A comparative study of multimodal MR in the differential diagnosis of AIDS-related central nervous system lymphoma and infection

Jingjing Li
Capital Medical University Affiliated Beijing Ditan Hospital
Ming Xue
Beijing Ditan Hospital, Capital Medical University
Shuo Yan
BeiJing Ditan Hospital, Capital Medical University
Chunshuang Guan
Capital Medical University Affiliated Beijing Ditan Hospital
Ruming Xie (mingrux@163.com)
Capital Medical University Affiliated Beijing Ditan Hospital
Budong Chen (budongchen@sina.com)
Capital Medical University Affiliated Beijing Ditan Hospital

Research article

Keywords: Lymphoma, AIDS-Related, Central Nervous System, Magnetic Resonance Imaging, Diffusion Magnetic Resonance Imaging

Posted Date: June 1st, 2020

DOI: https://doi.org/10.21203/rs.3.rs-29816/v1

Version of Record: A version of this preprint was published on February 10th, 2021. See the published version at https://doi.org/10.1186/s12879-021-05779-4.

Abstract

Background: To compare the ability of multimodal magnetic resonance(MR) to differentiate acquired immune deficiency syndrome-related(AIDS-related) central nervous system lymphoma (ARL-CNS) from infection.

Methods: Clinical data and multiple MR imaging were analyzed retrospectively. Nine cases of ARL-CNS and ten cases with central nervous system infection were included.

Results: In conventional MR, there was a statistical significance in whether the lesion involved the paraventricular/corpus callosum. The Fisher values were 0.020 and 0.033 for the lymphoma and infection groups, respectively. In multimodal MR, there were significant differences in the ADC(apparent diffusion coeffecient) values(high/low) and SWI-ITSS grades between two groups, with *p*values of 0.003, 0.001 and 0.001. The sensitivity, specificity and accuracy of conventional MR in the diagnosis of ARL-CNS were 88.9%, 70.0% and 78.9%, respectively. The conventional sequence combined with the DWI/ADC sequence in the diagnosis of ARL-CNS had a sensitivity of 100.0%, a specificity of 60.0% and an accuracy of 78.9%. The sensitivity, specificity and accuracy of the conventional sequence combined with the SWI-ITSS sequence in the diagnosis of ARL-CNS were 100%, 70.0% and 84.2%, respectively.

Conclusion: Multimodal MR is of great value in distinguishing ARL-CNS from infection.

Background

AIDS (acquired immunodeficiency syndrome) is an immunodeficiency syndrome caused by human immunodeficiency virus (HIV) infection. AIDS patients often suffer from various fatal opportunistic infections and tumors.The incidence of malignant tumors such as lymphoma issignificantly increased in these patients[1]. AIDS-related central nervous lymphoma(ARL-CNS) and infectionscan present as multiple diseases and ringenhancement in conventional magnetic resonance (MR)[2, 3]. The lack of specificity in clinical symptoms and laboratory tests makes diagnosis difficult.

The purpose of this article is to investigate the application of multimodal MR in ARL-CNS and infection. Conventional MR can show the distribution, quantity, morphology and enhancement mode of the lesions. DWI and ADC values can infer benign and malignant lesions. 3D-pCASL can show cerebral blood flow in lesion areas. SWI can identify the deposition of low-signalparamagnetic substances in lesions.

1. Materials And Methods

1.1 Object of study

The multimodal MR data of AIDS patients in our hospital from October 2018 to February 2020 were collected, including nine cases of ARL-CNS and ten cases of infectious diseases that were difficult to

diagnose.All cases underwent biopsy or surgery to obtain pathological results.This study was reviewed by the ethics committee.The clinical and imaging features of the patients were summarized.

All AIDS diagnoses conformed to the "Chinese guidelines for AIDS Diagnosis and Treatment (2015)" [3, 4]. The time from onset of symptoms to MR examination in the ARL-CNS group was 10-120 days, with an average of 57.8 days. Patient age ranged from 25 to 52 years, with an average of 37.9. There were seven males and two females. The occurrence time of the infection group was 1-120 days, with an average of 40.8 days. In this group, patient age ranged from 24 to 52 years, with an average of 34.1 years. There were nine males and one female. The clinical symptoms lacked specificity. The most common was fever (nine cases, 47.4%), followed by headache/dizziness (six cases, 31.6%),adverse limb movement (four cases, 21.1%), vision loss(three cases, 15.8%) and transient loss of consciousness (two cases, 10.5%).

