Imaging of Lymphoma of the Central Nervous System, Spine, and Orbit

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• Lymphoma • Primary CNS lymphoma (PCNSL)
• Non-Hodgkin lymphoma • Magnetic resonance (MR)
• Computed tomography (CT) • Spectroscopy • Perfusion
• Diffusion tensor

Both systemic lymphoma and primary central nervous system (CNS) lymphoma (PCNSL) may directly involve the neuraxis. These non-Hodgkin lymphomas (NHL) are usually caused by the malignant transformation of B lymphocytes, although some systemic T-cell lymphomas can also have high rates of CNS involvement. A total of 10% to 15% of patients with systemic lymphoma have CNS disease caused by disseminated disease. This number may vary depending on the definition of CNS involvement by imaging, clinical, or cerebrospinal fluid (CSF) criteria, with most disseminated disease manifesting in the CSF.

PCNSL represents 1% of all lymphomas, less than 5% of all NHLs, and only 3% to 5% of all primary brain tumors.[1] The increased incidence that has occurred since the 1990s cannot be explained simply by increased imaging.[2] Most PCNSL are aggressive malignancies of the diffuse large B-cell lymphoma type. Patients with PCNSL should have disease that is restricted entirely to the brain, eye, and spinal cord; careful extent of disease evaluation in patients with presumed PCNSL discovers a reservoir of systemic disease in 4% to 8% of the patients.[3,4]

Lymphomas are aggressive malignancies that require rapid diagnosis. Imaging findings that are suggestive for lymphoma should preclude corticosteroid therapy and facilitate stereotactic biopsy rather than resection. Evidence of CSF or ocular involvement or vitrectomy may be used to provide the tissue diagnosis if present without brain biopsy.

PART I: INTRACRANIAL LYMPHOMA

Clinical Features

The clinical prodrome is relatively short, as most cases are diagnosed within 1 to 2 months after the onset of symptoms. The presentation is determined by the location and size of the tumor, and may include nonspecific focal neurologic deficits, behavioral and personality changes, headaches, hydrocephalus, or seizures. Although systemic lymphoma can present with focal enhancing mass lesions like PCNSL, systemic lymphoma

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more typically manifests with disseminated leptomeningeal disease.

Prognosis

The overall survival of patients with PCNSL is significantly worse than that in patients with similar types of extranodal NHL. The most widely accepted prognostic factors are age and performance status at time of diagnosis.[5] Poor prognostic factors include disease in deep brain structures, decreased performance status, increased patient age, increased serum lactate dehydrogenase, and increased CSF protein.[6] With an increased number of risk factors, the 2-year survival falls from 80% to 48% to 15%.[6]

Imaging Evaluation

The initial study for most patients with new neurologic signs or symptoms is a noncontrast CT scan, particularly for patients with acute findings or who present to the emergency department. This noncontrast CT is then followed by a contrast study. PCNSL involves the supratentorial brain in 87% of cases.[7] Typical locations include the cerebral hemispheres, periventricular white matter, deep gray matter, corpus callosum, subependymal region, and adjacent to other CSF spaces (**Fig. 1**). Lymphomas of the corpus callosum are nearly double the size of lymphomas at other locations.[8] Atypical locations for PCNSL include the brainstem, cranial nerves, cavernous sinuses, pineal gland, and pituitary gland (**Fig. 2**). The tendency to abut the ependymal surface in 28% to 38% or meningeal surface in 8% to 13% may reflect the PCNSL origin from the periadventitial cells of arterioles penetrating through the Virchow-Robin spaces in these regions (**Fig. 3**).[9,10,11,12] The imaging differences between immunocompetent and immunocompromised patients are summarized in **Table 1**.

Immunocompetent Patients

Lymphoma is usually hyperdense on noncontrast CT scans because of its high cellularity and nucleus-to-cytoplasm ratio. On MR imaging, this high cellularity results in tumors that are isointense to hypointense relative to gray matter on T1-weighted images, and isointense to hypointense on T2-weighted images.[9] With iodinated (CT) or gadolinium (MR imaging) contrast agent, more than two thirds of tumors reveal moderate to intense homogeneous enhancement and mild to absent peritumoral edema.[9,12] Focal tumors that are hyperintense on T2-weighted images and have moderate heterogeneous to absent enhancement may represent low-grade lymphomas.[13] Lymphoma may also uncommonly present as diffusely infiltrative or nonenhancing lesions.

Immunocompromised Patients

Disruption of the normal immune system from any cause (eg, HIV and AIDS; posttransplant pharmacologic immunosuppression; congenital diseases, such as IgA deficiency, severe combined immunodeficiency, and ataxia-telangiectasia) is an important risk factor for PCNSL.

The immunocompromised patient is more likely to have lymphoma occur in an atypical location. Intratumoral calcifications and blood products are uncommon but may be seen (**Figs. 4** and **5**). Nearly one half of immunocompromised patients have heterogeneous, often peripheral rim-enhancing tumors with cystic or necrotic components and marked peritumoral edema,[9] whereas some may have no enhancement at all. The presence of necrosis and heterogeneous enhancement are important differences between the imaging appearance of lymphoma in immunocompromised versus immunocompetent patients.

Differential Diagnosis

The typical imaging features of lymphoma can be used to narrow the differential diagnosis, initiate stereotactic biopsy, and prompt chemotherapy and radiation therapy. The different diagnostic clues are discussed next.

Signal intensity

Lymphoma shows prominent CT hyperdensity and MR imaging T2 shortening (hypointense signal) because of its high nucleus-to-cytoplasm ratio and relatively low intratumoral water content. This hypointense T2 signal distinguishes lymphoma from other lesions that usually demonstrate hyperintense T2 signal, such as gliomas, metastases, and demyelinating disease. Some highly cellular gliomas may also show hypointense T2 signal, but these are much more likely to contain blood products, have infiltrative margins, and reveal heterogeneous enhancement. Blood products are more typical for metastatic disease from melanoma, renal cell, breast, and lung carcinomas. These metastases are usually located at the gray-white junctions and often incite marked peritumoral edema, unlike the little peritumoral edema of lymphoma.

Corpus callosum

The main differential possibility for lymphoma centered at the corpus callosum is a glioblastoma multiforme. These high-grade gliomas show hemorrhagic and cystic-necrotic changes with heterogeneous enhancement in 95%, compared with lymphomas that are usually homogeneous with