

A Case of Intraventricular Primary Central Nervous System Lymphoma

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ABSTRACT

We report a case of primary central nervous system lymphoma presenting as multiple intraventricular masses in an immunocompetent 68 year old man with severe headache and unsteady gait. The diagnosis was obtained by analysis of the cerebrospinal fluid and subsequent surgical biopsy. This is an unusual appearance for primary central nervous lymphoma, with the majority of the cases presenting as solitary masses.

CASE REPORT

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A 68 year old male patient presented with headache, unsteady gait, and elevated blood pressure after an unwitnessed fall at home. Patient's history was significant for prostate cancer which was diagnosed and treated in 2006 and chronic anemia with no recent travel. Initial head computerized tomography (CT) without contrast performed through the emergency department demonstrated hyperdense masses (Hounsfield unit 40) in the right temporal lobe and right lateral ventricle with dilated right temporal horn (Figures 1a and 1b).

Subsequent contrast enhanced magnetic resonance imaging (MRI) revealed intermediate T1 and T2 signal lesions throughout the ventricular system (Figure 2a). The lesion in the right lateral ventricle obstructs the right temporal horn (Figure 2b). The lesions demonstrate homogenous enhancement (Figures 3) with subtle abnormal restricted diffusion and low apparent diffusion coefficient (ADC) signal (Figure 2c).

Additional work-up with HIV testing and CT scans of the chest, abdomen, and pelvis was negative. The patient underwent serial lumbar punctures with the third and final lumbar puncture demonstrating abnormal lymphoid cells suspicious for lymphoma (Figure 4). Subsequent surgical biopsy of the mass obstructing the right temporal horn was performed. The surgical specimen consisted of tan-white tissue with histologic diagnosis of primary central nervous system (CNS) diffuse large B cell lymphoma (Figure 5a). Immunohistochemical stains showed the tumor cells expressed CD 20 strongly and were negative for S100, GFAP, and pankeratin (Figure 5b). Subsequent staining revealed the tumor cells to be positive for CD10, bc12, and bc16, indicating a follicular center cell derivation.

Patient experienced a complicated hospital course after biopsy with new onset atrial fibrillation and episode of cardiopulmonary arrest leading to intubation. Per patient and family request, patient was transferred to hospice care. Patient expired after extubation.

DISCUSSION

Lymphoma of the central nervous system (CNS) can present with a range of symptoms and imaging findings which can challenge both the radiologist and clinician to come to a diagnosis. Fortunately, there are several key imaging characteristics of CNS lymphoma which can help differentiate it from other disease processes. Our patient presented with fairly general and non localizing symptoms including a diffuse headache over several weeks, weight loss, gait disturbances, and a recent fall and had no neurologically significant findings on clinical examination. Based on a differential provided by CT and MRI findings, further diagnostic tests including analysis of the CSF (cerebrospinal fluid) for cytology and a brain biopsy were performed to confirm the diagnosis. It is also important to recognize that despite characteristic radiologic features of CNS lymphoma, it remains a histologic diagnosis and requires either direct brain biopsy or histologic confirmation from the CSF.

When discussing lymphoma of the CNS it is important to distinguish between primary and secondary forms. Secondary CNS lymphoma is involvement of the CNS from a systemic lymphoma and is more common than primary central nervous system lymphoma (PCNSL). Among systemic lymphomas, non Hodgkin's lymphoma (NHL) is the form that more frequently spreads to the CNS. Up to 5-9% of systemic NHL involves the CNS and typically involves the leptomeninges [1,2]. PCNSL is rare among lymphoma and comprises only 1% of all lymphomas. However, among primary brain tumors in adults, PCNSL accounts for 3-5% and is the second most common primary adult brain tumor after gliomas [3]. Histologically, 95% of PCNSL are diffuse large B-cell lymphomas [4]. Neuroimaging shows several differences between the appearance of PCNSL in the immunocompetent versus the immunocompromised. Most cases of PCNSL in the immunocompetent are diagnosed between 45-70 years of age and men and women are equally affected. [4].