The pathology results of the ARL-CNS group were as follows: nine cases were B-cell lymphoma, including six cases of diffuse large B-cell lymphoma, one case of Burkitt lymphoma, and two cases of highly invasive B-cell lymphoma pathologically diagnosed due to less tissue. Of the nine cases, seven cases were positive for EBV nucleic acid, one case was negative and the other one was not tested.

The infection cases were difficult to diagnosis, and the effect of experimental treatments was poor. Some patients and their families requested pathology results. All ten cases were confirmed by pathology. There were three cases of toxoplasmosis, four cases of progressive multifocal leukoencephalopathy (PML), one case of tuberculoma (positive for acid-fast pus), and one case of brain abscess. Inflammatory/infectious changes were reported in one case, but the aetiology was unknown.

The inclusion criteria were as follows: inpatients who met the diagnostic criteria of the "Chinese guidelines for AIDS Diagnosis and Treatment (2015)" and patients with central neuropathy;patients who underwent MR scanning, including enhancement and multimodal MR examination. The exclusion criteria were as follows: patients with contraindications to MR examination; patients who had metal implants, and patients who did not agree to undergo the examination.

This study was approved by the Ethics Committee of Beijing Ditan Hospital, Capital Medical University. All the data were analyzed and presented anonymously.

1.2 Imaging examination.

GE Discovery MR750W 3.0 T was usedforMR examination. Multidirectional (axial, sagittal, coronal) scanning and multiparameter scanning were performed, including conventional MR T1WI, T2WI and enhanced examination. The contrast agent meglumine gadolinium was injected through the elbow vein or the dorsal hand vein (20ml for each patient), with an injection flow rate of 1.5-2.0 ml/s. Multimodal MR included 3D pseudo-continuous arterial spin labelling (3D-pCASL), DWI and SWI sequences. The DWI sequence parameters were: TR 4880ms, TE 77.4 ms, b=1000, matrix 256 × 256, FOV 240 mm × 240mm; 3D-pCASL: TR 4852 ms, TE 10.7 ms, matrix 128 × 128, FOV 240 mm × 240 mm, PLD 1.5 s delay; SWI: TR 77.6 ms, TE 42.56 ms, matrix 512 × 512, FOV 240 mm × 240 mm.

1.3 Image analysis.

Two deputy chief physicians performed blind evaluations of the conventional and multimodal MR images. They reached a consensus through further discussion when their opinions differed. The location, number, distribution and enhancement of the lesions were observed by conventional MR.

Multimodal MR analysis: All the original data were imported into a GE MR ADW4.6 workstation for correction and noise reduction. The DWI/ADC and cerebral blood flow(CBF) obtained in the solid maximum blood perfusion area and the ADC/CBF values of the tumor body were the most stable, and areas of cystic degeneration, hemorrhage, large vessels and artefact were avoided.

The ratio of CBF and ADC was obtained by measuring the fixed area and setting the control in the contralateral normal brain area. SWI image processing adopts the concept of ITSS[5], specifically referring to the thin line-like or dot-like structures with low signal intensity in tumors. The degree of ITSS was divided into 4 grades: grade 0, no ITSS; grade one, 1–5 dotlike or fine linear ITSSs; grade two, 6–10 dotlike or fine linear ITSSs; and grade 3, ≥11 dotlike or fine linear ITSSs in the continuous area within a tumor [5]. Due to the small number of cases in this study, SWI-ITSS 0-1 and ITSS 2-3 are discussed in combination.

1.4 Statistical methods

SPSS19.0 statistical software was used for routine analysis between two groups. The MR and multimodal MR imaging findings were analyzed using *Fisher's* method because the number of cases was less than 40. Statistically significant differences were defined as $p< 0.05$. The diagnostic sensitivity, specificity, and accuracy ofARL-CNS were calculated for conventional MR and conventional MR with DWI-ADC/SWI-ITSS.

2. Results

2.1 Conventional MR findings.

There was no significant difference in the distribution of supratentorial/subtentorial lesions between the two groups. There was no significant difference in the distribution of lesions under the cortex, involving ependyma/meninges, and whether there were multiple, ring, nodular or no enhancements. There were significant differences in lesions involving the paraventricular/corpus callosum. The Fisher values were 0.020 and 0.033, respectively. Conventional MR shows that there are many overlapping image features between these two patient groups. It is difficult to obtain a diagnosis using conventional MR manifestations (Table 1).

