Section: Radiodiagnosis

Original Research Article

CONVENTIONAL AND ADVANCED MAGNETIC RESONANCE IMAGING IN CENTRAL NERVOUS SUSTEM LYMPHOMA: EQUIVOCAL TO INVASIVE DIAGNOSIS?

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Received : 10/05/2026
Received in revised form : 17/06/2026
Accepted : 02/07/2026

Keywords:
Advanced MRI, Conventional MRI, Enhancement, Perfusion, Primary central nervous system lymphoma, Spectroscopy.

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DOI: 10.47009/jamp.2026.8.4.190

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (4); 1135-1138

ABSTRACT

Background: Primary central nervous system lymphoma (PCNSL) is an aggressive 2nd most common primary CNS tumor, next to gliomas that occurs in both immunocompromised and immunocompetent hosts. A brain biopsy is the gold standard for diagnosing PCNSL at present, but its invasive nature can cause morbidity and mortality. Thus, non-invasive imaging to avoid an unnecessary surgical procedure is the way forward. Advanced neuroimaging is useful for differentiating PCNSL with neoplasm such as glioblastoma, metastases, multiple sclerosis, tumefactive demyelination and brain abscesses, especially in atypical presentations. PCNSL may have characteristic imaging finding on conventional MR, however, it cannot unequivocally differentiate PCNSL from other brain neoplasm. **Aim:** The aim of the study was to evaluate MRI morphological characteristics in biopsy-proven PCNSL using conventional and advanced techniques. **Materials and Methods:** We retrospectively evaluated 11 patients using conventional and advanced MR imaging in a biopsy-proven PCNSL. The pretreatment MR images of patients with PCNSL confirmed with biopsy, are reviewed. We included only immunocompetent patients. All images were reviewed according to the location of the lesion, signal intensity, enhancement, MRS and perfusion characteristics. The presence of any calcifications, cystic or necrosis and hemorrhage were also examined. **Results:** PCNSL lesions enhanced homogenously in 09 cases, while nonhomogeneous enhancement was observed in 02 cases. The lesions showed iso to hypointense on T1W and T2W in 09 cases and hyperintense on T2W in 02 cases. Symmetrical lesions involving the genu or splenium of the corpus callosum referred to as "butterfly pattern" is seen in 06 cases. All the lesions showed restricted diffusion with corresponding low ADC values (0.4-1.0 □ 10^{-3} mm^2/s). Spectroscopy showed increased Cho peak, decreased NAA and Cr peak with elevated Cho/NAA (2-10) and Cho/Cr (2-5). Lipids peaks were noted in 3 cases. MR perfusion revealed modest reduction in rCBV (0.7-1.3) and rCBF (0.7-1.6) suggestive of lesions being hypo-perfused. Delayed percentage signal recovery overshooting baseline is seen in 09 cases. **Conclusion:** Combining advanced MR imaging with conventional imaging shows significant improvement in the morphological characterization of PCNSL. This study shows considerable accuracy of advanced MR imaging in identifying PCNSL and can become an important radiological diagnostic tool which can replace invasive surgical biopsy for diagnosis in near future.

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is an aggressive 2nd most common primary CNS tumor, next to gliomas that occurs in both immunocompromised and immunocompetent hosts. A brain biopsy is the gold standard for diagnosing PCNSL at present, but its invasive nature can cause morbidity and mortality. Thus, non-invasive imaging to avoid an unnecessary surgical procedure is the way forward. Advanced neuroimaging is useful for differentiating PCNSL with neoplasm such as glioblastoma, metastases, multiple sclerosis, tumefactive demyelination and brain abscesses, especially in atypical presentations. PCNSL may have characteristic imaging finding on conventional MR, however, it cannot unequivocally differentiate PCNSL from other brain neoplasm. The PCNSL

ISSN (O): 2687-5365; ISSN (P): 2753-6556

manifest as increased Cho peak, decreased N-acetylaspartate (NAA), increased choline/Cr, lactate and lipid peaks, diffusion restriction and relative hypoperfusion aiding in its differentiation from other brain lesions. Advanced MR imaging may, in the near future, substantially improve the diagnostic accuracy, ultimately facilitating a non-invasive method of diagnosis. It holds important especially in PCNSL as contrary to other malignant tumors, treatment is chemoradiation.[1]

Aim

The aim of the study was to evaluate MRI morphological characteristics in biopsy-proven PCNSL using conventional and advanced techniques.