The secondary involvement of the CNS with systemic lymphoma occurs at a median of 5-12 months after the primary diagnosis. Leptomeningeal spread is more common and occurs in approximately two thirds due to infiltration of the perivascular spaces. The remaining one third may present with parenchymal disease. Findings suggestive of leptomeningeal metastases include leptomeningeal, subependymal, dural, or even cranial nerve enhancement. For those patients with parenchymal disease, there may be single or multiple lesions associated with enhancement within the leptomeninges. The parenchymal lesions can have a periventricular or superficial location. [1,2]. Typically, in addition to CNS symptoms, these patients also have systemic symptoms of lymphoma at the time of diagnosis. Further workup with CT of the chest, abdomen, pelvis can help confirm the presence of systemic disease involvement [5].

As opposed to secondary CNS lymphoma, the lesions of PCNSL are nearly always found within the brain parenchyma. Purely intraventricular involvement is very rare. In the majority of immunocompetent patients, the lesions are solitary and most are supratentorial, with the posterior fossa being a

somewhat rare location. Multiple lesions have been reported in 20-40% of non-autoimmune deficiency syndrome (AIDS) PCNSL. In AIDS PCNSL, multiple lesions occur in 41-81% [1, 4, 6]. Most PCNSL (95%) will have a least one intra-axial lesion in contact with a CSF surface (ventricular or pial) [4, 5]. Some other uncommon features of PCNSL are necrosis, hemorrhage, cystic appearance, and ring enhancement. It is important to note however that ring enhancement can be seen in AIDS-related PCNSL and is difficult to distinguish from toxoplasmosis. Hemorrhage is also more frequently seen in the immunodeficient form of PCNSL. [2, 4].

The imaging characteristics of PCNSL are created by the hypercellularity of the tumor and its high nuclear to cytoplasmic ratio [1]. Just as our patient's initial CT showed a hyperdense lesion, classically, the lesions appear as hyperdense or isodense on non contrasted CT. The hyperdensity is nonspecific and can lead the incorrect consideration of hemorrhage within the lesion. Typical Hounsfield unit for acute hemorrhage is 60-90. However, the hyperdense appearance on CT can also help distinguish the tumor from metastasis and gliomas which tend to be more hypodense [6]. With contrast enhanced CT, these lesions almost always demonstrate enhancement due to disruption of the blood brain barrier.

On MRI, the typical appearance of PCNSL is hypointense to isointense on T1-weighted images (T1WI) and isointense to hyperintense on T2-weighted images (T2WI). In non AIDS patients, there is almost always homogenous contrast enhancement (90%) and it is uncommon to see ring enhancement. With the AIDS population, contrast enhancement is more irregular and ring enhancement may be seen in up to 75% of cases [1, 4]. PCNSL is sometimes referred to as a "ghost tumor" because corticosteroid administration has been reported to cause lesions to disappear or lose their contrast enhancement [3,4,6].

Mass effect tends to be mild to moderate despite occasional significant edema surrounding the tumor [6, 7, 8]. Diffusion weighted imaging (DWI) can also provide additional information. Due to the highly cellular nature of these tumors, there is often restricted diffusion making the lesions appear high intensity on DWI and hypointense on apparent diffusion coefficient (ADC) [1,4]. Our patient's tumor demonstrated mild restricted diffusion. Unfortunately, restricted diffusion itself is very nonspecific for PCNSL and can be seen with multiple other disease processes.

The top differential for intraventricular CNS lesions includes central neurocytoma, meningioma, ependymoma, choroid plexus papilloma, and metastasis [9].

Ependymomas constitute 3%-9% of all neuroepithelial neoplasms and can present at any age, with age range of 1 month to 81 years [10]. Approximately 30% are supratentorial. Of those ependymomas that occur intraventricularly, 58% originate in the fourth ventricle, whereas the remaining 42% are located in the lateral and third ventricles [10]. On nonenhanced CT images, ependymomas are usually isoattenuated, partially calcified masses. The solid

component tends to enhance, with calcification in 40-80% [9]. On MRI the mass appears isointense on T1 and hypointense on T2 with heterogeneous signal due to calcification, hemorrhage, and cystic components. Multiple intraventricular ependymomas can be seen with leptomeningeal spread of tumor, usually from an infratentorial source.

