

## Assessment of Primary Brain Lymphoma Using Multimodal Magnetic Resonance Imaging and Proton Magnetic Resonance Spectroscopy

### Abstract

**Objectives:** The primary lymphoma of the central nervous system is a cancer rare. The diagnosis of this tumoral entity must be considered as an emergency considering the therapeutical involved. Therefore, we report this entity while reporting diagnostic challenges. **Patients and Methods:** Unfortunately, the conventional clinical and imaging signs can be confusing and might contribute to delay the diagnosis process of potentially curable pathological entity. The diagnosis confirmation in immunocompetent patients is based on a stereotaxic biopsy. **Results and Conclusion:** In this paper, we report a case illustrating the contribution of multimodal imaging including diffusion-weighted magnetic resonance imaging (MRI), diffusion tensor MRI, perfusion MRI, and proton MR spectroscopy to the diagnostic approach of the atypical primary lymphoma of the central nervous system.

**Keywords:** *Intraparenchymal tumor, multimodal imaging, primary brain lymphoma*

### Introduction

The primary lymphoma of the central nervous system is cancer rare; it represents 1% of all lymphomas, <5% of all non-Hodgkin lymphoma, and 3%–5% of brain tumors. The existence of an immunodepression is a well-established risk factor despite the congenital or acquired origin.<sup>[1]</sup> The brain lymphoma incidence has considerably increased these last two decades. The AIDS epidemiological increase and dissipation elucidates partially this occurrence of the brain lymphoma. Indeed, an increase of incidence in similar proportions was also indicated in the immunocompetent population. The origin of this phenomenon in the immunocompetent population is not yet elucidated. The brain lymphoma diagnosis is sometimes difficult, especially in outside of a known seropositive HIV context or unusual imaging and radiological presentation.<sup>[1]</sup> Therefore, we report an atypical case of multiple lesions in a patient with tuberculosis history of declared that was treated and cured. The case illustrates the contribution of the multimodal magnetic resonance imaging (MRI) and proton magnetic resonance spectroscopy (MRS) to the diagnostic approach of real atypical

primary lymphoma of the central nervous system.

### Patients and Methods

The following patient recruitment was achieved according to local institutional guidelines approvals. Consent of the patient was obtained.

The patient was 43-year-old male that consented to be part of this study; he was initially admitted in emergency department of our hospital for convulsive crises while reporting a history of tuberculosis that was declared to be cured. The thoracoabdominal computed tomography (CT)-scan did not reveal any abnormality. The brain MRI demonstrated a multiple intraparenchymatous lesions localized in parietal bilateral and lenticular left localization. The lesions showed an oval shape with well delimitation. The lesions demonstrated an hyposignal in T1-weighted MRI images, hypercentral signal, and iso-peripheral signal in T2-weighted MRI images. Lesions borders associated franc edema with light deviation of the median to the right side, as well as a peripheral contrast enhancement after injection of gadolinium [Figure 1]. Considering these anatomicopathological facts, three diagnoses were evoked and included infectious necrotic lesions, primary necrotic tumors, and secondary necrotic tumors.

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The diffusion MRI presented a light hypersignal in the lesion with a decreased apparent diffusion coefficient (ADC); this reflected high cellularity character of the lesion. The fractional anisotropy maps and diffusion tensor MRI tractography demonstrated ejection of the white matter fibers [Figure 2] directing to lymphoma diagnosis. The perfusion maps analysis of contrast enhanced and surrounding lesion edema did not show any relative increase of the cerebral blood volumes, and the perfusion curve demonstrated a continues enhancement of perfusion above the threshold [Figure 3]. Indeed, these findings strengthened the orientation toward the central nervous system lymphoma diagnosis. The MRS studies highlighted a massive presence of free lipid, decreased N-acetyl

aspartate (NAA), increased rate of choline, which is a marker of membrane proliferation [Figure 4]. The spectra of the also abnormal since the rates choline/NAA were above superior to 1, with presence of lactate translating an acceleration of the anaerobic glycolysis connected to high cellular proliferation [Figure 5]; this last argument was against any hypothesis of infection and showed the infiltrating character of the lesion, besides this MRS results allowed also to discard any metastasis hypothesis.