2.2 Multimodal MR findings.

3D-pCASL sequences derived from cerebral brain perfusion (CBF). There was no significant difference between the ARL-CNS group and the infection group. There was no significant difference in DWI signal

between the two groups, but there was a significant difference in the low ADC values, the high ADC values and the SWI-ITSS grade, with *p*values of 0.003, 0.001 and 0.001, respectively. Multimodal MR can help distinguish ARL-CNS from infectious lesions, as shown in Table 2. It also suggests that in clinical work, the interpretation of the DWI signal must be combined with the ADC value to reach a more accurate conclusion. ADC can distinguish whether high DWI signal is truly caused by diffusion limitations or by the T2WI penetration effect.

2.3 Multimodal MR Combined with Conventional MR in ARL-CNS diagnosis.

There was nosignificant difference between the groups in terms of 3D-pCASL/CBF.A discussion of the diagnostic value of ASL combined with the conventional sequence is beyond the scope of this paper. ARL-CNS was positive under the following definitions:conventional MR lesions involving the corpus callosum or located near the ventricle; high DWI signal and low ADC signal; and SWI-ITSS sequence levels 2-3.The sensitivity, specificity and accuracy were calculated for the conventional MR, the conventional MR combined with DWI/ADC, and the conventional MR combined with SWI-ITSS in the diagnosis of ARL-CNS. For the conventional MR in the diagnosis of ARL-CNS,the sensitivity, specificity and accuracy were 88.9%, 70.0% and 78.9%, respectively. For the conventional MR combined with DWI/ADC sequence, the sensitivity, specificity and accuracy of ARL-CNS diagnosis were 100.0%, 60.0% and 78.9%, respectively. For the conventional MR combined with the SWI-ITSS sequence, the sensitivity, specificity and accuracy of ARL-CNS diagnosis were 100.0%, 70.0% and 84.2%, respectively.

3. Discussion

3.1 Epidemiological studies.

HIV is a neurotropic virus, and the central nervous system is vulnerable to it. It was found that more than 90%of AIDS patients pathological changes in neurological systemafter autopsies, which may involvethe brain, spinal cord, peripheral nerves and muscles[6].Additionally, 11% of AIDS patients are complicated with central nervous system diseases, and 15% have central nervous system lymphoma (ARL-CNS)[7]. After HIV infection, the incidence of ARL-CNS rate is as high as 4-10%[8].Among these patients, the incidence of non-Hodgkin lymphoma(NHL) is significantly higher than that of Hodgkin lymphoma(HL). The prognosis of ARL-CNS is poor,with amedian clinical remission time of 4.2 months and a median survival time after clinical symptom relief of 1.6months[7].Targeted treatment can improve prognosis, so early diagnosis is very important.

3.2 Diagnosis and Differential Diagnosis of ARL-CNS and Intracranial Infection.

The number of CSF cells in patients with ARL-CNS usually increased only slightly, with an increase in protein, and sugar and chlorine levels within the normal range. These signs overlap with those of AIDS complicated with intracranial infectious diseases.Clinical manifestations of ARL-CNS are also not specific, leading to difficulties in diagnosis. ARL-CNS and infectious diseases present as multiple lesions

in conventional MR. It is also very difficult to differentiate two diseases by radiology, which primarily manifested annular or nodular enhancement of MR[1, 9-12].

3.2.1 Conventional MR in Diagnosis and Differential Diagnosis of ARL-CNS.

ARL-CNS usually shows multiple lesions by conventional MR. The lesions are typically located slightly more supratentorial than subtentorial. They can also be located around the ventricle, beside the midline, or under the cortex. The current study shows that lesions involving the paraventricle are statistically significant. Those involving the corpus callosum are even more suggestive of an ARL-CNS diagnosis. ARL-CNS can easily invade the ependyma, pia mater and dura mater and can spread along it, which is similar to the findings of Kasamon[10]. The *p*value involving the ependyma was 0.057, buta larger sample size was required to clarify whether there is a difference between two groups. Most ARL-CNS originates in the perivascular space and shows multicentric infiltrative growth to the periphery, forming a typical "cuff-like" pattern. Tumor mass effect is relatively light, while e peritumoral edema can be light or heavy. Normally, the signals of T1WI and T2WI have no specificity. Masses without necrosis tend to be isointense relative to the grey matter. Hemorrhage is common in ARL-CNS, which is considered to be an inhomogeneous high signal in T1WI.

