

MRI in central nervous system infections: A simplified patterned approach

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Abstract

Recognition and characterization of central nervous system infections poses a formidable challenge to the neuro-radiologist. Imaging plays a vital role, the lesions typically being relatively inaccessible to tissue sampling. The results of an accurate diagnosis are endlessly rewarding, given the availability of excellent pharmacological regimen. The availability of numerous magnetic resonance (MR) sequences which provide functional and molecular information is a powerful tool in the hands of the radiologist. However, the plethora of sequences and the possibilities on each sequence is also intimidating, and often confusing as well as time consuming. While a large number of reviews have already described in detail the possible imaging findings in each infection, we intend to classify infections based on their imaging characteristics. In this review we describe an algorithm for first classifying the imaging findings into patterns based on basic MR sequences (T1, T2 and enhancement pattern with Gadolinium), and then sub-classify them based on more advanced molecular and functional sequences (Diffusion, Perfusion, Susceptibility imaging, MR Spectroscopy). This patterned approach

is intended as a guide to radiologists in-training and in-practice for quickly narrowing their list of differentials when faced with a clinical challenge. The entire content of the article has also been summarised in the form of flow-charts for the purpose of quick reference.

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Key words: Central nervous system; Infection; Magnetic resonance imaging; Magnetic resonance spectroscopy; Perfusion weighted magnetic resonance imaging; Diffusion weighted magnetic resonance imaging

Core tip: The plethora of magnetic resonance sequences available with the radiologist today provides a wealth of information about anatomical, pathological, physiological, functional and molecular aspects of the brain. While this provides an opportunity to transform patient management, the vast number of possibilities can be bewildering, particularly for the radiologist in-training. It is often easy to get lost in the details while forgetting the larger picture. In this article we first classify the infections into broad imaging patterns, and subsequently sub-classify them based on more advanced sequences (molecular and functional imaging). The flow-charts in the article are intended as a source of quick reference to the radiologist when faced with a clinical challenge.

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INTRODUCTION

Central nervous system (CNS) infections are a significant

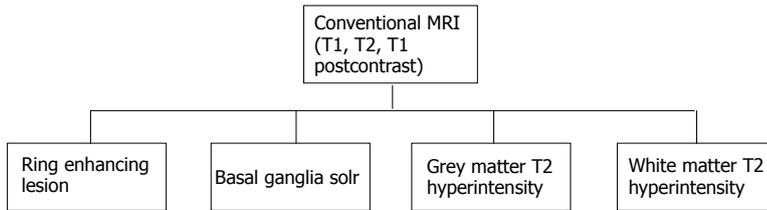


Figure 1 Classification of abnormalities on conventional magnetic resonance imaging sequences in suspected central nervous system infections.

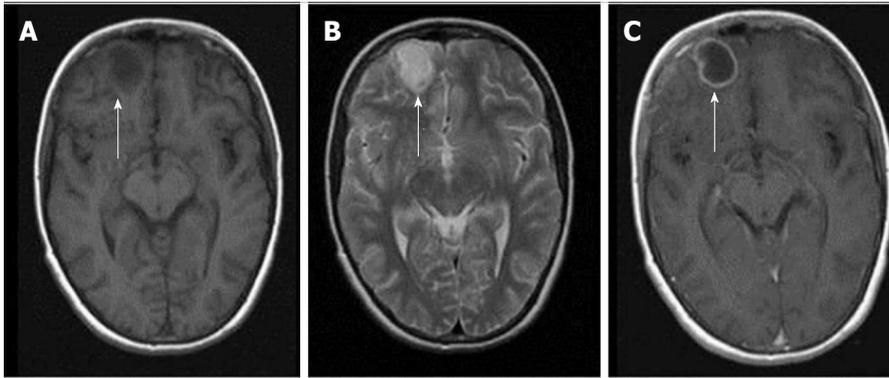


Figure 2 Ring enhancing lesions. T1 (A), T2 (B) and T1 (C) post gadolinium images from the magnetic resonance of an acutely ill child with fever. A ring enhancing lesion is seen in the right frontal lobe. This patient had a bacterial brain abscess. The differential diagnosis of this appearance would include a brain abscess of any etiology.

cause of mortality and morbidity world-wide. This is particularly true owing to its association with conditions of immunological compromise and the increasing incidence of human immunodeficiency virus (HIV) infection is further adding to the problem^[1]. Today with the availability of excellent antimicrobials, many of these disorders are potentially treatable, making early recognition imperative. Like in other disorders of the CNS, non-invasive imaging based diagnosis is the key as possibility of a tissue diagnosis by means of fine needle aspiration cytology (FNAC) or biopsy is difficult. Early diagnosis will also help to minimize long term complications related to the disease and its treatment.

The primary imaging modality, like in most CNS disorders is magnetic resonance imaging (MRI)^[2]. Coming to an exact etiological agent on the basis of conventional MRI sequences with Gadolinium enhancement is always difficult due to overlapping imaging characteristics. With the possibility of molecular and functional imaging with newer MRI techniques however, the radiologist today is better equipped to handle this dilemma. Though the use of such multiple MRI sequences adds lots of information to narrow the differential possibilities, this vast information is difficult to recall when faced with a clinical problem.