Choroid plexus papillomas account for 0.4%-0.6% of all intracranial tumors, with the lateral ventricle being the common site and more than one mass occurring in only 5% [11]. Clinical presentation relates to elevated intracranial pressure predominantly due to increased CSF production by the tumor. Imaging findings include an isodense to hyperdense, lobulated appearance on noncontrast CT. Calcifications can be found in approximately 24% [11]. On MRI the lesions tend to be isointense to hypointense on T1 with variable T2 signal and prominent flow voids. Rare case reports have been published of multiple choroid plexus papillomas.

Central neurocytomas constitute approximately 0.25%-0.5% of all intracranial tumors with the mean age at presentation of 29 years [9]. Lesions predominantly involve the lateral and third ventricles, and half of the cases involve the lateral ventricles near the foramen of Monro. The imaging appearance is of a well-circumscribed, intraventricular mass with internal cyst-like areas. On CT images, the lesions are hyperattenuated. Cyst-like areas are noted in two-thirds of the cases, while calcification is present in half of the cases. Moderate enhancement is typical. On MR images, the solid portions of the tumor are isointense to cerebral cortex on T1-weighted images and isointense-to-hyperintense on T2-weighted images. Heterogeneous signal can be due to prominent flow voids. A broad attachment to either the lateral ventricle wall or the septum pellucidum is almost always present.

Metastases to the choroid plexus are rare, accounting for 0.9-4.6% of all cerebral metastases [13]. The most common sources are renal cell and lung carcinoma with other sources including melanoma, gastric carcinoma, colon carcinoma, and lymphoma [13]. The most common site is the lateral ventricle. Imaging findings include isodense to hyperdense appearance on CT with hypointense T1 signal and hyperintense T2 signal on MRI. Metastases tend to homogeneously enhance.

Intraventricular meningiomas are rare, comprising only 0.5-3% of all meningiomas [14]. They are most commonly found in the lateral ventricles, and more frequently on the left than the right. The intraventricular meningiomas arise from arachnoid cells contained within the choroid plexus. The masses tend to present in patients age 30-60 with a 2:1 female to male ratio [14]. Most of the clinical presentation occurs from increased intracranial pressure. Imaging findings include hyperdense appearance on CT with 50% containing calcification. On MRI meningiomas demonstrate isointense to hypointense T1 and T2 signal with avid enhancement.

Intraventricular presentation of PCNSL is quite rare. Most of the intraventricular lesions occur as solitary masses and have overlapping imaging characteristics. The most important

role of imaging in PCNSL is directing clinicians to perform a stereotactic biopsy or obtain CSF in order to obtain a histologic diagnosis and avoid futile attempts at resection [4]. Resection does not play a therapeutic role in PCNSL and can worsen neurologic deficits [15]. Overall, prognosis has improved over the past several decades and PCNSL is a very chemosensitive and radiosensitive tumor. Most oncologists agree upon a methotrexate chemotherapy regimen in addition to whole brain radiation, although there is increased risk of neurotoxicity with radiation [3,15].

TEACHING POINT

Primary central nervous system lymphoma (PCNSL) can have a range of imaging characteristics which are non specific but can aid in distinguishing this lesion from others encountered within the central nervous system, such as the intraparenchymal and supratentorial location and typical lack of necrosis, hemorrhage, cystic appearance, and ring enhancement (except in autoimmune deficiency syndrome (AIDS)- related PCNSL). It is important for the radiologist to communicate PCNSL in the differential diagnosis so clinicians can obtain tissue via brain biopsy or cerebrospinal fluid cytology as PCNSL remains a histologic diagnosis.