Differential diagnosis:

Toxoplasmosis infection is one of the most common intracranial opportunistic infections in AIDS. The serum toxoplasma IgG test is often either a false negative or false-positive result. The clinical diagnosis is more difficult when the experimental therapeutic effect is poor. Toxoplasma gondii circulated through the blood to the brain, mainly at the junction area of the grey matter and white matter. The supratentorial/subtentorial region can be involved, but rarely the ventricles, ependyma and meninges. MR typically presents multiple intracranial annular enhancement foci, which often involve the basal ganglia[2]. In typical cases,T2WI and enhanced scanning show "target signs", but the incidence is less than 30%[13]. T2WI can show hypointensity, which is associatedto coagulative necrosis. Edema around the focus is severe.After 2-4 weeks of anti-Toxoplasma gondii treatment, the lesion is absorbed or reduced, and the edema effect is reduced. Effective experimental treatment can prompt a diagnosis. After treatment, the area is prone to bleeding easily and shows a high signal on T1WI, which increases the diagnostic difficulty of ARL-CNS.

AIDS complicated with cerebral tuberculosis:In AIDS patients, the incidence of cerebral tuberculosis is second only to pulmonary tuberculosis and lymphoid tuberculosis. The MR showed multiple dot or ring-enhanced lesions at the junction of gray and white matter. Meninges were easily involved, often with hydrocephalus. The annular enhanced wall of tuberculoma is more tensional than that of toxoplasmosis.

PML: PML is different from circular or nodular enhancement lesions such as ARL-CNS, toxoplasmosis and tuberculoma. Here, we are discussing PML because there were four cases in the infection group. PML is an opportunistic demyelination of the central nervous system caused by JC virus infection. PML typical presents as bilateral multiple and asymmetrical white matter lesions. These lesions can involve any part

of the supratentorial and infratentorial white matter. Bilateral cerebral hemispheres are often involved, the parietal lobe being the most severely affected, followed by the frontal lobe.Supratentorial leukoencephalopathy is most commonly associated with arcuate fibers(U-shapedfibers). The infratentorial involvement mainly affects the bridge arm, adjacent pons and cerebellum. The lesions have a low signal on T1WI and a high signal on T2WI. Typical lesions are "finger-shaped" and "scallop-shaped". In the current study, enhancement or mild peripheral enhancement were not observed in the lesions upon enhanced scanning.

Another opportunistic infection such as cryptococcus, which causes meningoencephalitis. Typical MR manifestations include thickening and enhancement of the frontal and parietal meninges and formation of a colloidal pseudocyst in the perivascular space of the basal ganglia. Clinically, a clear diagnosis can be obtained from cerebrospinal fluid positive for cryptococcus antigen or positive by ink staining. This condition is more easily distinguished from the above diseases and will not be further discussed here.

3.2. 2 Multimodal MR Differential Diagnosis.

DWI: Lymphoma without necrosis showed high DWI signal and a decreased ADC value, which indicated that diffusion was limited. The differences in ADC values of the ARL-CNS and infection groups were statistically significant. This finding is consistent with the study by Camacho[14], which showed that a high DWI signal and a decreased ADC value suggested ARL-CNS from toxoplasmosis. The limited diffusion of the solid portion may be due to the tumor cell structure with less cytoplasm, larger nuclei, more euchromatin, a lack of organelles, an abundance of ribosomes, a high nuclear-cytoplasmic ratio, a low water content, rich reticular fibers and other pathological characteristics. The main component of reticular fibers is collagen, which contains little water content. These pathological characteristics lead to the limited diffusion of water molecules in the tumor body and high DWI signal[15]. In our group, seven cases of infectious lesions were hyperintense on DWI, but their ADC values were also hyperintense, indicating that the diffusion was not limited. The cause of DWI hyperintensity was the T2 penetration effect, suggesting that ADC value shouldbeattachedimportancein clinical work. The ADC value excludes the influence of the T2 penetration effect on DWI signals and makes the interpretation of diffusion-weighted imaging more reasonable.