The purpose of this review is to provide a rational MRI approach to narrow the list of differentials, to quickly classify and characterize CNS infections. The flow-charts presented in this review guides the radiologist to first recognize the pattern of findings on routine MRI sequences and subsequently narrow the differential diagnosis based on the addition of other MR parameters such as diffusion weighted imaging (DWI) and MR spec-

troscopy (MRS).

CLASSIFICATION

Most infections in the CNS may be classified in one of the following categories based on their T1, T2 and contrast enhancement characteristics (Figure 1) as follows (an image demonstrating a typical lesion in each category has been provided in Figures 2-5): Ring enhancing lesions (Figure 2), Basal ganglia space occupying lesions (Figure 3), Grey matter hyperintensities (Figure 4), White matter hyperintensities (Figure 5).

RING ENHANCING LESIONS

Peripheral ring-like enhancement is a common finding in CNS imaging. Ring enhancing lesions on conventional MRI sequences have a long list of differentials ranging from infectious processes to high grade necrotic neoplasm. Glioblastoma multiforme represents the most important condition. Abscesses are usually associated with a thin smooth rim, in contrast to the nodular irregular rim seen in Glioblastoma multiforme. Satellite lesions are commonly seen in abscesses, unlike necrotic neoplasm^[1]. Recent work by some investigators has suggested a role for susceptibility weighted imaging (SWI) in this differentiation. They found that a smooth, complete rim of susceptibility is seen in abscesses in contrast to incomplete irregular rims seen in necrotic neoplasm^[3].

All mature abscesses whether bacterial, fungal or pyogenic are hypointense on T1, hyperintense on T2 and show ring enhancement following intravenous Gado-

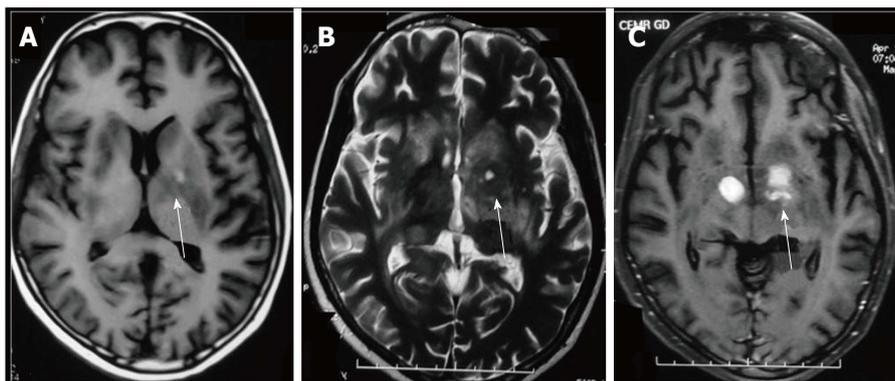


Figure 3 T1 (A), T2 (B) and Post gadolinium T1 (C) weighted images in an human immunodeficiency virus-positive patient with space occupying lesions in bilateral basal ganglia. Differentials for this appearance in such a patient would include Toxoplasmosis, Cryptococcosis as well as central nervous system (CNS) lymphoma. This patient had CNS lymphoma.



Figure 4 Fluid Attenuated Inversion Recovery Sequence in a patient with fever and altered sensorium shows hyperintensity predominantly in the grey matter of both temporal lobes and also in cerebellum. This patient was diagnosed with Japanese B Encephalitis. A similar picture may be seen in other viral encephalitis including herpes encephalitis.

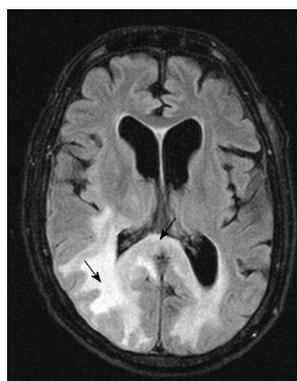


Figure 5 Fluid Attenuated Inversion Recovery Sequence image of a human immunodeficiency virus-positive patient shows hyperintensity predominantly involving the occipital white matter and splenium. The differential diagnosis for such an appearance would include human immunodeficiency virus encephalopathy, progressive multifocal leukoencephalopathy (PML) as well as other demyelinating conditions. This patient had PML.

linium injection. Further differentiation of abscesses for possible etiological cause may be made as follows.

DIFFUSION WEIGHTED IMAGING

DWI explores the molecular characteristic of diffusivity of particles within a region. It is based on the application of two gradients at a set interval of time, in such a way that only a molecule that experiences both gradients at the same position (does not exhibit motion between the two gradients) produces signal. Therefore regions of the brain that show “restricted diffusion” are hyperintense on DWI. This restricted diffusion appears as hyperintense area on DWI and needs to be corroborated with computer generated apparent diffusion coefficient (ADC) maps which show corresponding hypointense area. This corroboration rules out T2-shine through effect. Bacterial as well as tubercular abscesses show central diffusion restriction^[4,5] due to highly viscous necrotic tissue within (Figure 6). Fungal abscesses show intracavitary projections. The wall of abscess and the projections may demonstrate diffusion restriction^[5,6], though no restriction is seen in the abscess core (Figure 7).

DWI plays an important role in the differentiation of these abscesses from necrotic neoplasms, which usually demonstrate high ADC values within the core^[7].

