JMSR
Journal of Medical and Surgical Research

Research Article

ISSN: 2351-8200

JMSR 2016, Vol III; N°1 : 215- 222

RADIOLOGICAL APPEARANCES OF PRIMARY CNS LYMPHOMA

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Abstract

Primary central nervous system lymphomas (PCNSL) are uncommon tumours, accounting for only 2% of primary brain tumors. Recently many investigators have showed interest in MRI characteristics for aiding in diagnosis and stratify prognosis.

In this article, we aimed to review characteristic findings on traditional and advanced Imaging seen in immune competent patients with intracranial primary CNS lymphoma (PCNSL). CT scan and MRI examinations of 15 immunocompetent patients with biopsy-proven PCNSL were retrospectively evaluated. T1 and T2 signal characteristics as well as contrast enhancement features are described in all patients. Diffusion, perfusion and proton-MR-spectroscopy features are described in a subset of these patients.

Keywords: Primary Central Nervous System Lymphomas (PCNSL), Radiological Appearances.

Introduction

Primary central nervous system lymphomas (PCNSL) historically have accounted for approximately 2% of primary brain tumors. The review of literature regarding PCNSL strongly supports a protocol for stereotactic biopsy to establish diagnosis. Recently many investigators have shown interest in MRI characteristics for aiding in diagnosis and stratify prognosis.
In this article, we aim to review characteristic findings on traditional and advanced imaging of primary central nervous system lymphomas.

Material and methods

We report a retrospective study that evaluates 15 immune competent patients with PCNSL proven histologically, seen during the five year- period from January 2010 to December 2014.
MRI study of the brain was performed in all the patients either immediately or after a cranial CT scan. MRI evaluation was done on a 1,5T, including conventional sequences (FLAIR, T2- and T1-weighted images, post-contrast T1-weighted images) and diffusion-weighted MRI (DW-MRI) in all patients, while MR-spectroscopy and perfusion MR imaging were performed in 3 patients.

Results

The mean age of patients was 57 years old with gender distribution of 10 (67.6%) male and 5 (32.4%) female.
Of the total of 15 cases, the most common location was parietal lobe and least common was in the occipital lobe.

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All the lesions were in supratentorial compartment. Total number of cases in frontal lobe was 3 (20 %), parietal lobe was 4 (26.6%), temporal lobe was 1 (6.6%), corpus callosum was 3 (20%) and basal ganglia/Thalamus was 4 cases (26.6%).
9 patients had a solitary lesion (60%) and the other 6 patients have multiple lesions (40%).
Of the total 15 patients, 9 (60%) had hypodense lesion on CT scan as compared to 1 patient (6.7%) isodense and 5 patients (33.3%) with hyperdense lesion. None of the lesions showed calcification or bleeding. Contrast enhancement was uniformly present in all cases.
MRI data was available for all 15 patients. On T1 weighted images 12 cases (80%) were hypointense and 3 (20%) were isointense. The hyperintense lesions on T2 weighted images showed 2 (13.3%) isointense lesions and 13 (86.7%) lesions. 13 cases (86.7%) showed homogenous and intense contrast enhancement, 1 case (6.7%) showed moderate and heterogeneous contrast enhancement and 1 case (6.7%) demonstrated a punctuate enhancement. The edema was moderate-to severe.
Diffusion characteristics could be recorded for 15 cases: 2 cases (13.3%) had no diffusion restriction and 13 (86.7%) had diffusion restriction.
Perfusion-weighted MR imaging was performed in 3 patients and showed marked reduction in rCBV (relative to the contralateral normal-appearing white-matter) in all cases. The average rCBV was 0.75.
MR-spectroscopy was performed in 3 patients and consistently showed increased choline and decreased NAA along with the presence of lipid peak.