Many MRI and MRS aspects were revealed, these included anatomicopathological aspect of the lesion, the restricted diffusion measurements demonstrated in diffusion-weighted images and ADCs maps, the absence of any hypervascularization, enhanced perfusion curve above the threshold after the first passage of the bolus, high resonance of choline and lipids, the abnormal spectra around the lesions with high resonance of lactate. All these findings advocated the hypothesis of primary lymphoma of the central nervous system as most likely diagnosis. Therefore, a cerebral biopsy was scheduled. Unfortunately, the patient has quickly evolved critical stage and the patient died 10 days after imaging studies including MRI and MRS. The patient family refused any autopsy, while seropositive HIV was confirmed by biological assessment.

### Results and Discussion

The primary lymphoma of the central nervous system is cancer rare characterized by multiple intraparenchymatous lesions which are mainly of oval shape and well delimited. The lesions are peripherally enhanced by contrast agent injection. These aspects might suggest infectious necrotic abscesses, necrotic tumor, metastasis, or primary cerebral lymphoma. In addition in HIV-seropositive patients, it is remarkable to evoke toxoplasmic abscesses and lymphomas.<sup>[1]</sup>

Inhere reported case; the MRS highlighted a massive presence of lipids and a clear decrease of NAA spectra demonstrating the active neuronal loss. The high level of the choline peak reflected the presence of a suffering membrane and significant cellular proliferation. Besides, the spectra around lesions and remotely of contrast enhanced part of the lesion demonstrated were abnormal with arguments of

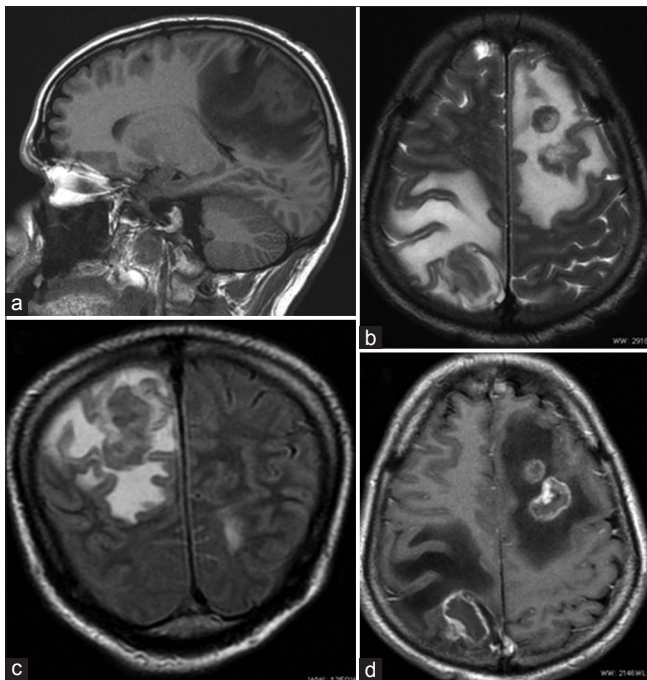


Figure 1: Brain structural demonstrated multiple intraparenchymatous lesions including parietal bilateral, lenticular left, shape rudely well-delimited oval showing an hyposignal T1 (a), hyper central signal and is-peripheral signal in T2. The lesion associated a lesional edemain axial in T2 weighted (b) and coronal fluid-attenuated inversion recovery in (c), a peripheral contrast enhancement was also demonstrated after injection of gadolinium (d)