MR SPECTROSCOPY

Spectroscopy provides information about metabolic alterations within a voxel by exploiting changes in the microenvironment produced by unique chemical characteristics of specific metabolites. Thus using this technique it is possible to infer the presence of a microorganism, based on the expected products of the microorganisms metabolism reflected in the metabolic signature.

The characteristic of the spectrum in bacterial abscesses is the presence of amino acid peak at 0.9 parts per million (ppm) [inverted peak at an time of echo (TE) 136 ms] representing valine, leucine and isoleucine (Figure 8)^[2]. The detection of succinate (2.4 ppm) and acetate (1.92 ppm) is proposed to indicate anaerobic organisms^[2].

Tuberculosis is characterised by lipid peaks at 0.9, 1.3, 2.0 and 2.8 ppm. The presence of lipids in the absence of other amino acids, lactate and succinate is strongly suggestive of tubercular abscess (Figure 9)^[5,8]. 0.9, 1.3, 2.0, 2.8, and 3.7 peaks correspond to specific chemical groups within metabolites found in these infections- 0.9 corresponds to a terminal methyl group, 1.3 to a methylene group, 2.0 and 2.8 to specific groups in fatty acyl chains and 3.7 to phosphoserine.

While lactate, acetate and succinate can all be seen

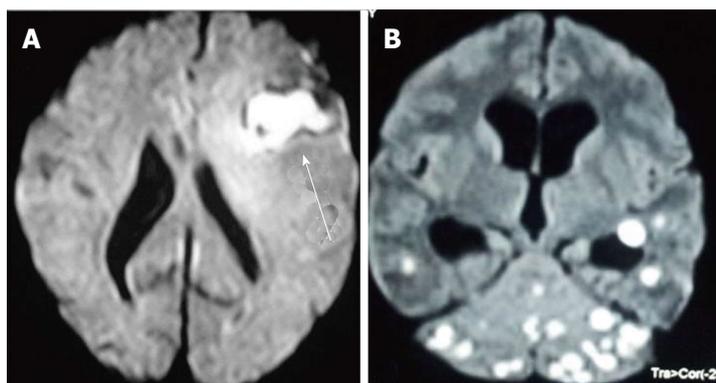


Figure 6 Diffusion weighted images show central restriction of diffusion in bacterial abscess (A) and tuberculomas (B) arrow.

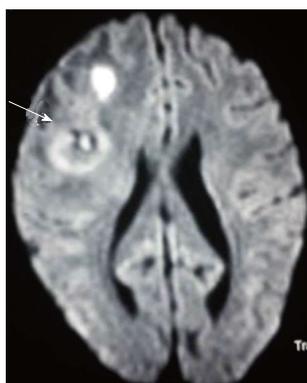


Figure 7 Diffusion weighted image in a diabetic patient shows diffusion restriction in the wall and intra-cavitary projection (arrow) in the centre of a fungal abscess.

in fungal abscesses, the presence of multiple signals between 3.6 and 3.8 ppm (representing Trehalose) has been seen in some forms of fungal abscesses (Figure 10)^[5]. The absence of choline peak on MRS provides important supportive evidence for an infective etiology as compared to neoplasms which show increased choline^[7,9].

MR ANGIOGRAPHY

Tubercular vasculitis results in extensive infarction due to inflammation of vessels coursing through the basal exudates (Figure 11)^[10]. Vascular involvement with formation of aneurysms is seen in fungal infections. These aneurysms are seen as irregular dilatation of vessel wall on MRA.

SUSCEPTIBILITY WEIGHTED IMAGING

The principle underlying SWI is the alteration of local magnetic field by substances that show paramagnetic properties. This is a gradient sequence, so molecules in the vicinity of a paramagnetic substance dephase rapidly, thus do not contribute to signal production. Voxels containing molecules with different magnetic susceptibilities are imaged when they are exactly out-of-phase, such that the whole voxel appears to be of low signal intensity^[2]. This is seen as an area of “blooming”. The presence of haemorrhage is often a clue to underlying fungal cause of

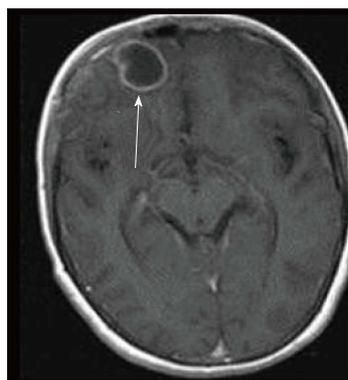
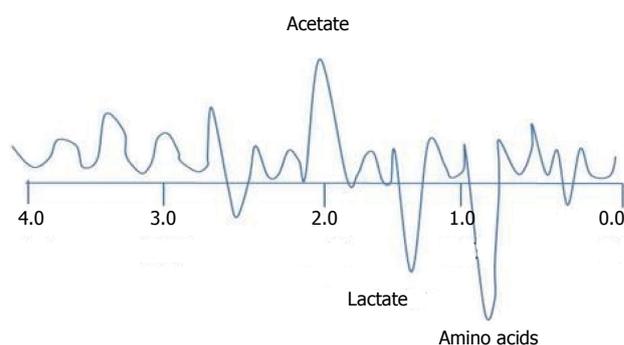


Figure 8 Representation of spectrum of metabolites in a bacterial abscess. Proton magnetic resonance spectroscopy obtained at a time of echo of 30 milliseconds shows the presence of amino acids. Succinate and acetate are seen in anaerobic abscesses.

infection (Figure 12) due to its angioinvasive nature^[11].