Discussion

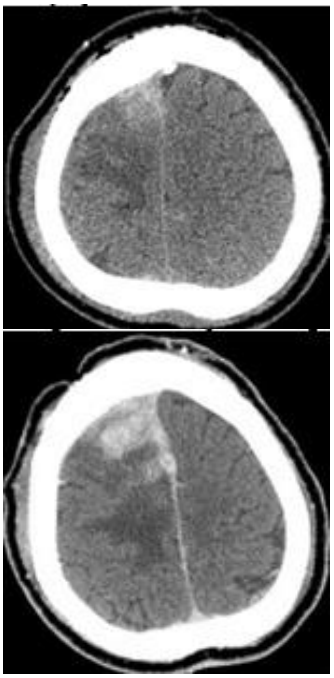
Primary CNS lymphoma (PCSNL) is a rare tumour, representing approximately 5% of primary brain tumours. It is a form of non-Hodgkin lymphoma limited to the CNS [1].
The overall incidence rate of PCNSL is 4 cases per million people per year. The peak incidence is between 60 and 70 years old for immunocompetent patients. The male: female
ratio is 1.5 : 1 [2, 3].
The etiology of (PCSNL) remains unclear: The CNS is devoid of endogenous lymphoid tissue. The only established risk factor is immunodeficiency and (PCSNL) is the most common brain tumor in this population. AIDS accounts for the largest group of immunocompromised patients with (PCNSL) and is an AIDS defining diagnosis [4].
Presentation can be with focal neurological symptoms or features of intracranial hypertension. The deep location of many tumours accounts for more frequent neurocognitive changes and rarer seizures [1].
PCNSL usually presents, solitary or multiple lesions mainly located at supratentorial level, usually in the periventricular regions, infiltrating the corpus callosum and the basal ganglia [5,6].
Multiple lesions are reported in 38%–55% of non-AIDSPCNSLs. Multifocal intra-parenchymal lesions without a dural involvement are very uncommon. Frontal lobe is affected in20%–43% of PNCLs, brain stem, or cerebellum in 13%–20%.Other localizations are leptomeninges, spinal cord, and eyes [6].

Imaging findings

PCNSL often has a characteristic appearance on both CT and MR imaging reflecting its hypercellularity and the high nuclear/cytoplasmic ratio.

Conventional CT and MR Imaging

CT has been the primary method for the evaluation of the PCNSL. Tumor results in hyperdensity (Figure1), but it may also appear isodense (Figure 2). There is usually a degree of associated oedema and mass effect resulting from these lesions is often as a result of the extent of oedema, rather than the lesions themselves [5].
However, CT is not a gold standard technique for diagnosis because a negative examination does not exclude CNS lymphoma and 13%–38%false-negative rate is reported (Figure 3) [6].



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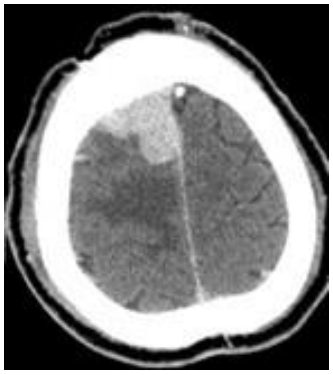

Figure 1: 55 years old man with progressive left hemiparesis. Non contrast cerebral CT scan image shows a hyperattenuated right parasagittal frontal lobe lesion with marked enhancement in post contrast series.

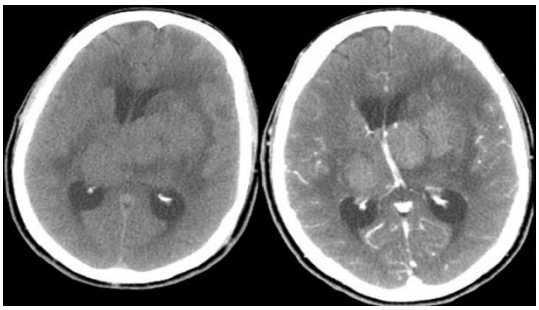

Figure 2: 48 years old man with increased intra cranial pressure. Axial cranial CT showing multiple isodense lesions in the basal ganglia with solid enhancement, associated to periventricular white matter vasogenic edema and mass effect displacing the midline.

On unenhanced T1-weighted imaging, lesions are typically hypo- or isointense and on T2-weighted MR imaging iso- to hyperintense to gray matter (Figure 4,5)[6]. On flair sequence, lesions are usually iso or hypointense to cortex (Figure 6)but may be hyperintense(Figure7)[7].

Most lesions show moderate-to-marked contrast enhancement [6]. No contrast enhancement on T1-weighted MR imaging has also been described in some rare cases of PCNSL [8, 9].We observed contrast enhancement in all our lesions. It was intense and homogeneous in 13 cases, moderate and heterogeneous in 1 case and punctuate in 1 case (Figure 8).