SWI is an imaging sequence based on differences in magnetic sensitivity and the blood oxygen level-dependent (BOLD) effect between tissues. SWI can sensitively display paramagnetic substances in tissues and has significant advantages in displaying microvascular structures and microhemorrhage foci. Hemorrhage and necrosis often occur in ARL-CNS and present as uneven, slightly high signal on T1WI and as multiple punctate/linear and patchy low signal on SWI. Refer to Park[5] for the classification of low SWI signal. The ITSS in ARL-CNS was statistically significantly higher (2-3 times) than in the infection group. There were 3 cases of toxoplasmosis in the infection group, one of which had internal hemorrhage after treatment. ITSS was divided into 3 grades, and the other 2 cases had ITSS grades of 0-1. The other infectious lesions, such as abscesses, tuberculoma, PML, and others, all had ITSS grades of

0-1. These findings are in accordance with those of Lai[16]. The combination of SWI and DWI plays an important role in differentiating brain tumors from infectious diseases.

The MR arterial spin labelling technique (ASL) technique uses water in arterial blood as an endogenous contrast agent by detecting magnetically labelled blood quality. When there is subcurrent passing through the region of interest, the change of tissue signal intensity reflects information of local tissues blood perfusion. With the continuous updates of technology, software and hardware, this technique is now in clinical practice.3D-pCASL is widely used as a safe and reliable method to quantitatively evaluate tumor blood perfusion[17]. Although brain lymphoma may invade vascular endothelial cells and even vascular walls, we found no obvious neovascularization, ASL hypoperfusion was apparent. Da Rocha[18] stated that hypoperfusion was a particular sign of lymphoma that was related to the lack of angiogenesis in tumor tissues and the extrusion and infiltration of microcirculatory vessels by tumor cells. Of the nine ARL-CNS cases, six showed hypoperfusion, a finding similar to that in previous studies of normal immune lymphoma. Among the ten cases of infectious disease, there were two cases of PML with high perfusion in the periphery, and the other eight cases showed low perfusion. There was no significant difference between two groups.

3.2.3 Improvement of diagnosis efficiency in multimodal MR combined with conventional MR

ARL-CNS and infectious lesions often present as multiple lesions on the conventional sequence.They can show supratentorial/subtentorial, subcortical, and/or periventricular, and the ependyma and meninges can be affected. Enhancement methods can be nodular or annular, causing difficulties in differential diagnosis. When the corpus callosum is involved, it is considered ARL-CNS. Infectious lesions such as PML can be considered when the lesions are not enhanced. However, the incidence is relatively low. It is difficult to diagnose ARL-CNS by conventional MR, with a sensitivity of 88.9%, a specificity of 70.0%, and an accuracy of 78.9%.Conventional MR combined with DWI/ADC has improved sensitivity, but its specificity is decreased and its accuracy is unchanged. DWI, as a more commonly used clinical sequence, has the advantages of a short time and insensitivity to motion artifacts. Additional DWI sequence scans can reduce the missed diagnosis rate of ARL-CNS. For AIDS patients, the nature of intracranial lesions is more complex. We recommend DWI sequence scanning to assess the possibility of ARL-CNS. The sensitivity, specificity and accuracy rate of the conventional sequence combined with SWI-ITSS were found to be 100%, 70.0%,and 84.2%, respectively. The sensitivity and accuracy of the conventional sequence combined with SWI were improved compared with the conventional sequence. However, the time required to scan the whole brain takes much longer, taking approximately 4 minutes. If every AIDS patient undergoes this sequence, it will undoubtedly cause great pressure to clinics and reduce work efficiency. Therefore,we recommend that when distinguishing ARL-CNS from toxoplasmosis or tuberculoma, this sequence should be scanned as soon as possible to obtain a correct diagnosis.

3.3 Shortcomings of this study

The sample size of the study was insufficient. The pathology results in the infection group were more and relativelycomplicated, which may have affected the determination of MR signs and the accuracy of the statistical results. The next step in this field of study is to increase investment in this research area to increase sample collection. In this way, more objective results can be obtained, leading to further clarity on the early clinical diagnosis of ARL-CNS.

Conclusions

For AIDS complicated with intracranial lesions, we recommend adding DWI / ADC sequence to conventional MR. SWI should be taken when distinguishing ARL-CNS from infection.

