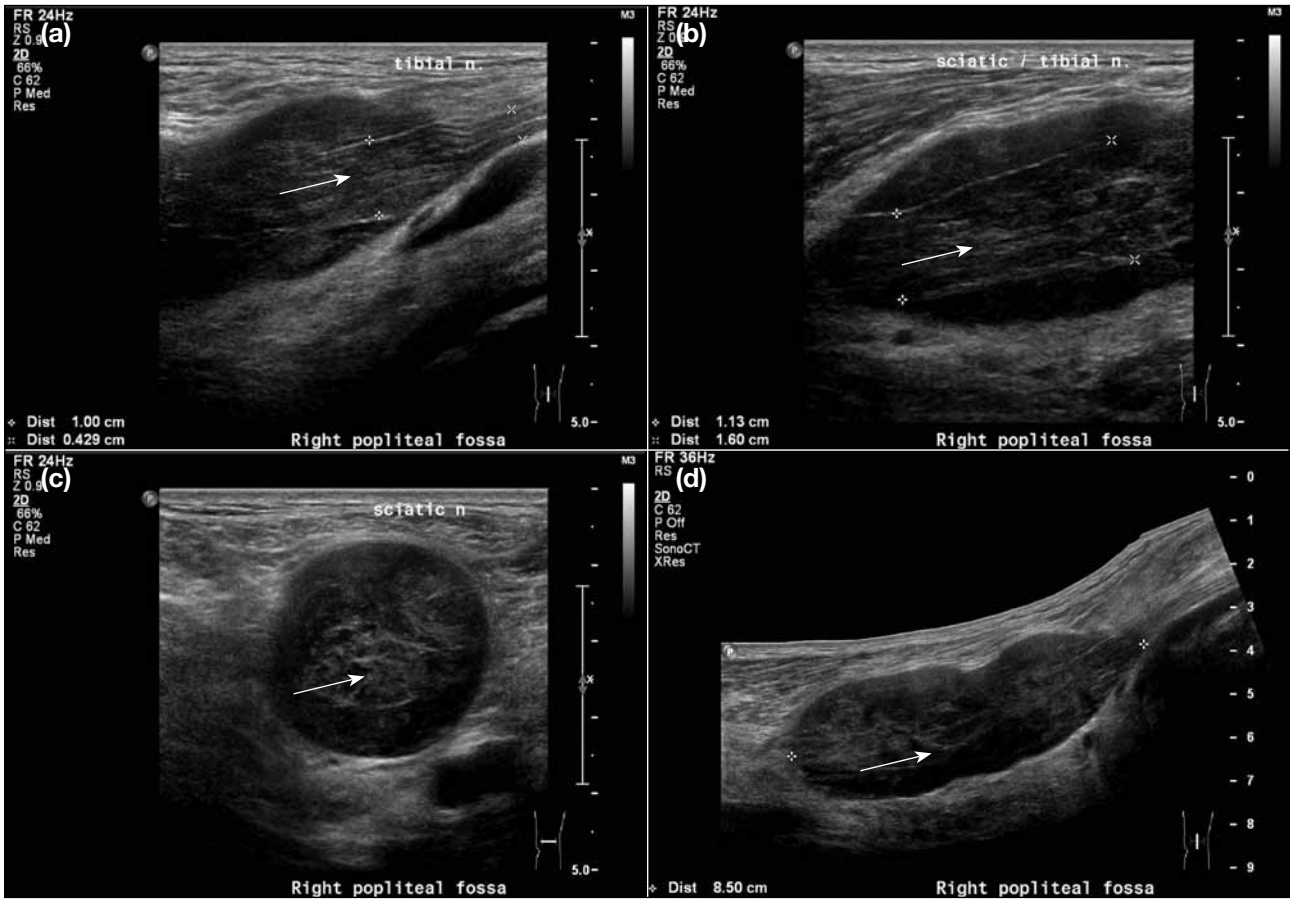

Figure 3. Ultrasonographic scans of the upper part of the right popliteal fossa of case 1. (a) A longitudinal scan shows an elongated hypoechoic mass superficial to the popliteal vessels surrounding a swollen proximal tibial nerve (arrow). (b) Longitudinal, (c) transverse, and (d) panoramic scans show an elongated hypoechoic mass surrounding the swollen distal sciatic nerve (arrows).

median nerve. The mass also abutted the brachial artery, with a positive Tinel sign. Ultrasonography of the right popliteal fossa (Figure 3) showed an elongated hypoechoic mass measuring approximately 2.8 x 2.9 x 8.5 cm in the upper part of the popliteal fossa superficial to the popliteal vessels. The mass surrounded the distal sciatic nerve and proximal tibial nerve, which were both swollen. The common peroneal nerve may also have been involved proximally; it was tender with a positive Tinel sign. These features suggested lymphomatous involvement or infiltration of the left median nerve and the right sciatic and tibial nerves. The ultrasonographic appearance was not typical of neurogenic tumours.