Edema is a common feature of PCNSL. Some published data reports the edema in 77% of the lesions, though usually less prominent than that in malignant gliomas or metastases [6]. In our series, the edema was mostly moderate-to severe, though; the mass-effect is less than what is expected for the same mass size.

Hemorrhage or internal calcifications within the tumor are a quite rare finding [9, 10].Necrosis is unusual in such tumours in the immunocompetent population [5].We did not encounter any similar case in our study.

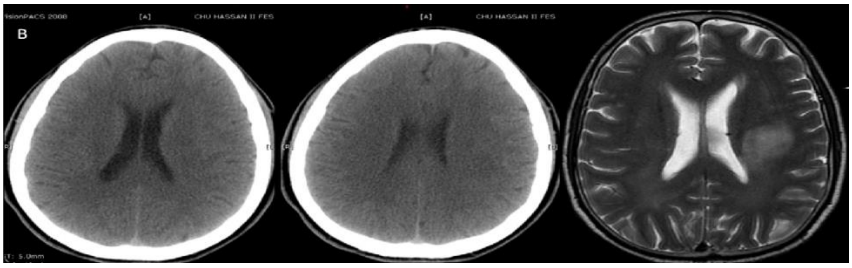

Figure 3: 43 years old women, with right hemiparesis. Negative CT examination with corresponding T2 WI showing a well-circumscribed lesion (confirmed PCSNL).

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Table I: Typical imaging features of primary and secondary CNS lymphoma

CT findings	Iso- or hypodense lesions with marked CE
MRI findings	T1: hypo- or isointenselesions, moderate-marked CE T2: iso- or hyperintense lesions; often hypointense to gray matter
Enhancement pattern	Non-AIDS patients: homogeneous CE, 90%; ring-CE, 0%-13% AIDS patients: irregular CE common; ring-CE, 75%

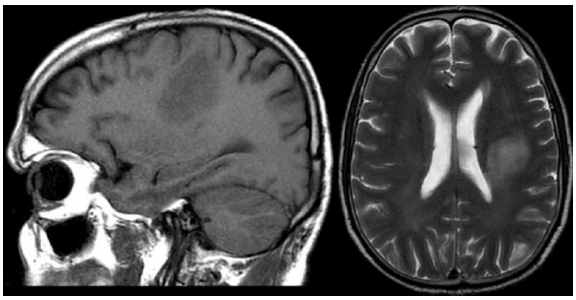


Figure 4: the same patient as figure 3. Hypo intense T1 and hyper intense T2 well circumscribed left posterior frontal lobe lesion.

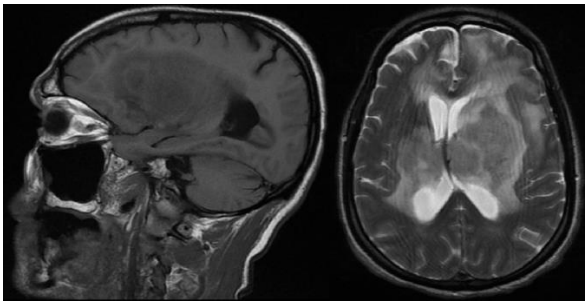
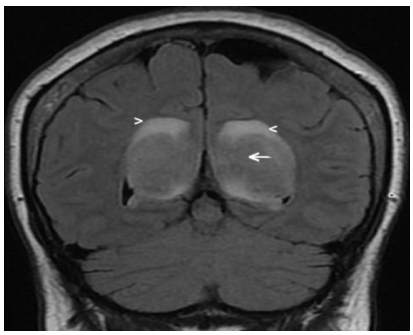


Figure 5: 50 years old man increased intracranial pressure. Sagital T1 WI without contrast



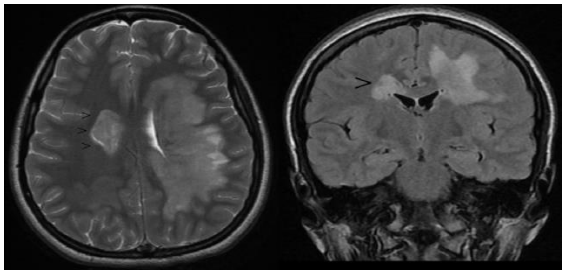


Figure 7: 47 years-old-man, signs of coma. Large hyperintense T2 and FLAIR lesion involving the left periventricular white matter and corpus callosum. Note the additional periventricular right lesion (arrowheads).