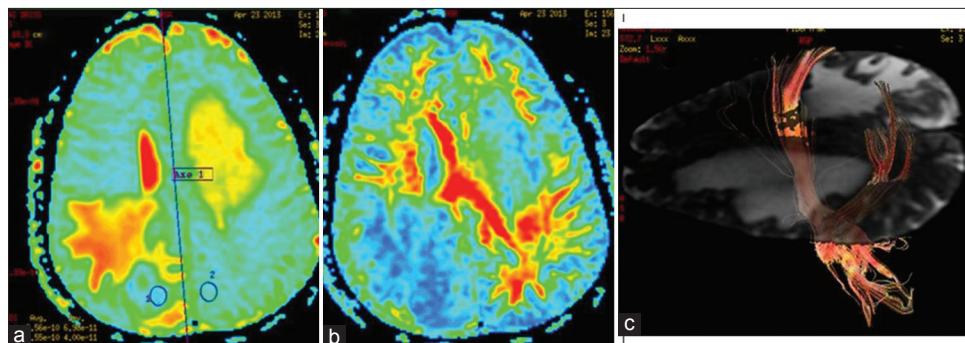
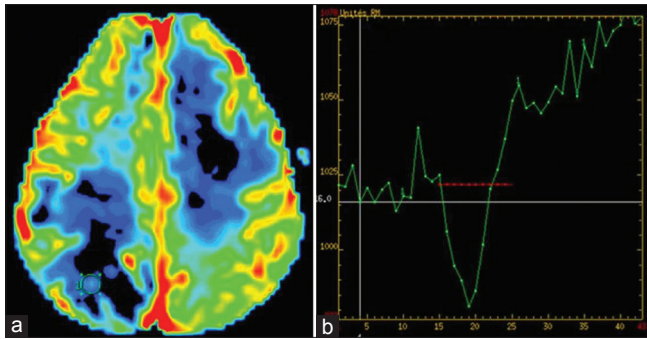
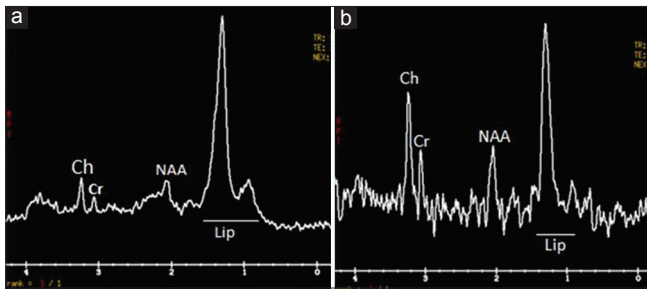


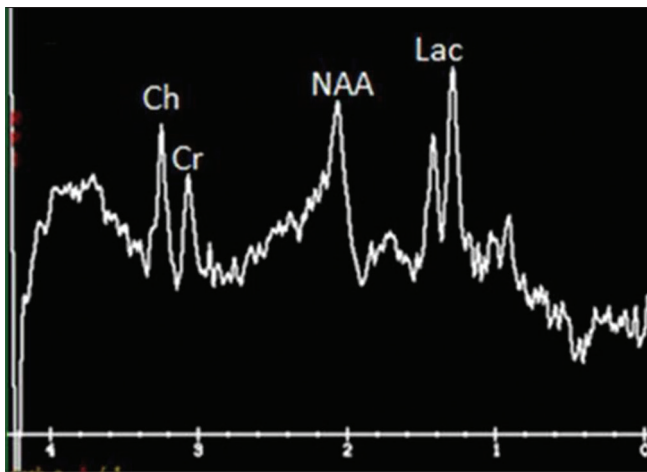
Figure 2: The apparent diffusion coefficient (map) demonstrated the lesion extents in (a), and the fractional anisotropy was lower in the lesion (b), while the diffusion tensor magnetic resonance imaging tractography showed ejection of the white matter fibers (c)



**Figure 3:** The perfusion magnetic resonance imaging allowed a color mapping of the relative cerebral blood volume relative cerebral blood volume in (a) with hypoperfusion, while the perfusion curve demonstrated to be above the threshold after the first bolus passage (b)



**Figure 4:** The proton magnetic resonance spectroscopy acquired spectra at short echo time of TE = 35 ms in the lesion, this showed a very high lipids peak at 1.35 ppm and another at 0.9 ppm in (a). The long echo time spectra with TE = 144 ms showed persisting lipids peak at 1.35 ppm elevated choline peak at 3.3 ppm and important rates of choline/creatine and choline/N-acetyl aspartate >1 in (b)



**Figure 5:** The proton magnetic resonance spectroscopy acquired spectra at short echo time of TE = 35 ms in the prelesion tissue showed the presence of a peak of lactate at 1.35 ppm, elevated choline peak at 3.3 ppm, and rates of choline/creatine and choline/N-acetyl aspartate >1

infiltrating effect by the tumor. Indeed, these findings are arguing the character noninfiltrating metastasis.<sup>[2-5]</sup>

The malignant lymphoma of the central nervous system cerebral might occur at any age, with a predilection during sixth and seventh decades of life with male predominance with gender ratio (male/female) of 1.5.<sup>[5-9]</sup> The topography is

mostly in the subtentorial and rarely cerebellar. Intraventricular localizations were exceptionally reported; while multiple localizations were reported in 25 in 50% of cases.<sup>[1-5]</sup>