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FIGURES

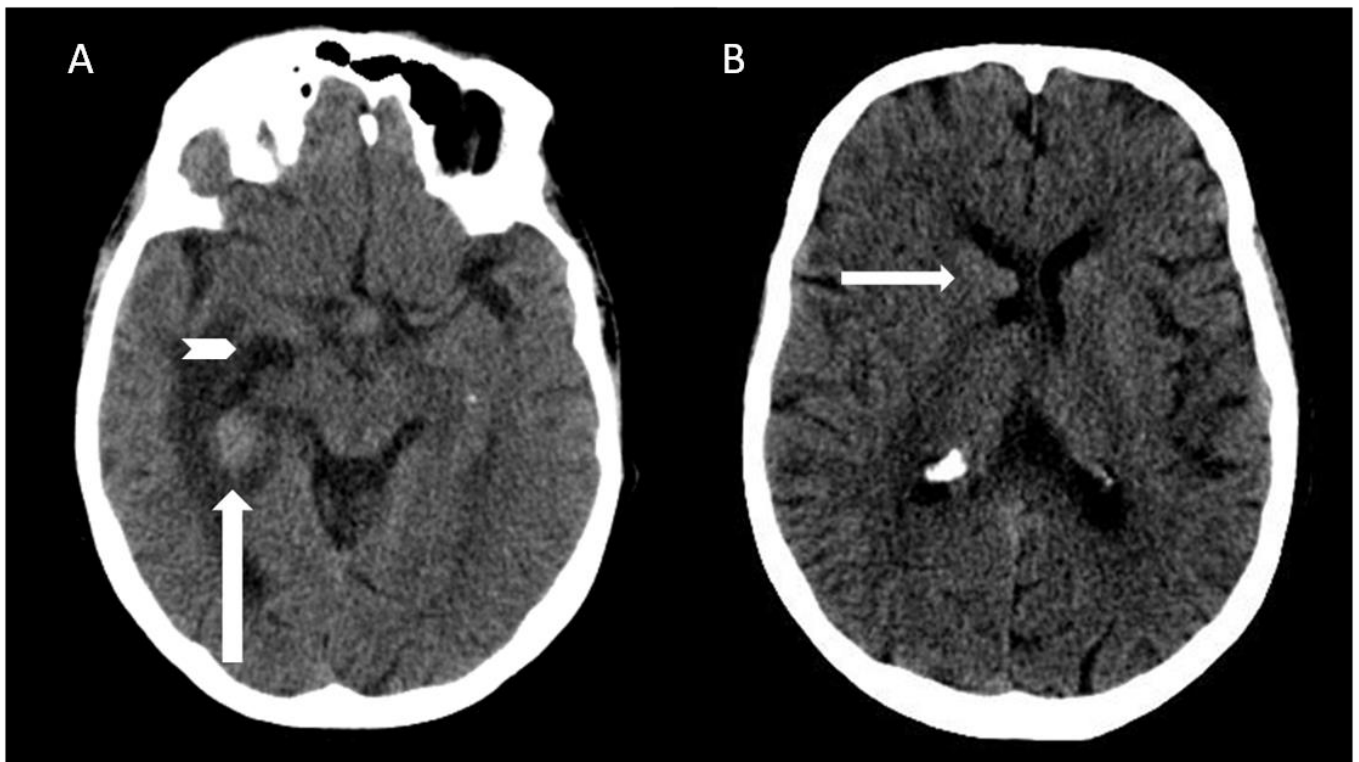


Figure 1: 68 year old man with primary CNS lymphoma. a) Axial CT image without contrast demonstrates 1.6 cm hyperdense mass in the right temporal lobe (arrow) with dilated right temporal horn (arrowhead). b) Axial CT image without contrast demonstrates 8 mm hyperdense mass in the right lateral ventricle adjacent to the caudate head (arrow). CT: Aquilion 120 kVp, 250 mA, 5 mm slices.