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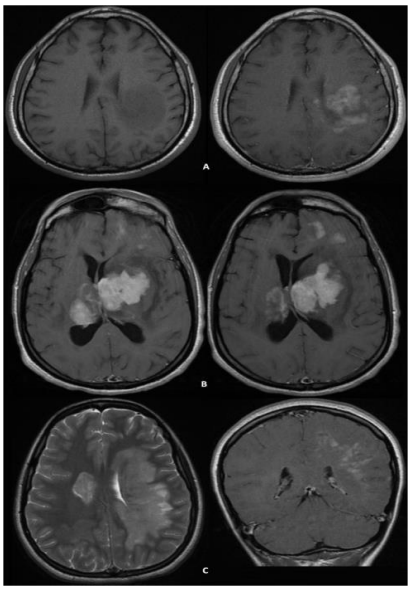


Figure 8: different types of enhancements. (A) Moderate and heterogeneous enhancement. (B) Multifocal strong patchy homogeneous enhancement. (C) Punctuate nodular enhancement.

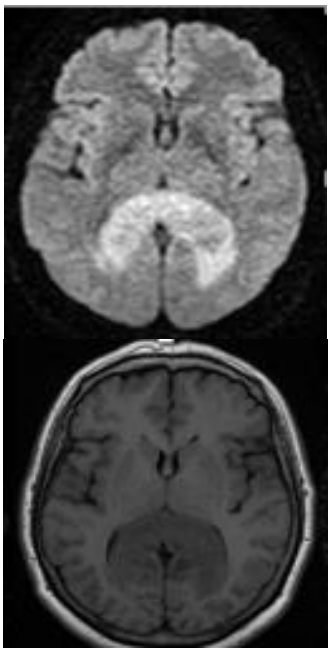
CNS lymphomas may have a characteristic appearance on traditional CT and MR imaging; however, none of these imaging characteristics will unequivocally differentiate CNS lymphomas from other neoplasms (eg, metastases from other malignancies, malignant gliomas, meningiomas) or non-neoplastic diseases (eg, multiple sclerosis, stroke, cerebral toxoplasmosis, pyogenic abscess) [6, 8]. Furthermore, the typical imaging characteristics may not be present.
DWI, perfusion MR imaging, and MR spectroscopy are increasingly used in clinical radiologic practice and may help to differentiate CNS lymphomas from other lesions of the brain [6].

Table II: Advanced imaging techniques in CNS lymphoma

Diffusion MRI	Restricted diffusion in lesions (hyperintense on DWI andhypointense on ADC maps)11,12 Low maximum CBV 12,15
Perfusion MRI	Characteristic intensity time curve related to leakage ofcontrast into the interstitial space15
MR spectroscopy	Elevated lipid peaks and high Cho/Cr ratios5,11,15

Diffusion weighted imaging (DWI)

DWI measures the diffusion of water molecules in biologic tissues. It is a surrogate marker of tumor cellularity. Highly cellular tumors, like CNS lymphoma, would demonstrate a restricted diffusion (hyperintense lesion on DWI and hypointense on ADC maps) [11, 12] (Figure 9).Differential diagnosis of lesions with these features is with ischemic stroke, central necrosis of brain abscess, high-grade gliomas, or some metastases. PCNSL lesions often have more restricted diffusion and lower ADC values than high-grade gliomas and metastases [12, 13].In our patient cohort, we observed subjective diffusion restriction (hyper-intensity on DWI and iso- to hypo-intensity on ADC maps) in 13 cases. This is consistent with what has been described in the literature.
In addition, pre-therapeutic ADC tumor measurement within the contrast-enhancing part of the tumor has been shown to be predictive of the clinical outcome (lower ADC meant shorter progression-free survival and overall survival) [14]. It also can be used as a biomarker to monitor response to treatment, where increasing ADC values suggest favorable response [6].