List Of Abbreviations

ARL-CNS=AIDS-related central nervous system lymphoma

SWI=Susceptibility Weighted Imaging

ITSS=degree of intratumoral susceptibility signal intensity

3D-pCASL=3D pseudo-continuous arterial spin labelling

EBV=epstein-barr virus

PML= progressive multifocal leukoencephalopathy

CBF= cerebral blood flow

NHL= non-Hodgkin lymphoma

HL= Hodgkin lymphoma

BOLD= blood oxygen level-dependent

Declarations

Ethic approval and consent to participate: This study was approved by the Ethics Committee of Beijing Ditan hospital, Capital Medical University (2019-No.0061-001).

The requirement for informed consent was waived for this retrospective study.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: This work is supported by "Budding" support program of youth talent development of Beijing Ditan Hospital, Capital Medical University.DTMY201810.

Authors' contributions: JJ L collected and analyzed patients' images and were major contributors in writing the manuscript. RM X and BD C made contributions on study concept and design, and BD C was the guarantor of integrity of the entire study. MX performed data analysis. SY contributed to literature research. CS G worked on statistical analysis. All authors read and approved the final manuscript.

Acknowledgments: We appreciate the help on English language editing by AJE.

References

1. Biggar RJ, Chaturvedi AK, Goedert JJ, Engels EA: **AIDS-related cancer and severity of immunosuppression in persons with AIDS**. *J Natl Cancer Inst* 2007, **99**(12):962-972.
2. Bowen LN, Smith B, Reich D, Quezado M, Nath A: **HIV-associated opportunistic CNS infections: pathophysiology, diagnosis and treatment**. *NAT REV NEUROL* 2016, **12**(11):662-674.
3. Kasamon YL, Ambinder RF: **AIDS-Related Primary Central Nervous System Lymphoma**. *Hematology/Oncology Clinics of North America* 2005, **19**(4):665-687.
4. Sun JJ, Lu HZ: **[Highlights of the third edition of Chinese guidelines for AIDS diagnosis and treatment(2015)]**. *Zhejiang Da Xue Xue Bao Yi Xue Ban* 2015, **44**(6):597-602.
5. Park MJ, Kim HS, Jahng GH, Ryu CW, Park SM, Kim SY: **Semiquantitative assessment of intratumoral susceptibility signals using non-contrast-enhanced high-field high-resolution susceptibility-weighted imaging in patients with gliomas: comparison with MR perfusion imaging**. *AJNR Am J Neuroradiol* 2009, **30**(7):1402-1408.
6. Vivithanaporn P, Heo G, Gamble J, Krentz HB, Hoke A, Gill MJ, Power C: **Neurologic disease burden in treated HIV/AIDS predicts survival: a population-based study**. *NEUROLOGY* 2010, **75**(13):1150-1158.
7. Bilgrami M, O'Keefe P: **Neurologic diseases in HIV-infected patients**. *Handb Clin Neurol* 2014, **121**:1321-1344.
8. Ota Y, Hishima T, Mochizuki M, Kodama Y, Moritani S, Oyaizu N, Mine S, Ajisawa A, Tanuma J, Uehira T *et al*: **Classification of AIDS-related lymphoma cases between 1987 and 2012 in Japan based on the WHO classification of lymphomas, fourth edition**. *Cancer Med* 2014, **3**(1):143-153.
9. Chen H, Lin F, Liu S, Da Y, Guo D: **Neurological manifestations, laboratory and neuroimaging features in HIV-infected patients**. *Neurosciences (Riyadh)* 2017, **22**(4):311-315.
10. Kasamon YL, Ambinder RF: **AIDS-Related Primary Central Nervous System Lymphoma**. *Hematology/Oncology Clinics of North America* 2005, **19**(4):665-687.