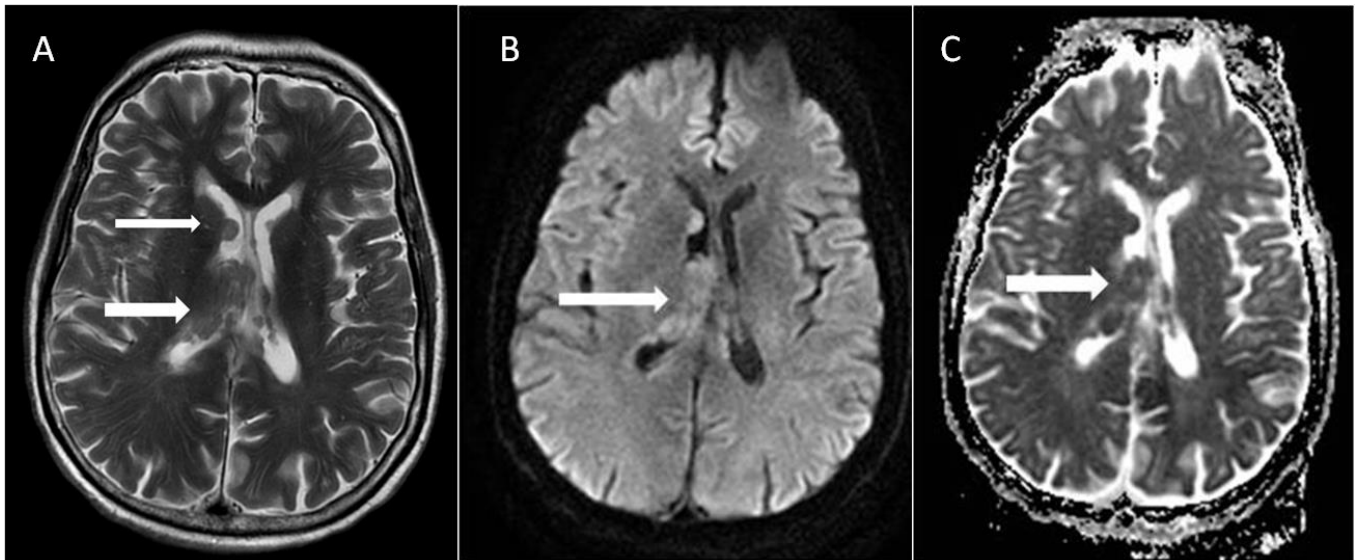


Figure 2: 68 year old man with primary CNS lymphoma.

- a) Axial T2 weighted MRI image without contrast demonstrates 8 mm and 1.3 cm intermediate signal lesions adjacent to the caudate in the right lateral ventricle (arrows). MRI: 3 Tesla magnet, T2 (TE 91.4869, TR 5000), axial, 5 mm slice.
- b) Axial DWI MRI image demonstrates slightly abnormal restricted diffusion in the right lateral ventricle lesions (white arrows). MRI: 3 Tesla magnet, Diffusion Weighted Imaging (TE 76.8, TR 7000), axial 5 mm slice.
- c) Axial ADC MRI image demonstrates slightly low signal in the right lateral ventricle lesions. MRI: 3 Tesla magnet, Apparent Diffusion Coefficient TE 76.8, TR 7000), axial 5 mm slice.