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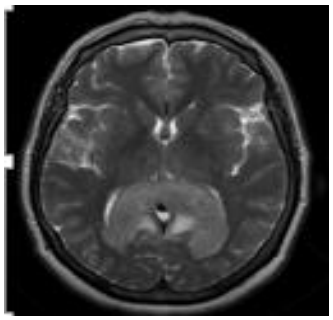

Figure 9: 62 years old women. Signs of increased intracranial pressure. Homogeneous hypointense T1 WI and hyperintense T2 WI mass in the splenium of the corpus callosum. DWI reveals high signal within the lesion, representing restricted diffusion due to the high cellularity of the tumor.

Perfusion-weighted MR imaging (MRP)

While contrast enhancement reflects leakiness of the vessels (disruption of the blood–brain barrier), perfusion assesses tumor vascularity. The documented importance of revascularization through angiogenesis for tumor growth has led to a growing interest in such imaging techniques. Perfusion MR and CT imaging visualize nutritive delivery of arterial blood to the capillary bed in the biologic tissue (e.g., tumors). Post processing of the acquired data allows for calculation of physiologic parameters, such as cerebral blood volume, cerebral blood flow, mean transit time, and time to peak [6]. PCNSLs demonstrate low CBV (Fig 10) and a characteristic intensity time curve, which is related to a massive leakage of contrast media into the interstitial space(Fig 11).[15] Furthermore, maximum relative CBV measured in tumor tissue, calculated as a ratio to contralateral normal-appearing white matter, is typically lower in lymphomas than in other brain tumors. This characteristic finding can help to differentiate glioblastomas and metastases from lymphomas which show significantly higher rCBV values. [12, 16]In our series perfusion-weighted MR imaging was performed in 3 patients and shows marked reduction in rCBV in all cases. This is consistent with what has been described in the literature.

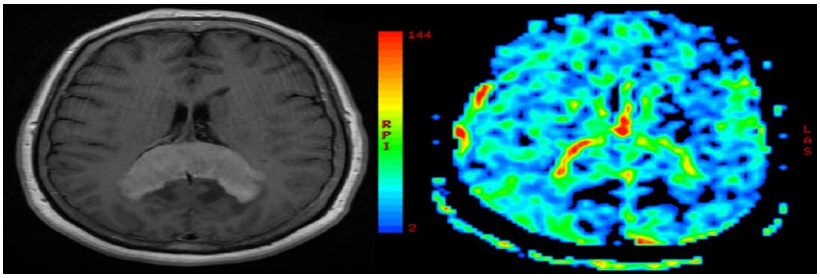

Figure 10: Same patient as in figure 9. Enhanced T1-WI MRI demonstrates a homogeneously enhancing mass in the splenium of the corpus callosum. Perfusion MR imaging shows a relative low perfusion within the contrast-enhancing tumor on the rCBV map, which indicates no significant localized neoangiogenesis.

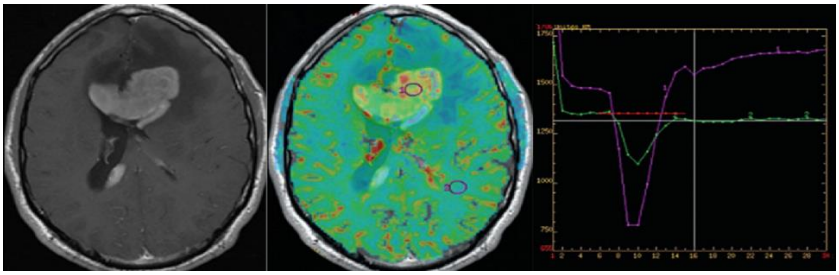

Figure 11: Multimodality cerebral MRI of a middle-aged man with a PCNS lymphoma. T1WI with contrast showing an homogeneous enhancing of two lesions in contact with the ventricles. MRI perfusion of the major lesion shows a weak increase of relative cerebral blood volume, which indicates no significant localized neoangiogenesis (no red area in the lesion). The first pass of the bolus agent curve indicates high blood-brain barrier permeability [1].

