



Case Report

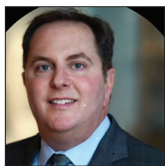
# Neurolymphomatosis of the brachial plexus from atypical primary central nervous system lymphoma lesions: A case report and review of the literature

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## ABSTRACT

**Background:** Primary central nervous system lymphoma (PCNSL) is an aggressive and extranodal non-Hodgkin lymphoma limited to the neuroaxis. In immunocompetent individuals, PCNSL is more common in older adults and lacks the association with the Epstein–Barr virus found in individuals with AIDS-associated PCNSL. Because the clinical presentation and radiographic findings of PCNSL are highly variable, stereotactic brain biopsy is typically required for definitive diagnosis. High-dose methotrexate, in combination with other chemotherapeutic agents with or without whole brain radiation, is the mainstay of treatment.

**Case Description:** A 70-year-old HIV-negative woman presented with confusion, acute flaccid left arm weakness, and left hand numbness. Head computed tomography without contrast demonstrated a 1 cm hyperdense round lesion in the suprasellar cistern that prompted further evaluation. Gadolinium-enhanced brain magnetic resonance imaging demonstrated enhancing lesions with heterogeneous signal intensity in the suprasellar, pineal, and right periaxial regions that did not explain the limb weakness and numbness. Serum and cerebrospinal fluid (CSF) studies were unrevealing, and a diagnosis of PCNSL was made following stereotactic biopsy. The patient's liver cirrhosis precluded chemotherapy, but treatment with whole-brain radiation was pursued.

**Conclusion:** The myriad clinical presentations and insidious course of PCNSL contribute to diagnostic difficulties, delays in treatment, and poor outcomes. Stereotactic brain biopsy is the primary method of PCNSL diagnosis since malignant cells are typically not detected in CSF. PCNSL should be considered in the differential diagnosis when immunocompetent elderly patients present with multiple intracranial lesions, even in the presence of lower motor neuron findings.

**Keywords:** Case report, Multifocal, Neurolymphomatosis, Primary central nervous system lymphoma

## INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is a rare type of non-Hodgkin lymphoma accounting for 1% of all lymphomas and 2% of all central nervous system (CNS) tumors.<sup>[1]</sup> The clinical presentation of PCNSL is variable. Patients typically present with focal neurologic deficits, symptoms of increased intracranial pressure, or altered mental status, which are findings that mimic many other CNS pathologies. Brain magnetic resonance imaging (MRI) findings of gadolinium-enhancing lesions are common but nonspecific for PCNSL and typically require

biopsy for histopathological confirmation, especially because cerebrospinal fluid (CSF) studies can be unrevealing.<sup>[8]</sup> We present a patient with an unusual constellation of neurologic deficits and radiographic findings ultimately diagnosed with and treated for PCNSL.

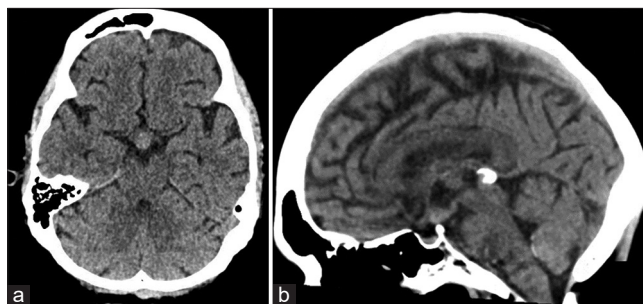
## CASE REPORT

A 70-year-old woman with atrial fibrillation, liver cirrhosis, Type 2 diabetes mellitus, hypertension, and venous thrombus treated with enoxaparin presented with a 5-day history of weakness in the left arm, numbness in the left fourth and fifth digits and medial palmar surface, and confusion. The patient also reported chronic vision loss in the right eye and denied headache or recent trauma.

On initial examination, the patient was alert; oriented to person, place, and time; and disoriented to situation. Cranial nerve testing revealed reduced visual acuity in the right eye. Motor strength testing revealed 4/5 strength in the left triceps, left wrist flexors and extensors, and left finger flexors and 3/5 strength in the left finger extensors. Reflex testing revealed an absent left triceps reflex. Sensation testing revealed decreased sensation to pinprick and light touch in the fourth and fifth digits of the left hand. There was no dysmetria or dysidiadokokinesia. Head computed tomography (CT) without contrast demonstrated a 1 cm hyperdense round lesion in the suprasellar cistern [Figure 1].