MATERIALS AND METHODS

We retrospectively evaluated 11 patients using conventional and advanced MR imaging (6 females, 5 males) in a biopsy-proven PCNSL, in the Department of Radiodiagnosis, JNIMS, Imphal, Manipur. The pretreatment MR images of patients with PCNSL confirmed with biopsy, are reviewed. We included only immunocompetent patients. All images were reviewed according to the location of the lesion, signal intensity, enhancement, MRS and perfusion characteristics. The presence of any calcifications, cystic or necrosis and hemorrhage were also examined.

RESULTS

PCNSL lesions enhanced homogenously in 09 cases, while nonhomogeneous enhancement was observed in 02 cases. The lesions showed iso to hypointense on T1W and T2W in 09 cases and hyperintense on T2W in 02 cases. Symmetrical lesions involving the genu or splenium of the corpus callosum referred to as "butterfly pattern" is seen in 06 cases. [Figure 1]

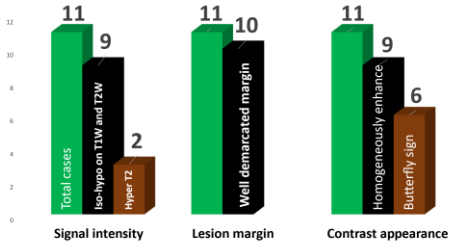


Figure 1: Morphological characteristics of PCNSL on MR imaging

All the lesions showed restricted diffusion with corresponding low ADC values (0.4-1.0 □ 10-3 mm2/s). Spectroscopy showed increased Cho peak, decreased NAA and Cr peak with elevated Cho/NAA (2-10) and Cho/Cr (2-5). Lipids peaks were noted in 3 cases. MR perfusion revealed modest reduction in rCBV (0.7-1.3) and rCBF (0.7-1.6) suggestive of lesions being hypo-perfused. Delayed percentage signal recovery overshooting baseline is seen in 09 cases. [Figure 2-8]

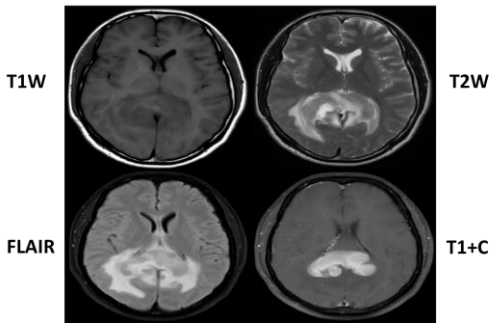


Figure 2: An axial T1W and T2 weighted MR images shows the splenial lesion appearing isointense with respect to gray matter. Bilateral parietal edema is T2W/FLAIR hyperintense. An axial T1W+C MR image after contrast shows homogenous intense enhancement

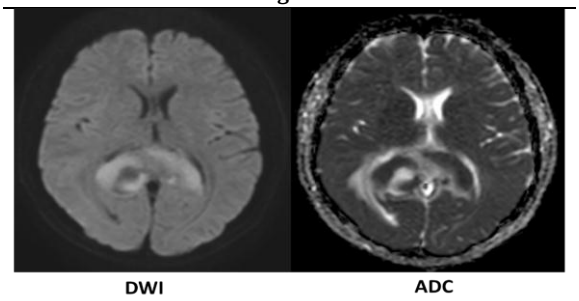


Figure 3: Diffusion-weighted imaging (DWI) reveals restricted diffusion within the tumor, with high signal intensity on DWI and corresponding low signal intensity on the ADC map

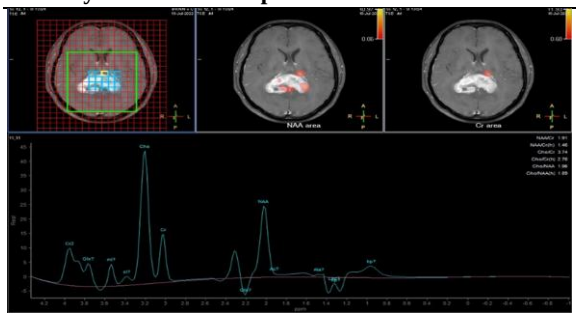
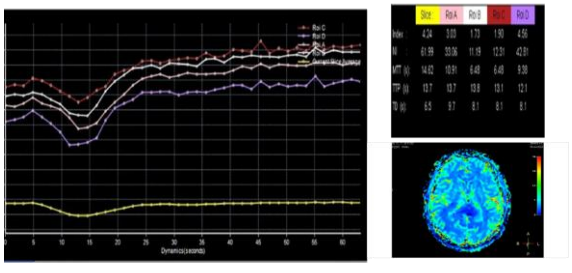


