

Lymphoma relapse presenting as neurolymphomatosis

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ABSTRACT

Neurolymphomatosis (NL) is a rare neurological manifestation of lymphoma characterized by malignant lymphoma cells infiltrating cranial or peripheral nerve, or their roots. We present the first reported Australian case of a patient whose initial presentation of relapsed mantle cell lymphoma was NL. Our case highlights that clinical and imaging findings of NL often mimic other neuropathies, and hence presents unique challenges that may lead to delayed diagnosis and management. We emphasize the importance of considering NL in the differential diagnosis and combining imaging with other diagnostic modalities such as lumbar puncture (LP) to aid in the diagnosis of NL particularly where there is acute neurological deterioration.

Key words: Mantle cell lymphoma, neurolymphomatosis, relapse

Introduction

We report the first Australian patient with NL associated with relapse of mantle cell lymphoma. The clinical manifestations of NL vary and hence, a high index of suspicion is required. We suggest that a combination of diagnostic modalities including LP is useful in aiding diagnosis and management in these patients.

Case Report

Our patient, a 72-year-old female, presented with 5 weeks of progressive bilateral leg weakness, with sharp pain in the L5 dermatome distribution bilaterally and progressive worsening left upper limb weakness over 5 months. She denied bowel or bladder disturbance, and there were no systemic symptoms.

Her past medical history included mantle cell lymphoma which was diagnosed more than a year prior, for which she

previously received six cycles of chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone). At the time of her presentation, she was in remission.

On examination, there was moderate weakness in the left upper limb; normal biceps and triceps reflexes bilaterally. There was increased tone at the knee and ankle; bilateral ankle clonus; mild lower limb weakness and absent bilateral knee and ankle reflexes. Babinski reflexes were negative. There was decreased sensation in the L4, L5, and S1 dermatome distributions bilaterally. Anal tone and peri-anal sensation were normal. There was no evidence of hepatosplenomegaly or lymphadenopathy on examination.

Magnetic resonance imaging (MRI) of the lumbar spine revealed a discrete lesion in the lumbar canal from L2-L5 [Figures 1 and 2]. The lesion was difficult to define as intra- or extra-medullary. The lesion demonstrated hyper-intensity on T1 and T2 [Figures 1 and 2] with vivid enhancement postgadolinium [Figure 3]. Brain, cervical, and upper thoracic MRI revealed no abnormality.

Routine blood tests were relatively unremarkable. Computed tomography (CT) of chest, abdomen, and pelvis was unremarkable.

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Figure 1: Sagittal T2-weighted image flair sequence L-spine



Figure 2: Sagittal T2-weighted image



Figure 3: Axial T1-weighted image contrast coronal, flair sequence

At the multidisciplinary meeting, it was suggested that the cauda equina be decompressed and that the lesion be biopsied ± excision depending on the frozen section result.

The patient was commenced on dexamethasone prior to surgery.

At surgery, decompressive laminectomies at L3, L4, and L5 were performed followed by a midline durotomy. The cauda equina nerve roots were found to be abnormally pale and grossly expanded filling the canal with no evidence of extrinsic or exophytic tumor. There was no surrounding cerebrospinal fluid (CSF) in this area. Nerve biopsy was not performed to avoid neurological damage. A lumbar drain was passed cranially, and CSF was taken intra-operatively. A dural patch was sewn in to allow for the expanded nerve roots. CSF analysis revealed, elevated white cells, protein, and decreased glucose. CSF flow cytology showed 100% monoclonal population of B lymphocytes expressing CD19⁺, CD20⁺, and CD5⁺.

Following surgery, the patient was considered not medically fit for systemic or intrathecal chemotherapy. She received radiotherapy with palliative intent. Postoperatively the patient’s pain had improved with some modest improvement in the patient neurology.