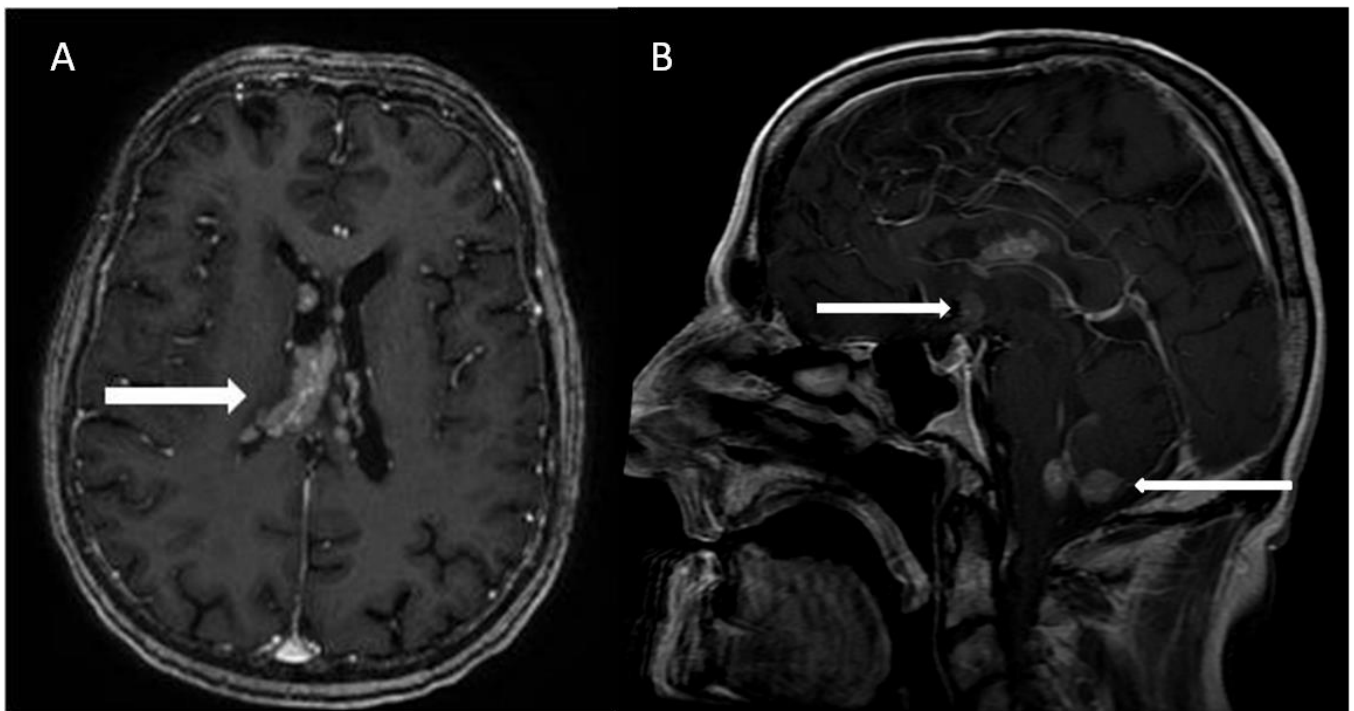


Figure 3: 68 year old man with primary CNS lymphoma.

- a) Axial FSPGR postcontrast MRI image with contrast demonstrates two larger and greater than ten smaller homogeneously enhancing lesions throughout the right lateral ventricle (arrow) and the left lateral ventricle. MRI: 3 Tesla magnet, FSPGR Bravo 3D postcontrast (TE 3.496, TR 8.916), axial, 20mL Prohance, 1.20 mm slice.
- b) Sagittal T1 weighted MRI image with contrast demonstrates three 1.3 cm homogeneously enhancing lesions in the fourth ventricle outflow and foramen magnum (arrow) as well as the floor of the third ventricle (arrowhead). MRI: 3 Tesla magnet, T1 postcontrast (TE 12, TR 516.668), axial, 20mL Prohance, 5 mm slice.

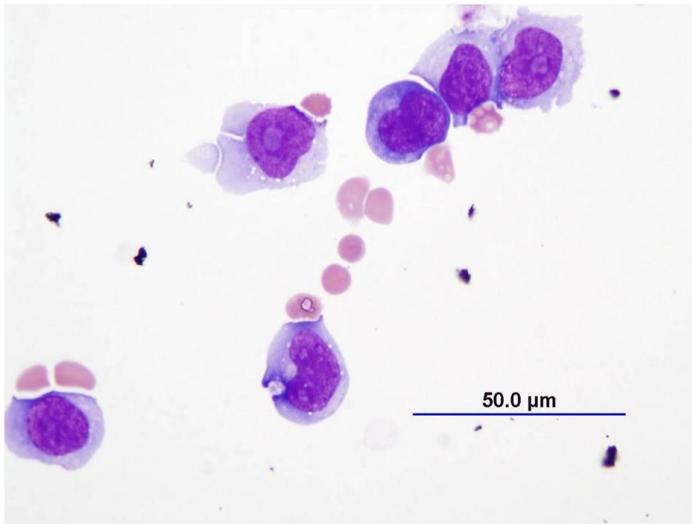


Figure 4 (left): 68 year old man with primary CNS lymphoma. Wright-Giemsa stained cytocentrifuge preparations of the CSF at 50 x magnification demonstrate scattered large, atypical lymphoid cells with ovoid to indented to irregular nuclear membranes, medium to coarse chromatin, one to multiple nucleoli and moderate, basophilic cytoplasm with occasional small vacuoles.