The presence of a complete, smooth hypointense rim on SWI favours a diagnosis of an abscess against a necrotic neoplasm. A brief summary of approach to a peripherally enhancing lesion is presented as a flowchart (Figure 13).

BASAL GANGLIA SPACE OCCUPYING LESIONS

A number of CNS lesions are seen characteristically involving the region of basal ganglia. The differential diagnosis in this category includes cryptococcosis, toxoplasmosis and primary CNS lymphoma. Cryptococcosis usually does not show enhancement after gadolinium injection. Further characterisation often requires additional

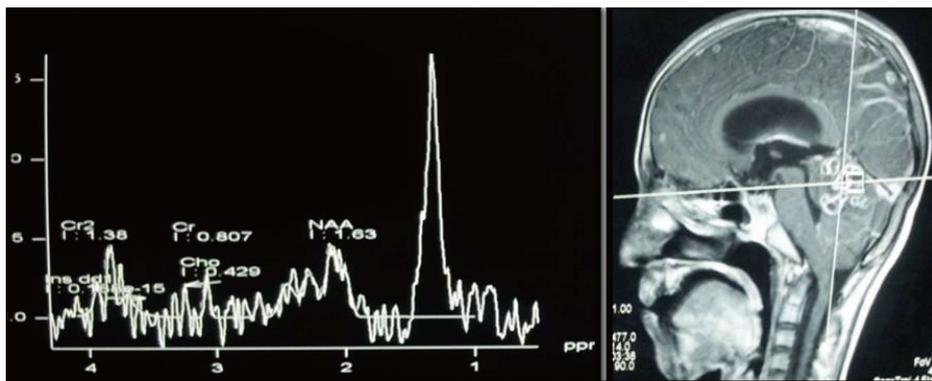


Figure 9 Proton spectroscopy at echo time of 135 ms from a tuberculoma shows a lipid peak at 1.3 ppm.

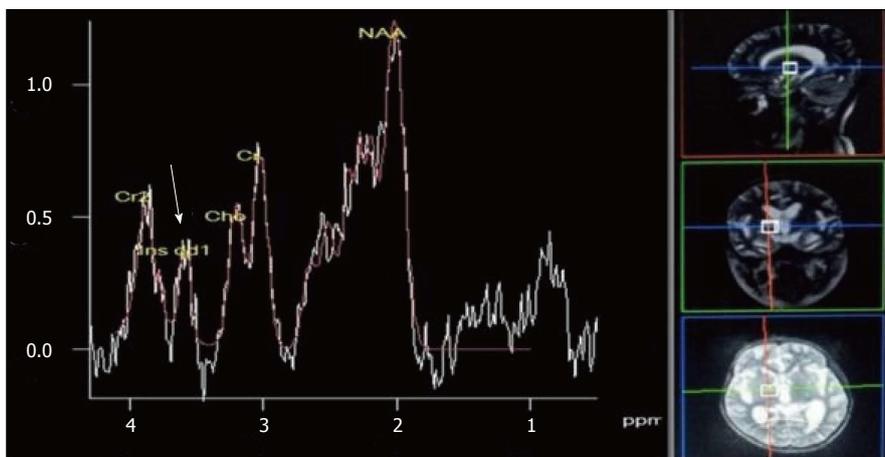


Figure 10 Proton magnetic resonance spectroscopy at time of echo of 30 ms shows multiple peaks between 3.6 and 3.8 ppm in the spectrum obtained from a cryptococcoma (fungus) representative of trehalose peak (arrow).

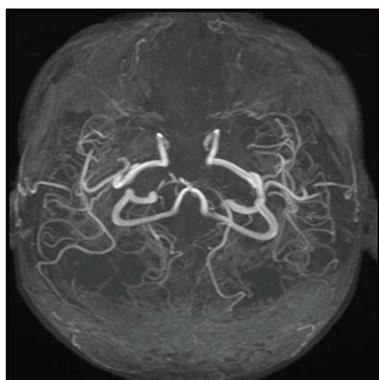


Figure 11 Time of Flight magnetic resonance angiography in a patient with tubercular meningitis. Bilateral anterior cerebral arteries are not seen whereas bilateral middle cerebral arteries are markedly attenuated suggesting vasculitis. The patient presented with extensive cerebral infarction.



Figure 12 Foci of blooming (arrow) noted within the abscess is suggestive of haemorrhage and points to a fungal cause.

sequences.

DWI

Toxoplasmosis does not usually show significant restriction of diffusion, though a wide range of ADC value have been encountered^[2,12]. A proposed explanation is

the lack of viscous contents within these lesions. Peripheral areas may show hyperintensity due to the presence of haemorrhage^[13]. Lymphoma which usually are highly cellular, shows restricted diffusion^[2,12], helping differentiation from toxoplasmosis (Figure 14). The paucity of intercellular spaces results in a decreased diffusivity of water molecules within these lesions. Cryptococcosis is also known to show restricted diffusion within the pseu-