The patient's limb weakness and numbness localized to either the C7/8 nerve roots or the middle and lower trunks of the brachial plexus. Our differential diagnosis included a lateralized mass in the extradural or intradural extramedullary spinal canal or idiopathic brachial neuritis. While the patient had several risk factors for embolic stroke, including atrial fibrillation and diabetes, the specific patterns of sensory loss in the left upper extremity and loss of the left triceps reflex were more suggestive of either nerve root or brachial plexus pathology. On hospital day 2, the patient developed a pupil-sparing right CN III palsy. The next day, the right pupil became dilated to 4 mm and nonreactive to light.

The new cranial nerve palsy combined with the previously seen lesion on head CT without contrast broadened the differential diagnosis to include neoplastic, infectious, and inflammatory etiologies, especially those with a predilection for invading the subarachnoid space. Considerations included leptomeningeal disease from metastatic carcinoma or lymphoma as well as PCNSL due to the patient's age and multifocal nature of her symptoms, as well as tuberculosis, histoplasmosis, coccidioidomycosis, or cryptococcosis, and sarcoidosis. The patient then underwent gadolinium-enhanced brachial plexus, brain, and spine MRI in addition to lumbar punctures and several blood tests.



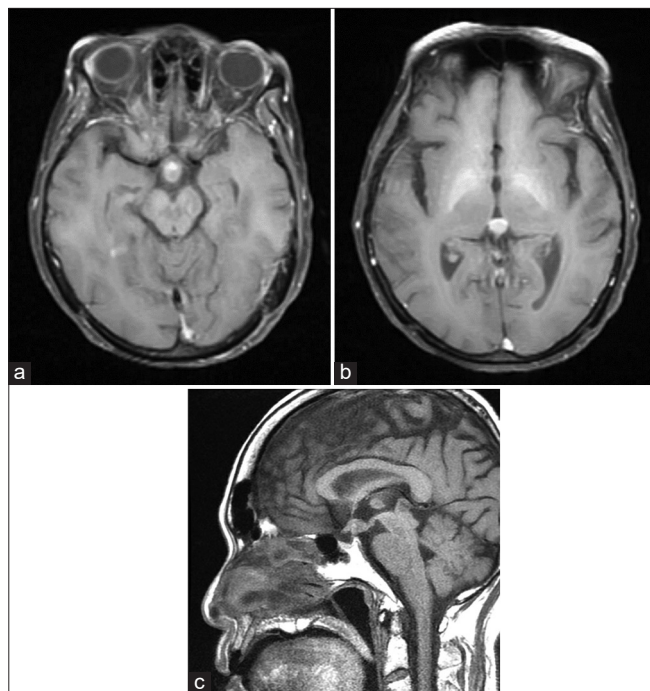
**Figure 1:** Initial (a) axial and (b) sagittal head computed tomography without contrast demonstrating a 1 cm hyperdense round lesion in the suprasellar cistern.

The patient's Vitamin B12, Vitamin B6, folate, and lead levels were within normal limits. RPR was nonreactive and HIV-1 was negative. Hemoglobin A1c was mildly elevated to 6.7%. The ophthalmology service performed a slit-lamp examination, which showed only rare drusen. Gadolinium-enhanced brachial plexus and spine MRI were unrevealing. Gadolinium-enhanced brain MRI demonstrated enhancing lesions with heterogeneous signal intensity in the suprasellar, pineal, and right periaxial regions concerning for a lymphoproliferative, infectious, or inflammatory process and no evidence of ischemic stroke [Figure 2]. One week later, repeat gadolinium-enhanced brain MRI demonstrated an increase in the size of all enhancing lesions [Figure 3] in addition to focal right frontoparietal dural thickening. Chest/abdomen/pelvis CT with contrast demonstrated multiple nodules in the thyroid concerning for metastases. CSF studies from two serial lumbar punctures, with respective volumes of 28 mL and 6.5 mL, demonstrated lymphocytic pleocytosis, elevated protein, and elevated IgG index but neither malignant cells nor other inflammatory and infectious markers. The neurosurgery service performed a stereotactic biopsy of the lesion in the right periaxial region, which established the diagnosis of diffuse large B-cell lymphoma.

The patient was treated with whole-brain radiation (30 Gy in 10 fractions) rather than high-dose methotrexate due to the patient's decompensated liver cirrhosis.<sup>[7]</sup> The patient had difficulty tolerating radiation due to severe, intractable nausea, and vomiting. Post-radiation head CT without contrast demonstrated reduction in the size of the intracranial lesions [Figure 4]. Her mental status did not significantly improve, and the patient was ultimately discharged home with family and palliative care.