Magnetic resonance imaging (MRI) of the left arm (Figure 4) and right knee (Figure 5) was performed with similar findings. Left arm and right popliteal enhancing masses were found along or close to the neurovascular bundles. The signal characteristics of the lesions were not typical of neurogenic tumours. Lymphomatous

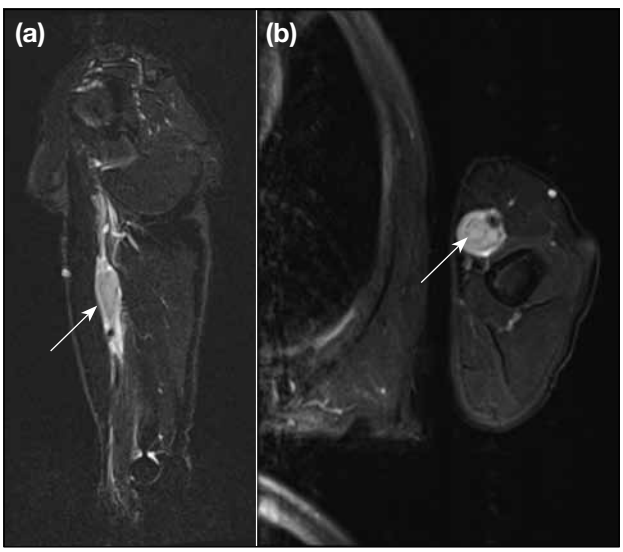

Figure 4. T2-weighted magnetic resonance images of (a) sagittal and (b) axial sections of the left upper arm of case 1 show an infiltrating mass (arrows) encasing the median nerve.

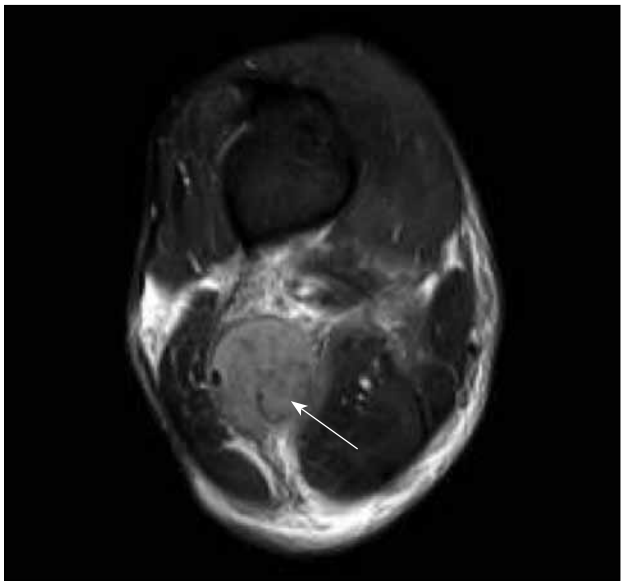

Figure 5. An axial enhancing magnetic resonance image of the right popliteal fossa of case 1 shows an infiltrating mass encasing the swollen distal sciatic nerve (arrow).

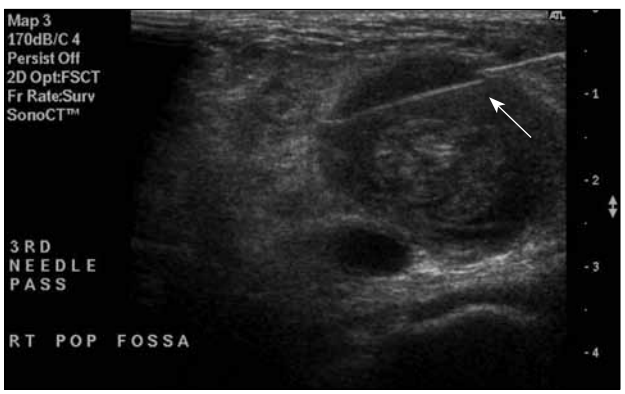

Figure 6. Ultrasonography-guided core biopsy of the right popliteal fossa lesion (arrow) of case 2.

involvement of the nerves was the likely diagnoses. Ultrasound-guided fine needle aspiration was performed for the right popliteal lesion. Biopsy was not done because of shooting pain described by the patient. The cytological results showed large B cell lymphoma.

Case Two

A 69-year-old man was diagnosed with diffuse large B cell lymphoma in 2008 with presenting symptoms of right tonsillar mass. Tonsillar biopsy confirmed diffuse large B cell lymphoma. Eight cycles of chemotherapy with R-CEOP were planned, but chemotherapy was stopped after four cycles as the patient had a cerebellar infarction.