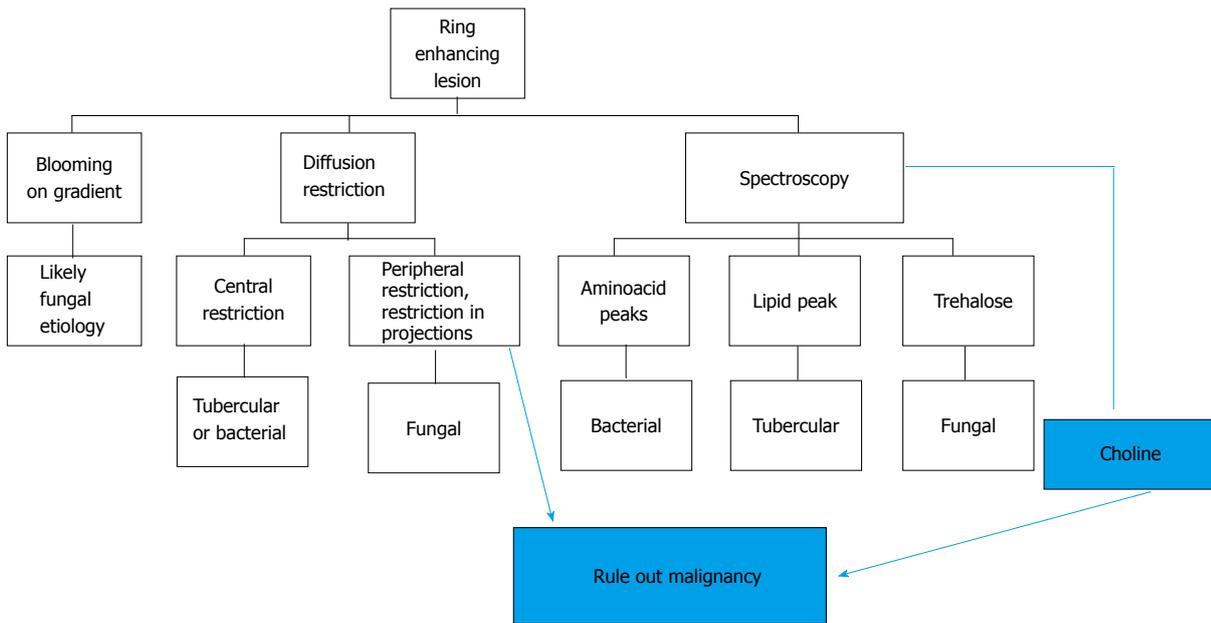


Figure 13 Approach to ring enhancing lesions.

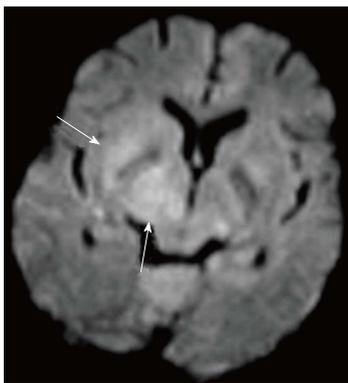


Figure 14 Diffusion weighted image from the Brain magnetic resonance imaging of an human immunodeficiency virus-positive patient with lymphoma shows restriction in the right lentiform nucleus and the thalamus (arrow).

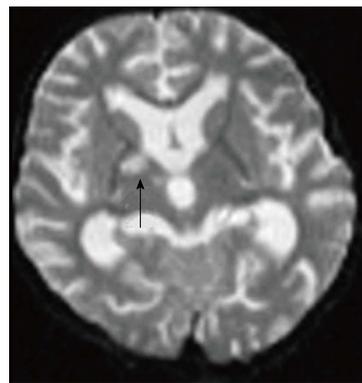


Figure 15 Apparent diffusion coefficient map showing free diffusion with in a cryptococcoma (arrow) in a human immunodeficiency virus-positive patient.

docysts^[2] owing to the viscosity of gelatinous material. Cryptococcomas have been shown to exhibit peripheral diffusion restriction akin to a necrotic brain tumour^[14], though often they may not show any restricted diffusion^[12] (Figure 15).

MRS

Presence of peak between 3.6 to 3.8 ppm (trehalose) has been observed in cryptococcosis (which is a fungus)^[5] (Figure 10). Toxoplasma lesions (Figure 16) show markedly elevated lipid and lactate with diminished levels of all other metabolites^[2]. Lymphoma (Figure 17) shows mild to moderate increase in lipid and lactate with markedly elevated choline peak^[2].

MR perfusion

Toxoplasmosis shows normal or decreased cerebral blood volume (CBV). Primary CNS lymphoma on the other

hand shows elevated CBV^[12].

SWI

Presence of hemorrhage (blooming on gradient echo sequences) points towards toxoplasmosis, as lymphoma rarely show hemorrhage before treatment^[12,15] (Figure 18). A brief summary of the approach to space occupying lesions in the basal ganglia is presented as a flowchart in Figure 19.

GREY MATTER HYPERINTENSITY

T2/ FLAIR hyperintensity involving the grey matter may be seen in encephalitis as well as infarction. This differentiation is aided by diffusion and perfusion sequences (Table 1).