Discussion

Neurolymphomatosis (NL) makes up 10% of primary lymphoma of the nervous system.^[1] The incidence of NL at an Australian Tertiary Referral Hospital has been recently reported as three cases per 100 new intermediate or high-grade non-Hodgkin’s lymphoma (NHL) patients annually.^[2]

In NL malignant lymphoma cells directly infiltrate beyond the arachnoid mater of single or multiple cranial or peripheral roots, or nerves.^[2] B-cell NHL is the most common type of lymphoma associated with NL although few cases associated with T-cell NHL and acute lymphoblastic leukemia have been described.^[3] Of the sub-type, mantle-cell lymphoma is a rare cause and our patient is the first reported Australian case. It has been reported that the majority of NL patients had concomitant systemic lymphoma, and it is uncommon for NL to be the first manifestation of lymphoma.^[3] In our patient, there was no systemic lymphoma with only spinal nerve roots and CSF affected. Isolated involvement of spinal nerve roots is unusual, and only a minority of NL patients also have other central nervous system involvement.^[1] CSF analysis may be normal in NL patients^[1] or abnormal in the setting of patients without NL.^[1,3] The pathogenesis of NL with or without CSF/systemic lymphoma is unknown due to the rarity of NL.

NL patients have variable clinical presentations depending on the nerves involved, and sensorimotor neuropathy has been noted as the most common clinical feature.^[1,3]

Currently, there is no gold-standard diagnostic tool for NL. This has translated to some patients having delayed diagnosis (up to years) and hence treatment.^[1]

MRI is often the most useful common imaging modality for NL diagnosis and MRI findings include spinal root or nerve enlargement or enhancement.^[1] It should be noted that nerve thickening or enhancement is not specific for NL and can suggest inflammatory radiculopathies or peripheral nerve sheath tumors.^[1] MRI does not always provide optimal visualization of the individual nerves as in our case. Positron emission tomography (PET) imaging is usually used when other modalities are inconclusive. PET is unlikely to be 100% sensitive as radioactive uptake occurs with any process where there is an increased rate of glycolysis as in infection and inflammation.^[4] There has been at least 1 report of false-negative.^[2] Interestingly, there has been suggestion that PET and CT findings may be more appropriate for imaging NL in patients with suspected relapse of NHL than other diagnostic modalities.^[5]

For disease staging: MRI brain and spine and CT chest, abdomen, and pelvis should be performed.^[1] Most studies have recommended that PET imaging be used to measure treatment response.^[1,3,6]

Nerve biopsy is less commonly performed due to difficulties with accessing the involved nerve and neurological compromise.^[3,6] It may be appropriate where the benefits outweigh the risks; however in some patients, nerve biopsy shows nonspecific findings.^[7] Isolated cranial neuropathy presents a diagnostic biopsy dilemma.^[1]

CSF analysis typically shows elevated protein, low glucose, and elevated cell count; at the time of diagnosis, only a minority of NL patients had malignant cells in CSF.^[3] An abnormal CSF cell count does not necessarily correlate with positive cytology, and an abnormal CSF count has been evident in patients with no nerve involvement.^[1,3] Abnormal CSF does not show whether there are intrinsic changes involving the spinal cord or nerves, and hence, biopsy of the lesion may be useful. Electrical nerve monitoring should also be considered for aberrancy of the nerve roots and its branches.

The sensitivity of MRI, nerve biopsy, and CSF analysis has been reported as 40%, 80%, and 21%, respectively.^[2]

As this case highlights, preoperative MRI showing lumbar spinal nerve root infiltrates can mimic neural tumor. In the setting where there are characteristic clinical findings and MRI shows persistent enlargement, signal intensity abnormality, NL should be considered. We suggest that a combination of diagnostic modalities including CSF analysis be used, particularly where there is history of lymphoma. MRI is preferred as it is often performed to exclude other neuropathies. While PET has been recommended, it is not always easily accessible. LP is easy to perform, and there are minimal risks involved. Nerve biopsy and electrical nerve stimulation are also useful in detecting intrinsic changes involving the nerve roots.

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Conflicts of interest

There are no conflicts of interest.

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