Dear Editor,

Neurolymphomatosis is a rare clinical entity and has mainly been described as primary lymphomatous infiltration of the nerves and as a relapse or progression of disease after previous treatments. In this case report, we describe an unusual occurrence of neurolymphomatosis evolving in mid-cycle chemotherapy.

Case Report

An 80-year-old Chinese lady was diagnosed with diffuse large B-cell lymphoma (DLBCL) involving cardiac, nodal and bony disease. She was first investigated for chest pain with breathlessness and a 2D echocardiogram showed a large circumferential pericardial effusion as well as an echodense mass seen adherent and anterior to the right ventricle and right ventricle outflow tract (RVOT) region with RVOT compression. She underwent a left anterior thoracotomy, pericardial window, mediastinoscopy and biopsy; histology of her mediastinal lymph node was consistent with DLBCL.

18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) was performed using a GE Healthcare Discovery PET/CT machine with 10.0 millicurie of FDG injected. The scan was performed 75 minutes after the radiotracer administration. Hypocount measurement was 6.0 mmol/L prior to the scan. Findings showed a hypermetabolic nodular soft tissue thickening along the pericardium as well as pericardial effusion. Multiple foci of FDG uptake were also seen in the bones and in lymph nodes above and below the diaphragm. Bone marrow aspirate had no morphological evidence of lymphomatous infiltration but trephine showed mildly hypocellular trilineage haematopoiesis with minimal, concordant B-Lymphomatous infiltration. Flow cytometry noted approximately 3% atypical B lymphocytes which express CD19+, CD20+, SMIG+, predominantly CD5-, CD23-, FMC7- with lambda light chain restriction compatible with clonal B cells. The International Prognostic Index was 4. She was treated with her first cycle of R-CHOP chemotherapy regimen consisting of rituximab, cyclophosphamide, hydroxydaunorubicin (doxorubicin), Oncovin (vincristine) and prednisolone displaying good clinical improvement. A repeat 2D echocardiogram done 16 days later showed resolution of the cardiac mass and pericardial effusion.

The patient presented after her third cycle of R-CHOP with complaints of new onset glove and stocking numbness. Physical examination revealed hand numbness up to wrist and lower limb numbness up to mid-calf on both sides. A magnetic resonance imaging (MRI) study of the brain and spine was performed (Siemens MAGNETOM Avanto, 1.5 Tesla). Apart from degenerative changes such as disc bulges and lumbar spondylosis, the MRI study showed no overt leptomeningeal enhancement, or any intracranial abnormality detected and no MR features to suggest transverse myelitis. A lumbar puncture performed showed elevated protein 0.99 g/L (normal: 0.1 to 0.4 g/L) with absent white blood cell count. The cerebrospinal fluid was also negative for lymphomatous large cells. Nerve conduction studies showed evidence of bilateral absent H reflexes and prolonged right tibial and left peroneal F wave latencies which were compatible with early changes in Guillain-Barré syndrome. She was initially treated as for Guillain-Barré syndrome and completed 5 days of intravenous immunoglobulin (IVIG) with no improvement in symptoms. A subsequent FDG PET/CT study (9.4 millicurie of FDG injected, scan performed at 75 minutes post radiotracer administration with hypocount 5.9 mmol/min prior to scan) showed near complete resolution of the previous sites of disease (Fig. 1). However, new FDG-avid perineural soft tissue thickening were found in multiple peripheral nerves, suspicious for tumour. The nerves involved included the bilateral brachial plexi, right femoral nerve and left sciatic nerve. FDG uptake was also seen beginning from the L5 nerve roots with perineural thickening suspicious for tumour infiltration as opposed to inflammatory nerve conditions (Fig. 2). A repeat lumbar puncture was performed which then showed atypical lymphoid cells suspicious for lymphomatous involvement. Flow cytometry of the cerebrospinal fluid noted a population of atypical B-lymphocytes constituting approximately 30% of the analysed cells. The lymphocytes were CD19+, CD10-, CD5-, CD20+ and cytoplasmic lambda light chain restricted; suspicious of involvement of the cerebrospinal fluid by a B-cell lymphoproliferative disorder. The patient deteriorated neurologically and also developed a nosocomial pneumonia during her inpatient stay. The decision was made...
for palliation after consultation with the family and she then passed away shortly after terminal discharge.

**Discussion**

Neurolymphomatosis is a rare syndrome of peripheral nerve dysfunction secondary to infiltration by lymphoma, nearly always B-cell non-Hodgkin’s lymphoma.1,2 A high index of suspicion is required as presenting symptoms are varied; conventional radiology has only modest sensitivity, and pathological diagnosis is often difficult. A number of differential diagnoses need to be considered (e.g. nerve damage from herpes zoster, chemotherapy with vinca alkaloids such as vincristine, Guillain-Barré syndrome, radiation plexopathy, nerve root compression, amyloidosis and lymphoma-associated vasculitis).3 The diagnosis and localisation of neurolymphomatosis may be supported by FDG PET-CT imaging.3-8 There is no known standard treatment for neurolymphomatosis and management usually consists of either chemotherapy alone or combined with radiotherapy. Most institutes employ a methotrexate monotherapy regime or combined with other drugs particularly cytarabine. Early recognition and treatment of this rare neurologic manifestation of lymphoma may improve outcome.1,3-9 Previously reported cases of neurolymphomatosis have described cases as first presentation of malignancy and as relapse or progression of disease after previous treatment, including a single case report of cardiac lymphoma relapsing as neurolymphomatosis.8-9 It seems likely that the blood-nerve barrier presents a barrier to the entry of large molecules such as cyclophosphamide, doxorubicin, vincristine, and rituximab into these areas, possibly resulting in lymphomatous infiltration. Ours is a rare case demonstrating a disseminated lymphoma involving cardiac, nodal and bony disease responding well to standard treatment that subsequently evolved into neurolymphomatosis mid-cycle through chemotherapy.10 To the best of our knowledge, this is the second such reported case in the published literature. This report adds to the small but growing literature on neurolymphomatosis and care must be taken to correctly diagnose this clinical entity in such settings to avoid delays in therapy.

**REFERENCES**


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