Diffusion and perfusion

Reduced diffusion with increased perfusion points to an

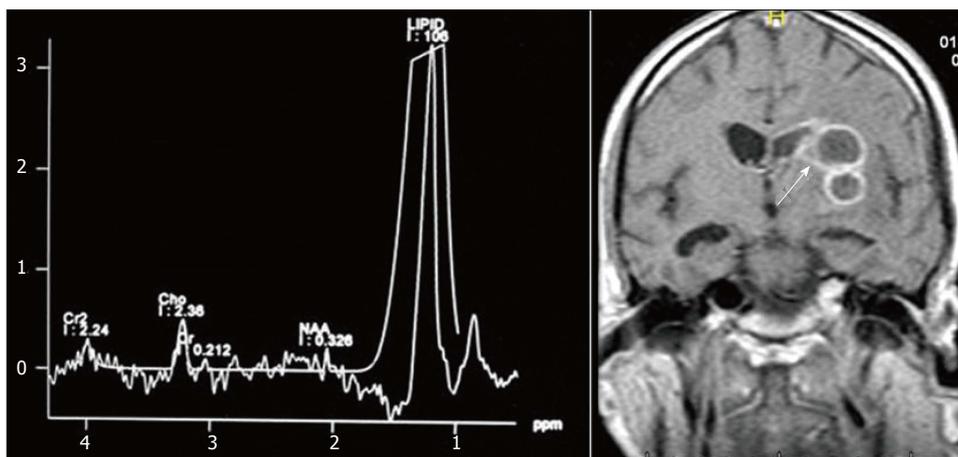


Figure 16 Proton magnetic resonance spectroscopy at echo time of 30 ms in a patient with toxoplasmosis shows a lipid lactate peak with diminished levels of all other metabolites (arrow).

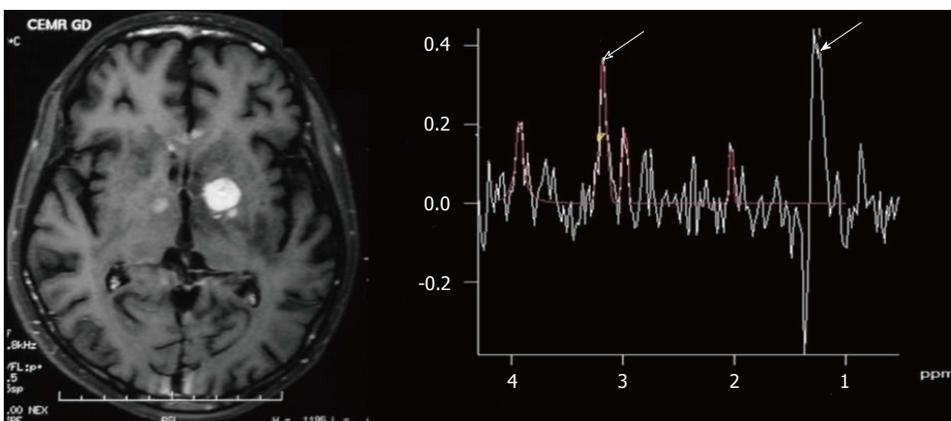


Figure 17 Proton magnetic resonance spectroscopy at echo time of 135 ms in a patient with primary central nervous system Lymphoma of basal ganglia showing elevated lipid, lactate (white arrow) and choline (open arrow).

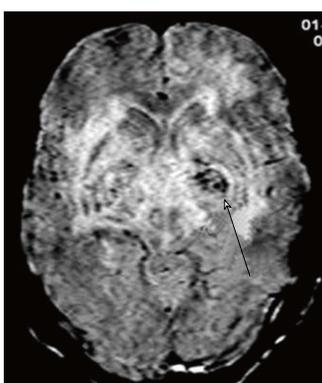


Figure 18 Gradient echo image in a patient with toxoplasmosis shows foci of blooming (arrow) suggestive of haemorrhage.

infective etiology. Reduced diffusion with decreased perfusion characterizes ischemic events. The further characterization of infection is typically based on characteristic neuro-anatomic location of the lesion on T2/FLAIR/DWI (Figure 20)^[2,16]. Prion disease can also show similar imaging manifestation. The imaging appearance of these encephalitis may be fairly non-specific. The dengue vi-

Table 1 This differentiation is aided by diffusion and perfusion sequences

	Diffusion	Perfusion
Infection	Restricted	Increased
Infarction	Restricted	Decreased

rus has been reported to show imaging features similar to Japanese encephalitis^[17] in regions where this virus is common. Cytomegalovirus can also show non-specific manifestations, though the predominant involvement of grey matter (more than white matter) is an important differentiating feature^[1]. The presence of a pencil-thin rim of enhancement in the subependymal region is considered to be a specific finding^[1]. Approach to lesions presenting with hyperintensity predominantly involving the Grey matter is presented as a flowchart in Figure 21.

WHITE MATTER HYPERINTENSITIES

The major diagnostic considerations are HIV encephalopathy (HIVE) and progressive multifocal leukoen-