The imaging and radiological characteristics of the primary lymphoma of the central nervous system in the CT-scan and in conventional MRI are not specific. However, the imaging often allows evoking the diagnosis in the imaging. Typically, in the CT-scan, the primary lymphoma of the central nervous system is expressed by one or several spontaneous hyperdense lesions, and sometimes isodense. The iodized contrast agent injection demonstrates contrast-enhanced lesions that are classically homogeneously enhanced.<sup>[2-7]</sup>

In conventional MRI, the lesions appear generally with aspect of an isosignal in T1-weighted MRIs and iso- or hypo-signal in T2-weighted MRI.<sup>[2-7]</sup> The immunocompetent patients demonstrate perfusion contrast enhancement with classical intense and homogenous aspects of signal with snowball or cotton lifeless. The immunosuppressed patients demonstrate mostly multiple and necrotic lesions without perfusion contrast enhancement or presenting an annular peripheral contrast agent enhancement such was revealed in our case.<sup>[1-7]</sup>

The diffusion MRI is marked by its sensitivity since it allows demonstrating 90% studied cases of primary lymphoma of the central nervous system, with an evident decrease of the value of the ADC reflecting the hypercellular character of this tumor type.<sup>[1-8,10]</sup>

Perfusion MRI reported a normal relative cerebral blood volume (rCBV) or decreased.<sup>[1-8,10]</sup> Therefore, the perfusion curve in the tumor presented a characteristic aspect of important increase above the threshold after the first passage of contrast agent bolus; this phenomenon is originated by an important loss of contrast agent bolus in the interstitial tissue. In this case, such contrast agent bolus perfusion behavior is correlated to inflammation and break of the blood-brain barrier and not to neovascularization phenomena. These studied abnormalities are limited to the tumor and are not observed in the surrounding tumoral space, which is illustrated well in our case.<sup>[2-14]</sup>

The MRS study usually presents a spectra marked by a significant rise of choline, important reduction in the peaks of NAA and creatine with a corresponding noticeable increase of choline/NAA and choline/creatine ratios. In addition, the free lipids peak was clearly demonstrated, due to the active presence of macrophages containing a strong rate of moving lipids, and which persists even on remote spectra of the contrast agent bolus enhancement, This confirms the infiltrating character of such type of lesions.<sup>[2-13]</sup>

In HIV seropositive patients, the differential diagnosis is resolved between primary lymphoma of the central nervous system and toxoplasmosis abscess. The diffusion MRI has a limited interest since it allows distinguishing both pathological entities with sometimes an ADC have values of the ratio of similar CDA, between 1 and 1.6.<sup>[3-14]</sup>

However, several studies reported that an ADC higher than 1.6 is supporting a toxoplasmic abscess,<sup>[2-14]</sup> and an ADC lower than 0.8 expresses strongly to the diagnosis of primary lymphoma of the central nervous system such as in our case.<sup>[2-14]</sup> The perfusion MRI is more remarkable because the toxoplasmic abscess presents an absence of hyperperfusion even a hypoperfusion,<sup>[2-14]</sup> while the primary lymphoma of the central nervous system presents a rCBV discreetly increased, on average around 1 and 2 times compared to normal and the perfusion characteristic curve with a passage over the basic line due to the inflammation and to the break of the blood–brain barrier.<sup>[1,12]</sup> Finally, the MRS is major tool because even if both pathologies involved in differential diagnosis have very similar features<sup>[9,14,15]</sup> with high peak and concentration of lipids and a decreased NAA. The case of normal choline, slightly increased and lower would correspond only to toxoplasmic abscesses.<sup>[1-17]</sup> On the other hand, the spectra of primary lymphoma of the central nervous system presents an elevated choline and concentration,<sup>[2-4]</sup> this increase of choline is linearly correlated to the histological proliferation index of Ki67.<sup>[2-4]</sup>

## Conclusion

The diagnosis of primary brain lymphoma by multimodal MRI and proton spectroscopy is well demonstrated. Hence, the primary lymphoma of the central nervous system demonstrated strong cellularity, absence of neovascularization, and the break of blood–brain barrier demonstrated by perfusion curve above the threshold of the first bolus pass, enhanced choline, high presence of free lipids, and lactate. The primary brain lymphoma presents a particular semiology in diffusion-weighted MRI, diffusion tensor MRI, perfusion MRI, proton MRS, this knowledge allows further improving the diagnosis and the follow-up.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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