Primary central nervous system lymphomas: CT, MRI and MR spectroscopy findings at presentation

Poster No.: C-2577
Congress: ECR 2015
Type: Educational Exhibit
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Keywords: Lymphoma, Imaging sequences, MR-Spectroscopy, MR, CT, Oncology, Neuroradiology brain, CNS
DOI: 10.1594/ecr2015/C-2577

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Learning objectives

1. to review typical as well as atypical CT and MRI findings of PCNLS
2. to illustrate the spectrum of appearances of PCNLS with selected case examples from our institution.
3. to emphasize role of spectroscopy in differential considerations
4. to briefly review the current literature.
Background

Primary central nervous system lymphoma (PCNSL) is a form of extranodal lymphoma defined as isolated involvement of the craniospinal axis in the absence of primary tumor elsewhere in the body. PCNSLs are typically involving the brain, less often the leptomeninges, eyes and spinal cord. These rare aggressive neoplasms of the brain represent about 3 percent of all primary brain tumors [1]; their incidence is significantly higher in the immunocompromised patients than in general population. Long-term immunosuppression in transplant patients, AIDS and autoimmune disease are conditions associated with increased risk of primary CNS lymphomas. Clinical presentation is variable and depends on localization and the immune status of the patient: more than half of patients have non-focal, non-specific symptoms like altered mental status, symptoms of increased intracranial pressure and/or generalized seizures. Focal neurologic deficit or partial seizures are uncommon, but possible symptoms.
Findings and procedure details

Our series consists of 70 patients admitted to our center for advanced MR exam whose findings included lymphoma in the differential diagnosis; In all patients, patochistological examination of lesion was done and only by 11 was PCNLS confirmed.

10 patients underwent presurgical in vivo single-voxel MRS at short echo time (TE, 35 ms) and multi-voxel MR spectroscopic imaging at long TE (144 ms).

3.1. Pathohistology

PCNSLS are large B-cell non-Hodgkin lymphomas, usually high or intermediate grade. The brain is the only tissue environment in which large B-lymphoma cells accumulate densely around tumor vessels so tumor exhibit angiotropism [2]. Confluent areas of tumor may show necrosis, with residual viable tumor cells being found mostly around blood vessels [3]. The degree of necrosis differs between the immunocompetent and the immunocompromised hosts, with the latter group harboring a higher percentage of intratumoral necrosis.

3.2 Anatomical distribution

PCNLS are typically located in supratentorial brain parenchyma: the most frequent locations are periventricular white matter, the basal ganglia and the corpus callosum, frequently abutting ependymal or subarachnoid surface. Bilateral basal ganglia (BG) involvement is common.

The brain stem or cerebellum or both are affected in 9%-13%, and the spinal cord, in only 1%-2% of patients [5].

3.3 Imaging findings

Characteristic imaging features of PCNSL are supratentorial contrast-enhancing mass, relatively homogeneous, with a diameter of at least 15 mm. Single tumor manifestations occur in 60-70% of patients, however, immunodeficient patients frequently have multiple lesions at diagnosis [1]. The lesions vary in circumscription. Hemorrhage within the tumor is a rare finding, more frequent in AIDS patients.

Perilesional edema can be present in variable extent, from moderate to extensive.

Non-Contrast Imaging: Due to its hypercellular nature, lymphomas are typically iso- or hyperdense masses on non-enhanced CT, and iso- or hypointense to gray matter on T1W. T2W signal intensity varies from hypo- to iso- to hyper- dense. T2W hypointensity
reflects low water content within the cells which have a high nuclear-cytoplasmic ratio.

Enhancement patterns: After administration of intravenous contrast in immunocompetent patients, lymphoma demonstrate pronounced uniform contrast enhancement. Contrast-enhancing, thickened ependyma may be seen indicating leptomeningeal infiltration.

Higher degree of necrosis correlates with hyperintensity on T2-weighted MR images and rim enhancement and absence of restricted diffusion.

Diffusion-weighted MR imaging: Lymphomas are hypercellular tumors with high nuclear-cytoplasmic ratio; therefore, PCNSL are frequently hyperintense on DWI and hypointense on ADC maps. In case of necrotic areas within the tumor the decrease in ADC values is not a consistent finding [4].