Figure 4: Proton spectroscopy spectrum in lymphoma depicting a decrease N-acetylaspartate, a decrease of creatine, an increase of choline



Perfusion

Figure 5: DCE T1 perfusion MRI shows a low rCBV, rCBF and MTT value within the tumour with ROC curves demonstrating the discriminating performance of T1-derived haemodynamic and kinetic parameters. Characteristic time-intensity curve overshooting the baseline, related to leakage of contrast into the interstitial space

ISSN (O): 2687-5365; ISSN (P): 2753-6556

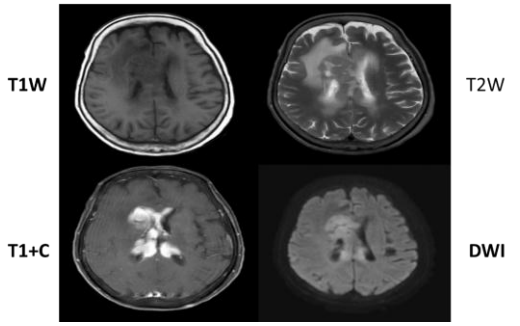


Figure 6: An axial T1W and T2 weighted MR images shows the genu and splenial lesion appearing isointense with respect to gray matter. An axial T1W+C MR image after contrast shows periventricular nodular homogenous intense enhancement. DWI demonstrates high signal intensity

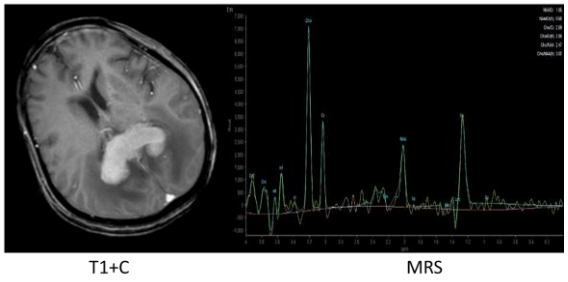


Figure 7: MRS in spenial lymphoma depicting a markedly elevated choline, decrease N-acetylaspartate, a decrease of creatine, and a prominent lipid peak

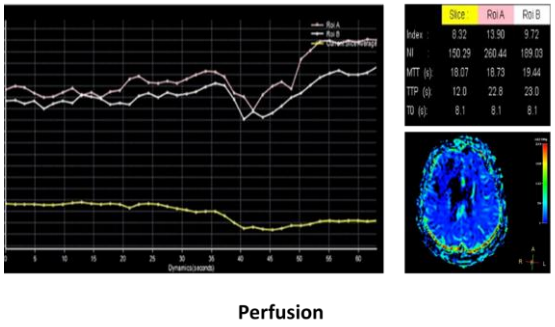


Figure 8: DCE T1 perfusion MRI after gadolinium reveals a low rCBV, rCBF and MTT value within the tumour with characteristic time-intensity curve overshooting the baseline

DISCUSSION

In conventional MRI Imaging, contrast-enhanced T1-weighted magnetic resonance imaging (MRI) is the imaging technique of choice in PCNSL. On the pre-contrast T1- weighted imaging, lesions are usually isointense or hypointense.[2] Strong homogenous enhancement is often present in PCNSL. Symmetrical lesions involving the corpus callosum are referred to as "butterfly pattern". PCNSL tend to show subependymal and leptomeningeal spread.[2-4] After steroids administration, lesions tend to shrink, causing non- visualization on MR imaging. It can also cause decrease gadolinium enhancement.[1,5] On MR imaging, PCNSL are usually characterized by their periventricular locations, well-demarcated margin, moderate to marked oedema, and intense homogeneous enhancement. On T2-weighted images, PCNSL appears isointense to hypointense in relation to gray matter, which is not common for most of the intracranial lesions[5].More commonly the nature of perilesional oedema is vasogenic. Ring enhancement is seen due to central necrosis and occurs virtually in the immunocompromised patients.[3,4]

In advanced MRI Imaging**,** PCNSL may have characteristic appearance on conventional MR imaging, however none of these images can unequivocally differentiate PCNSL from other brain tumours.[4] The dilemma arises especially when the PCNSL appear in uncommon locations, and or with unusual morphological findings. The main differential diagnosis is with GBM, metastases and demyelinating disease.