## DISCUSSION

PCNSL can present with a variety of signs and symptoms. In this case, the patient's initial presentation was secondary to distal neurolymphomatosis of the brachial plexus. The intracranial findings, with dominant lesions in the suprasellar

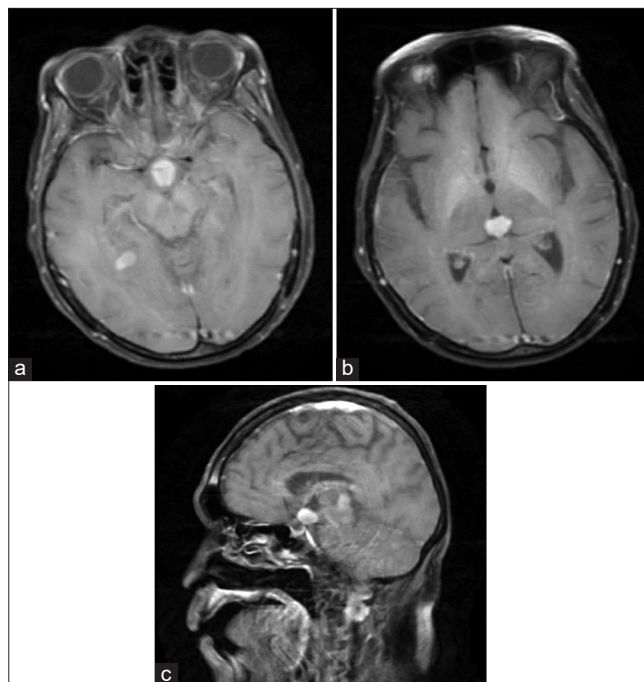


**Figure 2:** (a) Initial axial T1-weighted and gadolinium-enhanced brain magnetic resonance imaging (MRI) demonstrating enhancing lesions with heterogeneous signal intensity in the suprasellar and right periatrinal regions. (b) Initial axial T1-weighted and gadolinium-enhanced brain MRI demonstrating enhancing lesion with heterogeneous signal intensity in the pineal region. (c) Initial sagittal T1-weighted and gadolinium-enhanced brain MRI demonstrating enhancing lesions with heterogeneous signal intensity in the suprasellar and pineal regions.

and pineal regions, are atypical for the disease and could not explain the limb findings. We compare our experience with this patient to that reported in the literature.

PCNSL arises in the brain parenchyma, spinal cord, cranial nerves, eyes, or meninges; therefore, it can present with virtually any constellation of neurologic symptoms. The most common presenting symptoms are focal neurologic deficit (70%), altered mental status (43%), increased intracranial pressure (33%), seizures (14%), and vitreous involvement (4%).<sup>[1]</sup> While our patient did present with a focal neurologic deficit, her presentation is remarkable because the symptoms localized to the peripheral rather than CNS. The few reports of patients with neurolymphomatosis of the brachial plexus secondary to PCNSL are described in patients with either an established PCNSL diagnosis<sup>[2]</sup> or a long-standing history of brachial neuritis.<sup>[9]</sup> In contrast, our patient presented with 1<sup>st</sup> time, painless left arm weakness and numbness in the left fourth and fifth digits and medial palmar surface without a personal history of cancer.

PCNSL should be included in the differential diagnosis for all patients with imaging findings demonstrating multiple

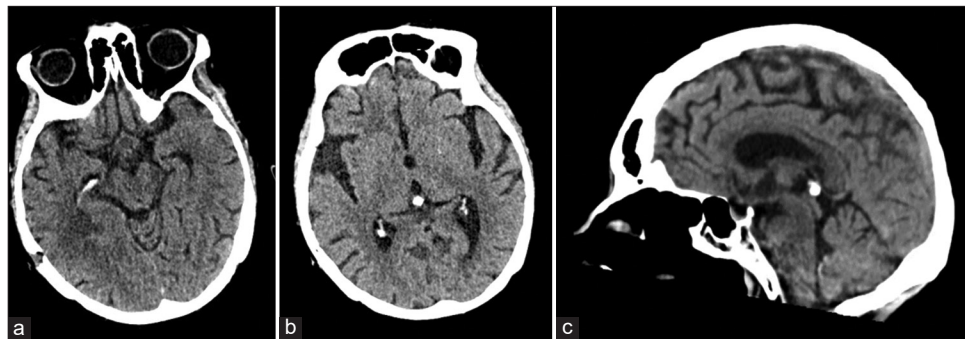


**Figure 3:** (a) Follow-up axial T1-weighted and gadolinium-enhanced brain magnetic resonance imaging (MRI) demonstrating enhancing lesions with heterogeneous signal intensity in the suprasellar and right periatrinal regions with interval increase in size. (b) Follow-up axial T1-weighted and gadolinium-enhanced brain MRI demonstrating enhancing lesion with heterogeneous signal intensity in the pineal region with interval increase in size. (c) Follow-up sagittal T1-weighted and gadolinium-enhanced brain MRI demonstrating enhancing lesions with heterogeneous signal intensity in the suprasellar and pineal regions with interval increase in size.