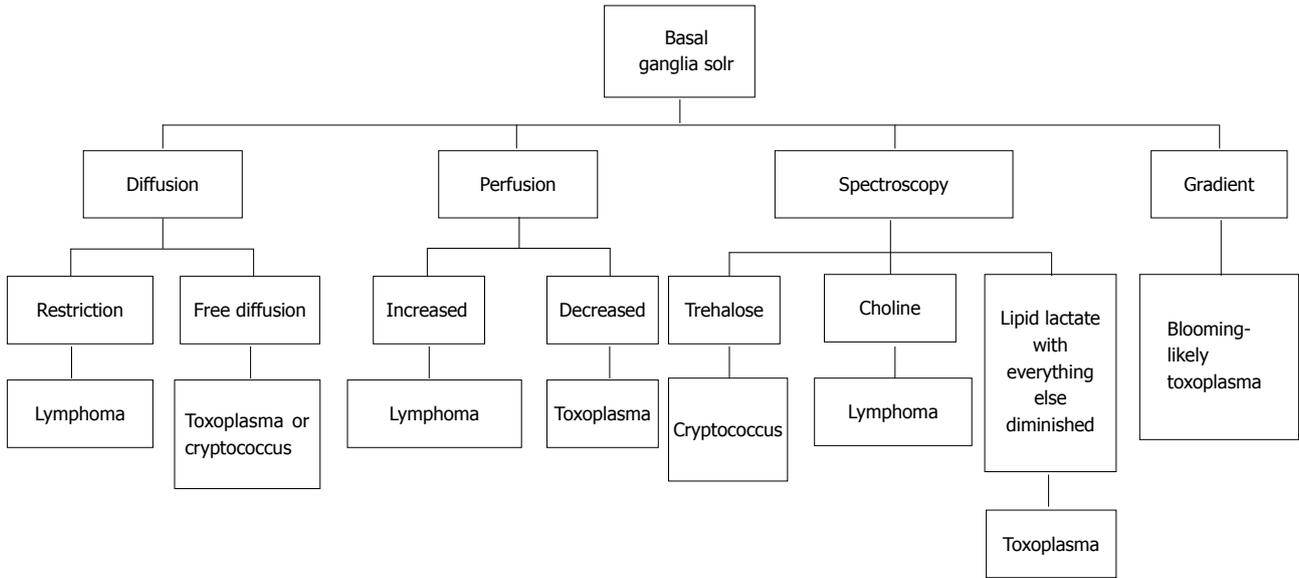


Figure 19 Approach to space occupying lesions in the basal ganglia.

Table 2 Role of additional sequences			
	T1	T2	T1 + contrast
HIV Encephalopathy	Isointense	Bilaterally symmetrical periventricular white matter hyperintensities	No enhancement
PML	Hypointense	Asymmetrical lesions involving subcortical and periventricular white matter	Faint peripheral areas of enhancement may sometimes be seen

HIV: Human immunodeficiency virus; PML: Progressive multifocal leukoencephalopathy.

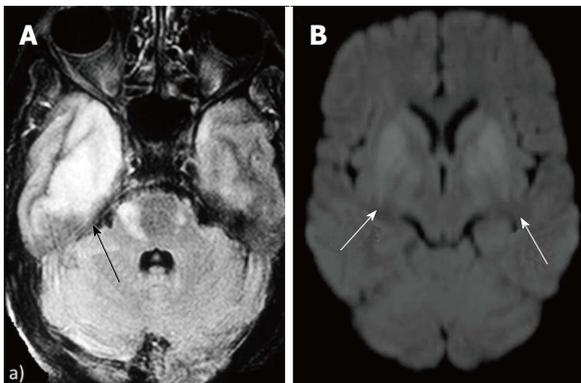


Figure 20 Fluid Attenuated Inversion Recovery Sequence hyperintensity (A) involving right temporal lobe (black arrow) in a patient with Herpes simplex virus encephalitis, diffusion weighted imaging (B) in a patient with Japanese encephalitis showing restricted diffusion in bilateral basal ganglia.

cephalopathy (PML) (Figure 22). Though both entities have characteristic imaging features on conventional MR sequences (Table 2), they may be difficult to differentiate due to overlapping features.

Magnetization transfer

Magnetization transfer (MT) reduction is seen in both PML and HIVE. In PML, it is due to demyelination whereas in HIVE it is primarily related to gliosis. Thus

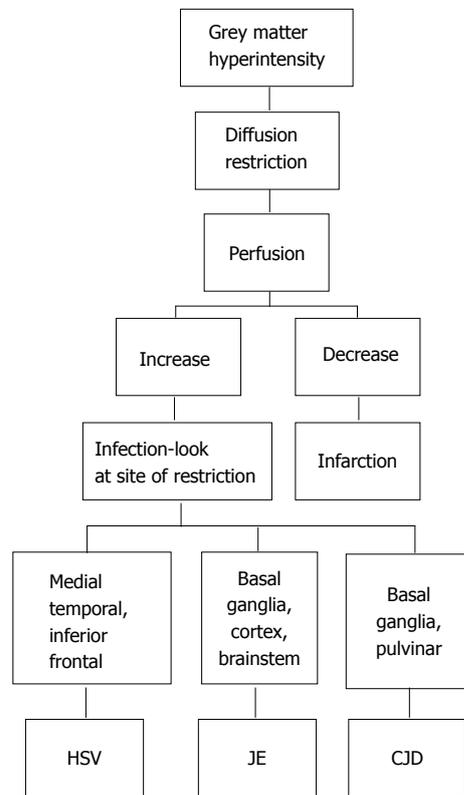


Figure 21 Approach to lesions presenting with hyperintensity predominantly involving the Grey matter.