High-resolution SWI is much more sensitive than conventional MR imaging for the visualization of small veins, blood products, and calcifications, which appear as low-signal intensity structures. This is helpful in differentiating PCNSL from high-grade gliomas, because microhemorrhages and calcifications are rare in PCNSL, whereas small hemorrhages are frequently seen in high-grade gliomas [5].

3.4 MRS characteristics

High Cho/Cr ratios and reduced Na are indicators of neoplastic origin, but nonspecific for lymphoma. These findings reflects increased cell membrane turnover and breakdown (increased Cho and lipids), and necrotic portions of the tumor (Lac and lipids) and can also be seen in high grade glioma or metastasis [6]. Increased Lac and lipids along with a prominent Cho peak, minimal NAA, Cr, and ml- depending on the amount of surrounding brain tissue in the voxel - (Figure X).

3.5 Differential diagnosis

Differential considerations include metastasis, ependymal spread of anaplastic glioma, demyelinating disorders, sarcoidosis, subacute infarcts; space-occupying lesions of infective etiology like toxoplasmosis should be considered in HIV-positive patients.

Involvement of the corpus callosum is suggestive of CNS lymphoma, but such involvement also occasionally occurs with anaplastic glioma and metastatic neoplasm. Lymphomas differ from glioblastoma multiforme because they usually have less peritumoral edema, are more commonly multiple and less commonly necrotic [7]. Metastasis have a predilection for the gray/white matter interface.

Subependymal enhancement should be actively sought on imaging studies as a potential clue to lymphomatous involvement.
**Fig. 1:** Typical features of PCNSL: Noncontrast and contrast CT images (1A and 1B) shows large solitary homogeneously enhancing mass. Axial T2W (1C) and T1W (1D) images shows that signal intensity of lesion is similar to gray matter. Moderate perilesional vasogenic edema is present.

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Fig. 2: Same patient as in Fig 1. Diffusion Weighted Imaging (Fig.2.A.) with ADC map (Fig 2.B) demonstrates restricted diffusion due to tumor hypercellularity and high nuclear/cytoplasmic ratio.

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**Fig. 3:** Axial contrast-enhanced T1-weighted MR image in patient with disseminated disease shows atypical intraventricular location with involvement of underlying periventricular white matter. Deep gray matter was also infiltrated.

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**Fig. 4:** Coronal FLAIR image (5.A) reveals space occupying lesion extending across corpus callosum. Multivoxel SE 144 spectroscopy (5.B), showing increased choline to creatine ratio, low N-acetylaspartate, heterogeneous distribution of lactate. Singlevoxel SE 144 and SE 35 spectroscopy: Fig 5.C Cho/Cr = 2.72 NAA/Cr = 0.68, Fig 5.D Cho/NAA= 4.33; ml/Cr= 1.1.

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Fig. 5: T2W (6A), GRE (6B), T1W pre- and postcontrast images (6C and 6D) reveals space occupying lesion, relatively homogenous except in small central area which is necrotic. On GRE images, susceptibility variations permits identification of subtle paramagnetic deposits. Microhemorrhages and calcifications are uncommon in PCNSL, but can be present, especially in immunocompromised patients.

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**Fig. 6:** Same patient as in Fig 5. Lesion was extirpated but follow-up CT exam 6 months later with noncontrast and postcontrast study revealed tumor recurrrens with bithalamic extension.

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**Fig. 7:** Diffuse angiocentric lymphoma in 45-years old female with altered mental status: T2W coronal and sagittal images shows infiltrative lesion with bilateral, relatively
symmetric involvement of frontal and temporal lobes, thalami, and corticospinal tract. Optic chiasm and optic nerve radiations were also involved.

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Fig. 8: Same patient as in Fig 7. Axial PROPELLER sequence reduces motion artefact and demonstrates diffuse infiltrative pattern of growth with bilateral symmetric FLAIR hyperintensities in basal ganglia and adjacent white matter.

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Conclusion

Solitary, homogeneously enhancing mass with predilection for the periventricular and superficial regions are features suggestive but not specific for PCNSL; also they may not always be present. Atypical appearance is more frequent in immunocompromised patients and may be misleading. DWI and spectroscopy have been shown to provide additional diagnostic information. Spectroscopy may aid the differentiation between CNS neoplasm and nonneoplastic lesion such as toxoplasmosis/ PML in immunocompromised patients. Proper characterization is mandatory in order to avoid misdiagnosis and an unnecessary extent of surgery.
References