intracranial lesions. The typical gadolinium-enhanced brain MRI of a patient with PCNSL shows isointense to hypointense lesions on T2 sequences that enhance intensely and homogeneously with well-defined borders on T1 with gadolinium sequences. PCNSL lesions also often demonstrate restricted diffusion on diffusion-weighted imaging.<sup>[7]</sup>

The frontal and parietal lobes are the most commonly involved sites followed by the periventricular region, corpus callosum, basal ganglia, and cerebellum.<sup>[3,5]</sup> Few have reported PCNSL infiltration of the suprasellar<sup>[11]</sup> or pineal<sup>[6]</sup> regions making simultaneous involvement an exceptionally unusual and, to the authors' knowledge, a previously unreported finding. One case of nodal non-Hodgkin lymphoma metastasizing to both the suprasellar and pineal regions has previously been described.<sup>[10]</sup> Concurrent lesions in these locations are most often associated with germ cell tumors in children; lymphoma should remain on the differential diagnosis, even if it is an exceedingly rare cause of such lesions.

In both case reports of neurolymphomatosis of the brachial plexus secondary to PCNSL, diagnosis of brachial plexus



**Figure 4:** (a) Follow-up axial head computed tomography (CT) without contrast demonstrating near-complete resolution of the lesions in the suprasellar and right periatrinal regions after whole-brain radiation. (b) Follow-up axial head CT without contrast demonstrating near-complete resolution of the lesion in the pineal region after whole-brain radiation. (c) Follow-up sagittal head CT without contrast demonstrating near-complete resolution of the lesions in the suprasellar and pineal regions after whole-brain radiation.

involvement could be made using gadolinium-enhanced brachial plexus MRI that showed hyperintense thickening of the brachial plexus on T2 sequences that enhance intensely and homogeneously.<sup>[2,9]</sup> However, its reported sensitivity is only 40%, and in medically stable patients, further evaluation may be performed with EMG/NCS and PET-CT to confirm clinical localization.<sup>[2]</sup> These patients had developed symptoms related to PCNSL at least 2 months before presentation while our patient experienced symptoms for less than a week at the time of presentation, which may be insufficient time for changes to manifest on MRI and may explain both the negative MRI findings in this case and the overall poor sensitivity of brachial plexus MRI for this disease process.

In patients who are not optimal surgical candidates because of either medical comorbidities or the deep or eloquent location of their lesions, a lumbar puncture may aid in diagnosis if the leptomeninges are involved. Analyzing CSF for neoplastic lymphocytes using either cytomorphologic or polymerase chain reaction analysis reveals evidence of leptomeningeal dissemination in only 15–20% of cases.<sup>[4]</sup> When CSF studies are nondiagnostic, as in this case, they may be repeated multiple times to improve diagnostic yield. We proceeded with brain biopsy to obtain a definitive diagnosis after two nondiagnostic lumbar punctures because the patient continued to deteriorate neurologically, and the lesions continued to enlarge on serial gadolinium-enhanced brain MRI.

## CONCLUSION

PCNSL is a rare, aggressive, and extranodal non-Hodgkin lymphoma of the neuroaxis with myriad clinical manifestations that complicate and potentially delay diagnosis. Diagnosis is most commonly made through stereotactic brain biopsy following an investigative path of

gadolinium-enhanced brain and spine MRI, body imaging to exclude systemic lymphoma, slit-lamp examination, and CSF analysis. We present a 70-year-old woman with rapid onset of motor and sensory disturbances, clinically localized to the brachial plexus, who subsequently developed a CN III palsy. Gadolinium-enhanced brachial plexus, brain, and spine MRI demonstrated enhancing masses in the suprasellar, pineal, and right periatrinal regions that did not explain the neurologic deficits, and CSF studies were nondiagnostic. Stereotactic brain biopsy confirmed PCNSL. An insidious course and nonspecific presentation contribute to the difficulty of diagnosing PCNSL and initiating treatment with chemotherapy and/or radiation in a timely fashion.

## Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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