



Primary Central Nervous System Lymphoma Presenting with Peripheral Neuropathy; A Rare Case of Coincident PCNSL and Mononeuritis Multiplex

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ABSTRACT

A 43-year-old male presented with diplopia and right sixth-nerve palsy. Brain magnetic resonance imaging (MRI) demonstrated a lesion in the right periventricular area. High-dose corticosteroid pulse therapy did not resolve the symptom. After one month, his diplopia progressed and he developed weakness of the left lower limb. Detailed examination revealed left sixth-nerve palsy, dropped foot, waddling gait, atrophy of the gluteal muscles and mild atrophy and weakness of the right upper limb. Neurological examination supported evidence of multiple cranial nerve palsies along with asymmetrical peripheral neuropathy. Electrodiagnostic studies were compatible with a mononeuritis multiplex. Rheumatologic evaluations were normal. Malignancy work-up were normal, except for some insignificant lymph nodes. Bone marrow aspiration and biopsy were normal. The second brain MRI detected multiple homogenous enhancing lesions in the right periventricular area. The result of stereotactic biopsy and immunohistochemistry staining demonstrated primary B-cell CNS lymphoma (PCNSL). Mononeuritis multiplex has not been reported as a paraneoplastic manifestation of PCNSL yet. In other words, it is not clear whether involvement of the peripheral nervous system in our patient is a paraneoplastic manifestation of PCNSL or a coincidence of PCNSL and hematologic lymphoma presenting with peripheral vasculitic neuropathy. It is recommended that future studies focus more on symptoms associated with PCNSL to recognize the exact relationship between PCNSL and peripheral neuropathy.

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Introduction

Primary central nervous system lymphoma accounts for approximately 3% of all primary brain tumors (1). Median age of diagnosis is 60 years in non HIV- infected patients (2). It can affect any part of the neuraxis including the eyes, brain, leptomeninges, or spinal cord. The only established risk factor for PCNSL is immunodeficiency (3). The diagnosis and patients evaluation can be established by guidelines provided by International PCNSL Collaborative Group (4). Corticosteroids, chemotherapy, and radiation are available treat-

ment options for PCNSL and surgery is not effective in this patients (3).

Case report

The authors report an unusual case of primary CNS lymphoma presenting with mononeuritis multiplex. This 43-year-old man presented with diplopia due to right sixth-nerve palsy two months prior the first admission. Brain MRI demonstrated a small, round-shaped, T1-isointense, T2-hyperintense lesion without gadolinium enhancement

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in the right periventricular area (Figure 1). High-dose corticosteroid pulse therapy was instituted according to suspicion of a demyelinating disease. However, his symptoms did not resolve.

After one month, his diplopia aggravated and he developed proximal and distal weakness of the left lower limb. Detailed examination revealed left sixth-nerve palsy, left foot drop, waddling gait, atrophy of the left gluteal muscles, as well as mild atrophy and weakness of the right upper limb. Fundoscopic examination was normal. Family history and past-medical history were unremarkable.

The patient was reassessed and neurological examination supported evidence of multiple cranial nerve palsies along with asymmetrical peripheral neuropathy. Electrodiagnostic studies were performed and the results were compatible with a mononeuritis multiplex. He was mildly anemic with a hemoglobin level of 12.1 g/dl. Results from kidney and liver function tests were within normal range. Cerebrospinal fluid (CSF) analysis showed lymphocytic (65%) pleocytosis (17 cells per mm³), elevated protein levels (204 mg/dl) and hypoglycorrhachia (42 mg/dl) with negative cytology. All rheumatologic evaluations including antinuclear antibodies (ANA), anti-double stranded DNA (anti-dsDNA), C3, C4, CH50, perinuclear anti-neutrophil cytoplasmic antibodies (P-ANCA), cytoplasmic anti-neutrophil cytoplasmic antibodies (C-ANCA), anti-sjögren's-syndrome-related antigen A(SS-A), anti-sjögren's-syndrome-related antigen B(SS-B), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were normal. Human immunodeficiency virus (HIV) serology was negative. Malignancy work-up including chest, thoracic, abdominal and pelvic computed tomography scans were normal, except for some insignificant mediastinal lymph nodes. Bone marrow aspiration showed active bone marrow with myeloid lineage hyperplasia and marrow biopsy was normal.