Diffusion weighted (DW) images give information on the movement of water molecules within the tissue. Cellularity of the lesions determining the factor of ADC values in the quantitative diffusion maps.[3,6] The higher cellularity of PCNSL shows homogeneous high signal on DW images, unlike GBM and metastases, which are heterogeneous.[2,6] The values in the quantitative ADC map are markedly low (0.4-1.0 □ 10^{-3} mm^2/s).

MR spectroscopy provides non-invasive in vivo biochemical information of the biological tissues. The spectral curves of PCNSL typically show significant increase in the lipid peak within the regions without necrosis, as the tumoral cells contents increase lipids.[3,4] Increased Cho peak, decreased NAA and Cr peak with elevated Cho/NAA and Cho/Cr reflecting cell proliferation and neuroaxonal damage are usually seen. These findings may also be seen in GBMs, however, the lipid peak is not as prominent as PCNSL, the increase in the lipid peak generally reflects considerable intra-tumoral necrosis.[6,7] Present of diffuse infiltration, beyond the contrast-enhancing areas occurs in PCNSL, helps differentiate it from metastases.[2,6] In demyelinating plaques, increase in the lipid peak is a normal finding but without a reduction in the other metabolites.[6]

Perfusion-weighted imaging (PWI) with contrast identifies the blood supply to the capillary bed of a lesion. Quantifying parameters like relative cerebral blood volume (rCBV), relative cerebral blood flow (rCBF) and mean transit time (MTT) are measured. PCNSL are known to have an angiocentric growth pattern, with neoplastic cells collecting around the existing vessels and almost absent tumoral neovascularization.[6,7] PCNSL typically show lower rCBV values, compared to glioblastomas and metastases, and slightly higher values than demyelinating lesion.[6] The signal time-intensity curve of perfusion maps is highly characteristic in PCNSL, i.e., overshooting the baseline, reflecting high permeability and massive loss of intravenous

ISSN (O): 2687-5365; ISSN (P): 2753-6556

contrast into the interstitial space, which is helpful in differentiating it from other lesions such as GBMs and metastases.

The present study aimed at evaluating MRI morphological characteristics in biopsy-proven PCNSL using possible imaging techniques that may discriminate PCNSL from other neoplastic lesions. Different indices like DCE T1 perfusion MRI, DWI, MRS along with traditional sequences are studied. Combining these multiparametric sequences show improvement in differentiating PCNSL from the other tumours.

In multiple studies, it has been found that PCNSL has lower ADC values when compared to the GBM. In the present study, mean values of ADC for lymphoma are (0.4-1.0 □ 10^{-3} mm^2/s). Previous few studies have reported less accuracy of diffusion for discriminating PCNSL from other tumors. Makino et al. reported no significant differences in the ADC values of PCNSL and GBM.[8] Some studies have shown that GBM has higher rCBV values as compared to those of PCNSL. Multiparametric analysis improves the discrimination of PCNSL from different tumour types more than individual imaging techniques alone. Corticosteroids is best avoided before imaging as they can shrink or vanish the tumor masking the imaging. The presnt study shows similar findings with the study by Anagha Joshi et al, in which PCNSL appear Iso – hypointense on T1WI, hypointense on T2WI and show homogenous enhancement.[9] All the lesions showed restricted diffusion with low ADC values. More restricted diffusion and lower ADC values than high-grade gliomas and metastases. MRS showed increased choline and decreased NAA, high Cho/Cr and Cho/NAA ratios with lipid peak in 50% of the cases. Perfusion demonstrates lower rCBV compare to high grade gliomas.[9] Cho/NAA is 2-10 and Cho/Cr 2-5 in our study. In the study by S. Lu et al, Lymphoma was suggested when the Cho/Cr ratio was >2.58, the Cho/NAA ratio was >1.73 rather than tumefactive demyelination.[10]

CONCLUSION

Combining advanced MR imaging with conventional imaging shows significant improvement in the morphological characterization of PCNSL. This study shows considerable accuracy of advanced MR imaging in identifying PCNSL and can become an important radiological diagnostic tool which can replace invasive surgical biopsy for diagnosis in near future.

Acknowledgments: We sincerely appreciate the cooperation of the patients for providing their biopsy report.

Ethics statement: The requirement for ethical approval was obtained from the institutional Ethical Committee (IEC) of Jawaharlal Nehru Institute of Medical Sciences, Imphal.

Declaration of conflicting interest: The authors declare that there is no conflict of interest.

Funding: This research received no grant from any funding agency in the public, commercial, or not-for-profit sectors.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556