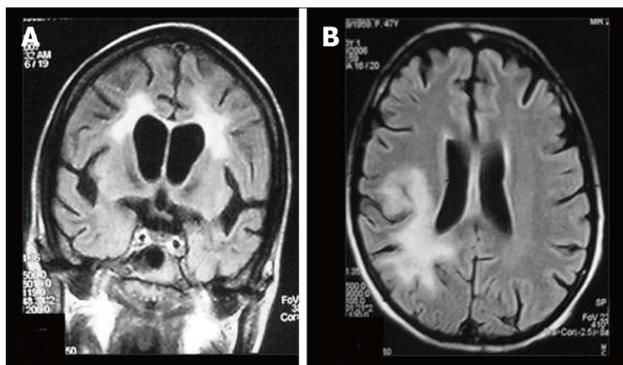


Figure 22 Fluid Attenuated Inversion Recovery Sequence image of a patient with (A) human immunodeficiency virus encephalopathy showing symmetrical periventricular white matter hyperintensity and (B) progressive multifocal leukoencephalopathy showing asymmetrical involvement of white matter, predominantly posterior subcortical white matter, with extension into the periventricular region.

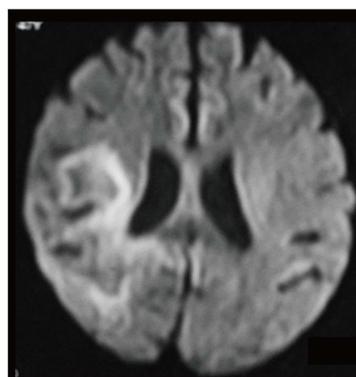


Figure 23 Diffusion weighted image in a patient with progressive multifocal leukoencephalopathy showing peripheral diffusion restriction.

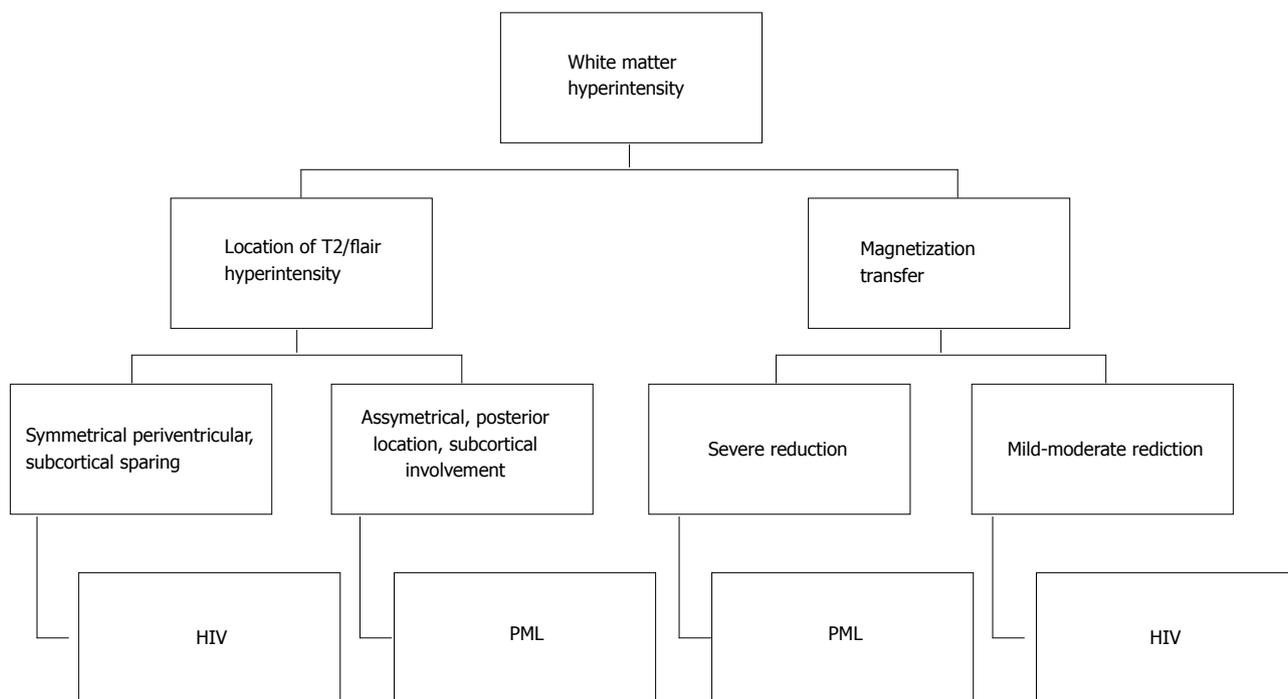


Figure 24 Approach to lesions presenting with hyperintensity predominantly involving the white matter. PML: Progressive multifocal leukoencephalopathy; HIV: Human immunodeficiency virus.

larger reduction in MT has been observed in PML as compared to HIVE^[18]. The major role of MT sequence in this setting is in early detection of disease.

Diffusion and diffusion tensor imaging

Fractional anisotropy is seen to be reduced in HIVE and PML before the morphologic changes in conventional sequences^[19]. Reduced diffusion is seen in the periphery and free diffusion in the centre of PML lesions^[12] (Figure 23).

MRS

Reduction of N-acetylaspartate is seen in HIVE even be-

fore the onset of symptoms. Raised choline and myoinositol is also seen in the spectra. A summary of suggested approach to these white matter lesions is presented as a flowchart in Figure 24.

CONCLUSION

Imaging features of CNS infections constitute a complex myriad. Their classification based on conventional MRI sequences, may provide a quick guide to narrowing the differential diagnosis followed by further sub-differentiation into single etiology using advanced MRI sequences

and techniques.

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