The second brain MRI detected multiple homogeneous enhancing lesions with restricted water diffusion on diffusion-weighted imaging (DWI) sequences in the right periventricular area (Figure 2-4). Meningeal enhancement was not observed.

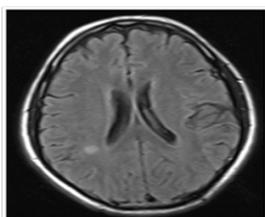


Figure 1. Small hypersignal change in the right periventricular area.

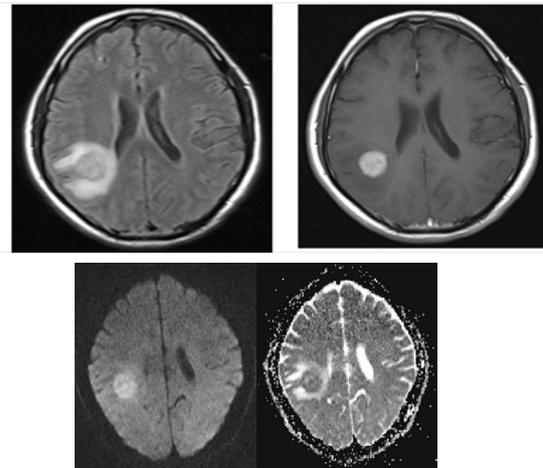


Figure 2, 3, 4. Lesion enlargement with gadolinium enhancement after one month.

In view of the MRI findings a stereotactic biopsy was performed. The result was consistent with lymphoproliferative disorder. Immunohistochemistry staining revealed diffusely positive creatinekinase (CK), negative CD20, positive CD3 and negative glial fibrillary acidic protein (GFAP), according to which the diagnosis of primary B-cell CNS lymphoma was confirmed. The patient was commenced on combination chemotherapy including cytarabine, vincristine, rituximab and methotrexate, followed by radiotherapy. After that, the disease progression diminished markedly.

Discussion

Primary central nervous system lymphoma is a rare malignancy of CNS accounting for 2.2% of all brain tumors (5). To date, numerous paraneoplastic manifestations associated with systemic non-Hodgkin's lymphoma have been reported (6). In a retrospective study, neurolymphomatosis was linked to systemic non-Hodgkin lymphoma in 90% and to acute leukemia in 10% of the subjects. It is the first manifestation of malignancy in 26% of the patients (7). Paraneoplastic syndromes, are rarely described in PCNSL, although it is very common in systemic lymphomas (8). A case of autonomic neuropathy was reported in 1995; a 68-year-old male with multiple enhancing lesions in brainstem, which was histologically consistent with large B-cell CNS lymphoma (9). In that study, autonomic nervous system function was evaluated by quantitative sudomotor axon reflex tests (QSART), which showed a dysfunction of the peripheral autonomic nervous system rather than a central autonomic disorder. This implies that autonomic dysfunction had been induced by the remote effect of tumor rather than a contiguous effect of tumor cells. Other paraneoplastic effects of PCNSL were myasthenia gravis, cerebral salt

wasting syndrome and leukoencephalopathy (9).

Conclusion

Mononeuritis multiplex has not been reported as a paraneoplastic manifestation of PCNSL yet. In other words, it is not clear whether involvement of the peripheral nervous system in our patient is a paraneoplastic manifestation of PCNSL or a coincidence of PCNSL and hematologic lymphoma presenting with peripheral vasculitic neuropathy. It is also possible that mononeuritis multiplex may be a complication of PCNSL due to a vasculitic process.

It is recommended that future studies focus more on symptoms associated with PCNSL to recognize the exact relationship between PCNSL and peripheral neuropathy.

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Conflict of Interest

The authors declare no conflict of interest.

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