In 2010, the patient presented with a right popliteal mass. Preliminary ultrasonography scan of the right popliteal fossa showed that the tibial nerve was thickened and had an internal heterogeneous echogenic pattern. A layer of soft tissue surrounded and encased the enlarged portion of tibial nerve. The tibial artery was closely related to the mass. The ultrasonographic features were thought to represent lymphomatous infiltration of the right tibial nerve. Ultrasound-guided core biopsy was done (Figure 6), and the pathology results confirmed diffuse large B cell lymphoma.

DISCUSSION

Neurolymphomatosis appears to be the least common neurological manifestation of lymphoma and is difficult to diagnose. Therefore, diagnosis is often delayed. Only 55% of patients in a combined series were diagnosed antemortem.[6] The final diagnosis requires integration of clinical presentation, imaging findings, and pathological results obtained from neural and extra-neural tissue, and cerebrospinal fluid. A high index of suspicion and familiarity with the clinical manifestations of this disease are necessary for the correct diagnosis.

Clinical Presentation

There are four broad clinical presentations, including painful polyneuropathy or polyradiculopathy, cranial neuropathy, painless polyneuropathy, and peripheral mononeuropathy. Clinical findings that suggest neurolymphomatosis, as opposed to a remote effect or inflammatory process, include severe pain, particularly when it affects all four limbs, asymmetric distribution, and rapid evolution.

Imaging Findings

There has been a decrease in the rate of postmortem diagnosis in recent years.[7] This is probably related to the improved resolution of current imaging techniques with increased precision and tissue definition. Therefore, imaging studies have the greatest clinical utility among the diagnostic tools. In practice, neurolymphomas can easily be misdiagnosed from imaging as neurogenic tumours at first presentation due to their prevalence. A combination of various imaging modalities is of the utmost importance in deriving the final diagnosis.

Normal peripheral nerves can be clearly demonstrated in high-resolution ultrasound images.[8] The nerve is seen as hypoechoic neuronal fascicles and echogenic surrounding connective tissue.[9] The most common tumours of peripheral nerves are neurofibromas and

schwannomas. Other benign and malignant peripheral nerve sheath tumours, such as neurofibromatosis, glomus, fibromatosis infiltration of the nerve, and metastases are rare. Most peripheral neurogenic tumours are ovoid with well-defined margins, and heterogeneously hypoechoic with cystic and solid components in the soft tissue mass on ultrasonography. In contrast, the lymphomatous infiltrated nerves show heterogeneous soft tissue encasement around the swollen affected nerves. The lesions appear more solid looking and normal hypoechoic clearly defined neuronal fascicles cannot be appreciated. A thin layer of echogenic connective tissue surrounding a normal peripheral nerve is absent. Ultrasonographic features of neurolymphomas are very different from typical neurofibromas or schwannomas.

MRI shows nerve or nerve root enlargement with or without contrast enhancement. These features were also found in the patients in this report. Involvement of the neural plexus is more difficult to detect,[10] as MRI may not be sensitive enough for small lesions.[11] This modality can yield abnormal findings in up to 80% of affected patients, particularly those with a known history of haematological malignancy.[12] MRI findings are not specific for neurolymphomatosis and similar findings might sometimes be seen in acute or chronic inflammatory radiculoneuropathies, inflammatory pseudotumour, and malignant tumours of the peripheral nerve sheath.[6] Interpretation of imaging studies should therefore be aligned with the clinical and laboratory findings.

PET-CT is a highly sensitive diagnostic method for identification of neurolymphomatosis, with 87.5% sensitivity.[7] Together with MRI findings, PET-CT may define the best target for biopsy. The role of PET-CT in the assessment of non-Hodgkin's lymphoma as a prognostic marker is under evaluation. Recent reports show encouraging results, especially in follow-up examinations after chemotherapy.[13]

Pathological Confirmation

Diagnosis of neurolymphomatosis usually requires histological demonstration of infiltrating malignant lymphocytes in a peripheral nerve. The diagnostic yield of biopsy can be as high as 88%.[7] Therefore, if imaging findings are inconclusive, nerve biopsy presents a reasonable approach for definitive diagnosis. However, nerve biopsy may fail despite widespread lymphomatous infiltration of the peripheral nerves.[14] Polymerase chain reaction–based testing for monoclonal rearrangement of immunoglobulin heavy-chain genes in B cell lymphomas can be used to diagnose neurolymphomatosis.[15]

In conclusion, non-Hodgkin's lymphoma involving the peripheral nervous system is a rare cause of peripheral neuropathy. Imaging studies are of the greatest clinical utility among all the diagnostic tools. The interpretation of imaging studies in the context of clinical presentation and laboratory tests is necessary.

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