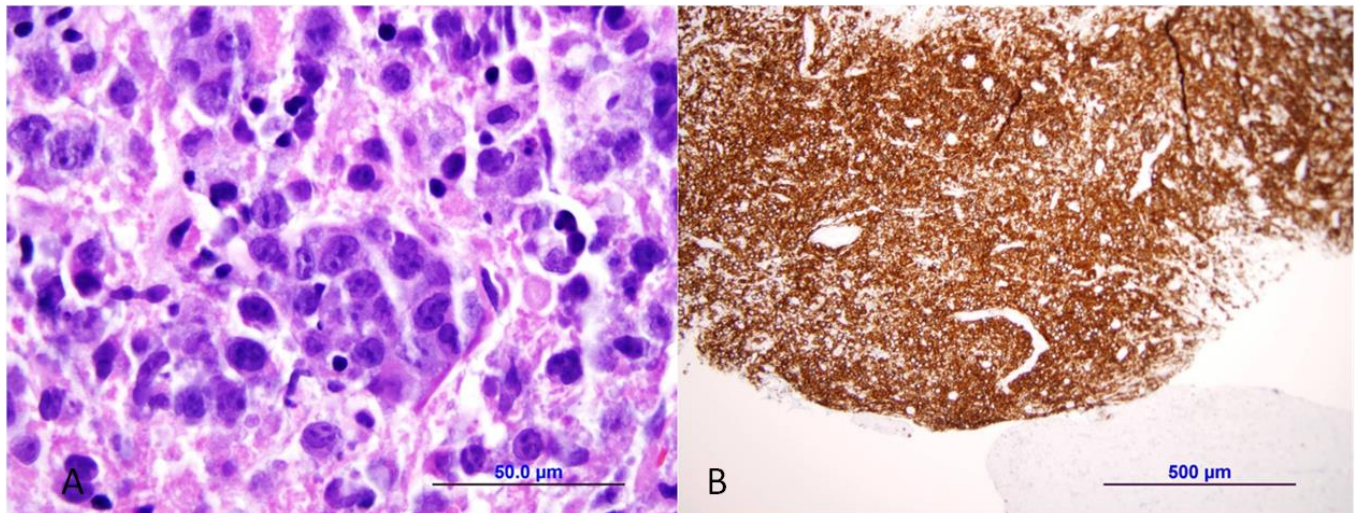


Figure 5: 68 year old man with primary CNS lymphoma.

- a) Hematoxylin-Eosin stained tissue biopsy from the temporal lesion at 50 x magnification demonstrates large, atypical lymphoid cells with ovoid to indented to irregular nuclear membranes, medium to vesicular chromatin, one to multiple nucleoli and moderate, cytoplasm in a background of necrosis.
- b) CD20 (pan B-cell) immunohistochemical stained tissue biopsy from the temporal lesion at 5x magnification demonstrates diffuse positivity of the atypical lymphoid cells.

Etiology	<ul style="list-style-type: none"> • 95% are diffuse large B- cell lymphomas. • May be seen in immunocompetent individuals or the immunocompromised.
Incidence	<ul style="list-style-type: none"> • Represents 1% of all lymphomas. • Accounts for 3-5% of primary brain tumors in adults. • Second most common primary brain tumor after gliomas. • Incidence has been rising in the immunocompromised for unclear reasons.
Gender Ratio	<ul style="list-style-type: none"> • Men and women are equally affected.
Age Predilection	<ul style="list-style-type: none"> • Typically between 45-70 years of age in the immunocompetent.
Risk Factors	<ul style="list-style-type: none"> • In immunocompetent patients, no specific risk factors have been identified. • An immunocompromised state (congenital, iatrogenic, or infectious) is a known risk factor. • Reported association between Epstein-Barr virus and primary CNS lymphoma in the immunocompromised.
Presentation	<ul style="list-style-type: none"> • Symptoms of increased intracranial pressure such as headache and nausea are found in 60%. • Behavioral changes can be seen in 24-73%. • Hemiparesis and ataxia/cerebellar symptoms are the most frequent focal neurological signs.
Treatment	<ul style="list-style-type: none"> • Histologic diagnosis that requires brain biopsy or pathologic confirmation by cerebrospinal fluid (CSF) cytology. • Methotrexate based chemotherapy regimen and typically whole brain radiation. • Surgical resection does not play a role in treatment of primary CNS lymphoma.
Prognosis	<ul style="list-style-type: none"> • The median survival duration with radiation therapy alone averages 18 months. • Methotrexate based chemotherapy alone results in median survival duration approaching 48 months. • The prognosis is improving with both radiation therapy and methotrexate based chemotherapy combined.
Findings on Imaging	<ul style="list-style-type: none"> • Typically solitary, supratentorial, and found within the brain parenchyma in the immunocompetent. • Isodense to hyperdense on non-contrast CT. • Hypointense to isointense on T1WI and isointense to hyperintense on T2WI with avid enhancement and most display some level of restricted diffusion. • Necrosis, hemorrhage, cystic appearance, and ring enhancement are rare especially in the immunocompetent. Ring enhancement and hemorrhage can be seen in the immunodeficient form. • Corticosteroid administration can cause the lesions to disappear or lose their enhancement, thus giving them the term "ghost tumors".