11. Bilgrami M, O Keefe P: **Chapter 90 - Neurologic diseases in HIV-infected patients**. In: *Handbook of Clinical Neurology.* Edited by Biller J, Ferro JM, vol. 121: Elsevier; 2014: 1321-1344.
12. Matinella A, Lanzafame M, Bonometti MA, Gajofatto A, Concia E, Vento S, Monaco S, Ferrari S: **Neurological complications of HIV infection in pre-HAART and HAART era: a retrospective study**. *J NEUROL* 2015, **262**(5):1317-1327.
13. Hamdeh S, Abbas A, Fraker J, Lambrecht JE: **Intracranial toxoplasmosis presenting as panhypopituitarism in an immunocompromised patient**. *AM J EMERG MED* 2015, **33**(12):1841-1848.
14. Camacho DLA, Smith JK, Castillo M: **Differentiation of Toxoplasmosis and Lymphoma in AIDS Patients by Using Apparent Diffusion Coefficients**. *AM J NEURORADIOL* 2003, **24**(4_x000a_):633.
15. You S, Yun TJ, Choi HJ, Yoo R, Kang KM, Choi SH, Kim J, Sohn C: **Differentiation between primary CNS lymphoma and glioblastoma: qualitative and quantitative analysis using arterial spin labeling MR imaging**. *EUR RADIOL* 2018, **28**(9):3801-3810.
16. Lai P, Chung H, Chang H, Fu J, Wang P, Hsu S, Hsu S, Lin H, Chuang T: **Susceptibility-weighted imaging provides complementary value to diffusion-weighted imaging in the differentiation between pyogenic brain abscesses, necrotic glioblastomas, and necrotic metastatic brain tumors**. *EUR J RADIOL* 2019, **117**:56-61.
17. Dai W, Garcia D, de Bazelaire C, Alsop DC: **Continuous flow-driven inversion for arterial spin labeling using pulsed radio frequency and gradient fields**. *MAGN RESON MED* 2008, **60**(6):1488-1497.
18. Da RA, Sobreira GB, Da SDRT, Maia JA, Chiattone CS: **Modern techniques of magnetic resonance in the evaluation of primary central nervous system lymphoma: contributions to the diagnosis and differential diagnosis**. *Rev Bras Hematol Hemoter* 2016, **38**(1):44-54.

Tables

Table 1. Routine MR Manifestations in ARL-CNS and Infection Group

Groups	Supra vs infratentorial		Multiple	Distribution (Involved or Not)					Enhancement pattern		
	Supra	Infra		under the cortex	paraventricular	corpus callosum	ependyma	meninges	nodular	ring	no
ARL-CNS	9	3	8	4	8	4	5	3	6	3	0
Infection	7	7	6	9	3	0	1	1	2	6	2
P value	0.211	0.370	0.303	0.057	0.020	0□033	0.057	0.303	0.070	0.650	0.211

Table 2. Multimodal MR manifestations of ARL-CNS group and infection group

Groups	ASL/CBF		DWI			ADC			SWI-ITSS	
	low	high	low	high	equal	high	low	equal	0-1	2-3
ARL-CNS	6	3	1	8	0	0	9	9	1	8
Infection	8	2	2	7	1	7	2	1	9	1
P value	0.628		1.000	0.582	1.000	0.003	0.001	1.000	0.001	