MR spectroscopy (MRS)

MR spectroscopy obtains biochemical information noninvasively from biologic tissue. Within a defined volume of interest, signals may be registered from chemical nuclei within the body; the most commonly used nuclei are protons (hydrogen). In PCNSL, proton MR spectroscopy has demonstrated elevated lipid peaks combined with high Cho/Cr ratios (Fig 12). [5, 11, 15]
In our patients, MRS consistently showed increased choline and decreased NAA along with the

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presence of lipid peak. This is compatible with what has been reported.
Elevation of lipid peak is typically a signature of cell death; however, a lipid dominated spectrum is found in PCNSL that is not macroscopically necrotic and due to macrophage content. [15, 17]
These can, however, also be seen in glioblastoma multiforme and metastases but may help in differentiating PCNSL from other lesions. [15]
We also noticed a transition zone of abnormal spectra outside the enhancing area reflecting the infiltrative pattern of lymphoma which extends beyond the contrast-enhancing region. This might aid in differentiating PCNSL from metastasis but not from high grade glioma.

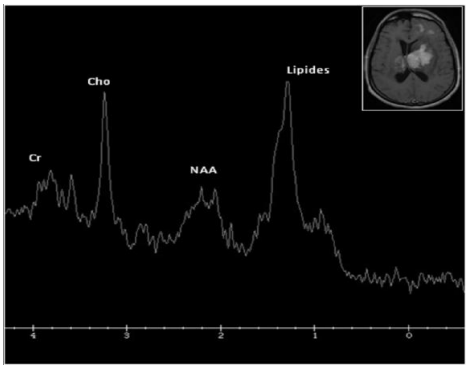

Figure 12: Same patient as in figure 2, the single voxel, short Time Echo MRS demonstrates an exaggerated lipid peak in a solid mass. Lipid peaks are typically demonstrated in necrotic lesions, but in solid PCNSL lesions the peak is due to the increased macrophage content. MRS demonstrates also a decreasing value of NAA and elevation of choline

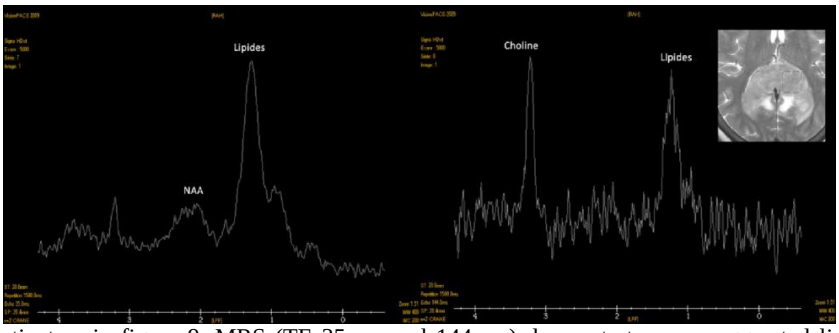

Figure 13: Same patient as in figure 9, MRS (TE 35 ms and 144 ms) demonstrates an exaggerated lipid peak, increased concentration of choline and decreased concentration of N-acetyl aspartate in this solid mass

Stereotactic brain biopsy and treatment for PCNSL

Since the clinical and neuroimaging presentation of PBL can be varied and the differential diagnostic possibilities are therefore large, no patient should be treated for PCNSL without definitive histological proof of diagnosis. Stereotactic brain biopsy is the most appropriate method for the diagnosis of PCNSL. However, open brain biopsy may be necessary in those patients who have lesions located in areas of the brain that are difficult to access (eg, brainstem). If possible, the procedure should be performed before corticosteroids have been administered.
The standard treatment for PCNSL has not been defined yet for the lack of adequate randomized studies. Retrospective series have shown a very significant survival advantage for the combination chemoradiotherapy. First-line chemotherapy consists in high dose methotrexate followed by radiotherapy. This strategy allows a 5-year survival of 25%–40%versus 3%–24% with the radioboost alone [19].

Conclusion

CNS lymphomas may have a characteristic appearance on traditional CT and MRI imaging; however, none of these imaging characteristics will unequivocally differentiate CNS lymphomas from other primary and secondary brain tumors (high-grade gliomas and metastases) or non-neoplastic diseases (multiple sclerosis, stroke, cerebral toxoplasmosis, pyogenic abscess). Furthermore, the characteristic imaging features on traditional imaging may be absent, at that time new imaging techniques (MRS, PWI and DWI) which are increasingly used in clinical radiologic practice, may play important role in the diagnosis of PCNSL and differentiating it from other brain lesions.

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