Table 1: Summary table for primary central nervous system lymphoma

Diagnosis	Location	CT	MRI T1WI	MRI T2WI	Contrast
Primary CNS Lymphoma	<ul style="list-style-type: none"> Typically solitary, supratentorial, and intraparenchymal in the immunocompetent. 	<ul style="list-style-type: none"> Isodense to hyperdense 	<ul style="list-style-type: none"> Hypointense to isointense 	<ul style="list-style-type: none"> Isointense to hyperintense 	<ul style="list-style-type: none"> Homogenous enhancement Can see ring enhancement and necrosis in immunocompromised form
Central Neurocytoma	<ul style="list-style-type: none"> Typically found in the lateral ventricle, usually in its anterior portion near the foramen of Monro. 	<ul style="list-style-type: none"> Hyperdense Cyst-like areas and calcifications. 	<ul style="list-style-type: none"> Isointense 	<ul style="list-style-type: none"> Hyperintense cystic areas and hypointense solid areas 	<ul style="list-style-type: none"> Moderate enhancement
Metastasis	<ul style="list-style-type: none"> Lateral ventricles more than third ventricle 	<ul style="list-style-type: none"> Isodense to hyperdense 	<ul style="list-style-type: none"> Hypointense 	<ul style="list-style-type: none"> Hyperintense 	<ul style="list-style-type: none"> Homogenous enhancement
Meningioma	<ul style="list-style-type: none"> Lateral ventricles, left more than right 	<ul style="list-style-type: none"> Hypodense 	<ul style="list-style-type: none"> Hypointense to isointense 	<ul style="list-style-type: none"> Hyperintense 	<ul style="list-style-type: none"> Transient contrast enhancement during active demyelination
Ependymoma	<ul style="list-style-type: none"> Fourth ventricle 	<ul style="list-style-type: none"> Hypodense; Calcification in 40-80% 	<ul style="list-style-type: none"> Isointense to hypointense 	<ul style="list-style-type: none"> Hyperintense 	<ul style="list-style-type: none"> Heterogeneous enhancement due to cystic change, flow voids, calcification, or hemorrhage
Choroid Plexus Papilloma	<ul style="list-style-type: none"> In adults occur more often in the fourth ventricle 	<ul style="list-style-type: none"> Isodense to hyperdense 	<ul style="list-style-type: none"> Typically hypointense 	<ul style="list-style-type: none"> Hyperintense 	<ul style="list-style-type: none"> Intense enhancement with heterogeneous signal due to flow voids, calcification, or hemorrhage

Table 2: Differential diagnosis table for primary central nervous system lymphoma

ABBREVIATIONS

ADC = Apparent diffusion coefficient
 CNS = Central nervous system
 CSF = Cerebrospinal fluid
 CT = Computerized Tomography
 DWI = Diffusion weighted imaging
 NHL = Non Hodgkin's lymphoma
 MRI = Magnetic Resonance Imaging
 PCNSL = Primary central nervous system lymphoma
 T1WI = T1-weighted images
 T2WI = T2-weighted images

KEYWORDS

Primary CNS lymphoma; intraventricular masses

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