Figures

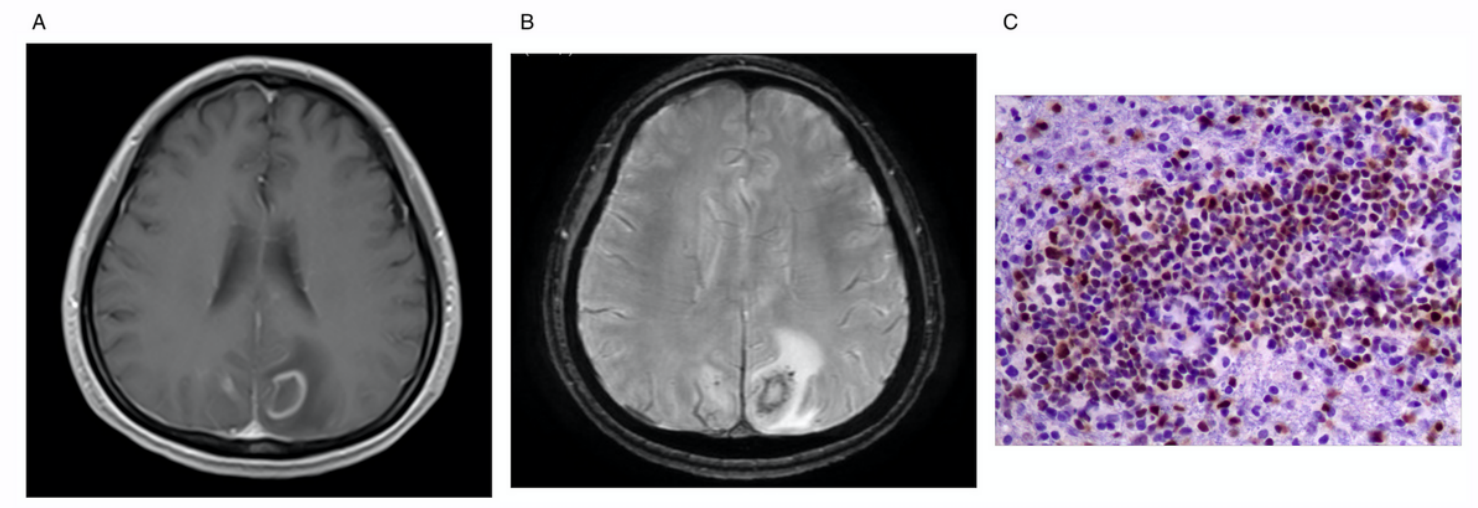

Figure 1

Case 1, a middle age female patient. Figure 1A-1C is enhanced T1WI, SWI and biopsy pathology. On contrast-enhanced T1WI, the left parietal subcortical showed ring enhanced nodule. On SWI, multiple punctate and fine line like low signal (TISS Level 3) were found in the lesion. The pathological diagnosis was diffuse large B-cell lymphoma.

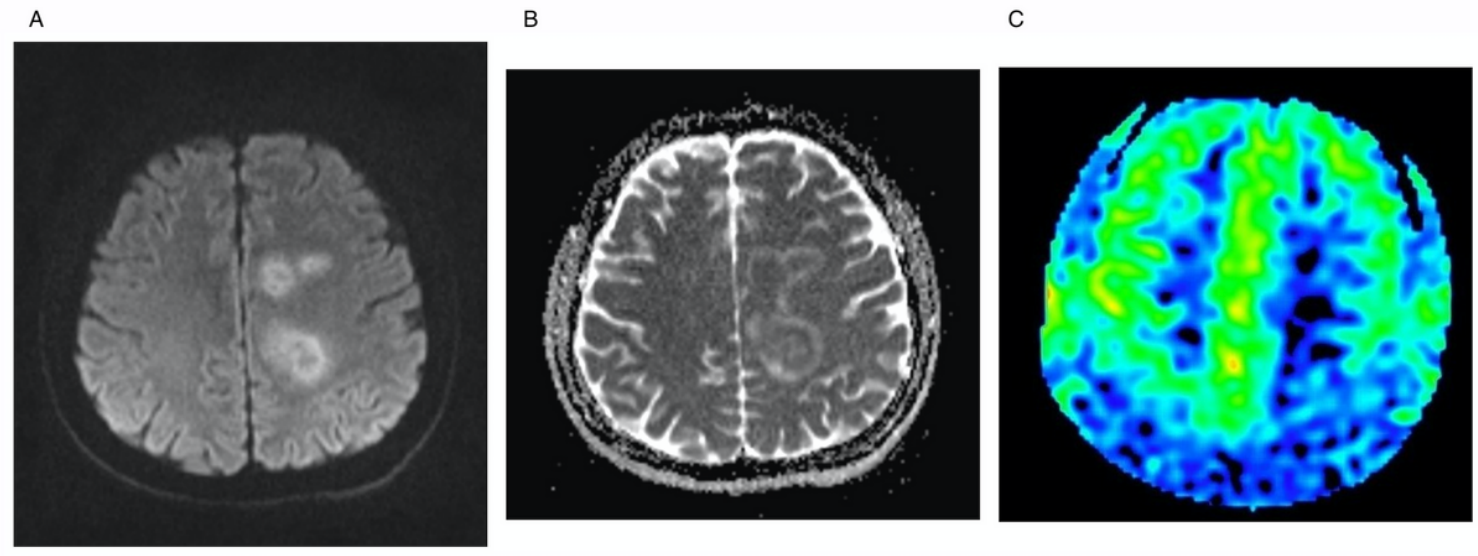

Figure 2

Case 2, a young man. Figure 2A-2C shows DWI, ADC and CBF (post-processing result of ASL sequence). Irregular lesions were found periventricular of the left lateral ventricle, with high signal on DWI, low singal on ADC, and decreased on CBF. The lesion was confirmed high invasive B cell lymphoma by biopsy.