ROLE OF MRI IN WHITE MATTER DISEASES- CLINICO-RADIOLOGICAL CORRELATION

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ABSTRACT

BACKGROUND

The diagnostic process is difficult as there are many different white matter disorders (inherited and acquired). MRI has high diagnostic specificity to study the pattern of brain structures. MRI is more useful in demonstrating abnormalities of myelination.

MATERIALS AND METHODS

Our study developed a practical algorithm that relies mainly on the characteristics of brain MRI. Our study included clinically-suspected patients with demyelination during a period of one year.

RESULTS

Our study included 25 clinically-suspected patients (out of total of 400 patients) with demyelination during a period of one year (February 2016 to January 2017).

- Multiple sclerosis accounted for the majority of cases (36.0%) followed by acute disseminated encephalomyelitis (20%).
- In multiple sclerosis, majority of the patients presented in the third decade of life with a definite female preponderance (M:F-1:2).
- The most common symptom and site of involvement were visual impairment (73.3%) and periventricular area (80%), respectively.
- Other causes like PML, PVL, CPM, reversible posterior leucoencephalopathy, leukodystrophies and motor neuron disease comprised the remainder of the cases.

CONCLUSION

MRI due to its excellent grey white matter resolution is very sensitive in detecting subtle demyelination, the sensitivity being still further enhanced by FLAIR sequences. MRI in correlation with the clinical signs and symptoms is an ideal modality in early diagnosis of white matter diseases.

KEYWORDS

White Matter Lesion, Elderly, Periventricular, Deep White Matter, Juxtaventricular, Juxtacortical.

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BACKGROUND

Only very few studies on white matter diseases have been done in India.

However, with the introduction of MRI and increasing awareness of the disease, more and more cases of multiple sclerosis and other demyelinating diseases are being diagnosed.[1]

The pattern of brain structures involved, as visualised by MRI, has proven to often have a diagnostic specificity.[2]

MR findings in major categories of white matter diseases were analysed for sensitivity in detecting the presence of an abnormality.[3]

MRI plays a vital role in early diagnosis of many of these diseases. MRI is superior to CT in the evaluation of white matter diseases due to its grey white matter resolution and multiplanar imaging capability.

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Classification of White Matter Disease

1. Primary demyelination- Loss of normally formed myelin with relative preservation of axons.
2. Secondary demyelination- Destruction of both axons and myelin (associated with known aetiology of systemic disorder).
3. Leukodystrophies (dysmyelination)- Defective formation and/or maintenance of myelin.

Primary Demyelinating Diseases

1. Multiple sclerosis.
2. Inflammatory demyelinating pseudotumor.

Secondary Demyelinating Diseases

1. **Infectious Agents/Vaccinations-**
   - Acute Disseminated Encephalomyelitis (ADEM).
   - Progressive Multifocal Leucoencephalopathy (PML).
   - HIV encephalopathy.
   - Subacute Sclerosing Panencephalitis (SSPE).

2. **Nutritional/Vitamin Deficiency-**
   - Central pontine myelinolysis.
   - Vitamin D12 deficiency.
   - Vitamin E deficiency.
   - Beriberi.
   - Marchiafava-Bignami disease.

3. **Physical/Chemical Agents or Therapeutic Procedures-**
   - Hexachlorophene intoxication.
   - Thallium intoxication.
   - Radiation changes (early delayed effects).
   - Periventricular leucoencephalopathy associated with combined chemotherapy and radiation therapy.
   - Disseminated necrotising leucoencephalopathy.

4. **Genetic Abnormality-**
   - Abetalipoproteinemia.
   - Ataxia - telangiectasia.
   - Ataxia with vitamin E deficiency.
   - Friedreich's ataxia.

5. **Others-**
   - Binswanger disease (subcortical arteriosclerotic encephalopathy).
   - Polycystic lipomembranous osteodysplasia with sclerosing leucoencephalopathy.

***Leukodystrophies (Dysmyelination)-**

1. **X-LINED-**
   - Adrenoleukodystrophy.
   - Adrenomyeloneuropathy.
   - Pelizaeus-Merzbacher disease.

2. **Autosomal Recessive-**
   - Krabbe disease (globoid cell leukodystrophy).
   - Canavan disease (spongy degeneration of brain).
   - Metachromatic Leukodystrophy (MLD).
   - Cockayne syndrome.
   - Neonatal adrenoleukodystrophy.
   - Aicardi-Goutieres syndrome.

3. **Unknown Inheritance-**
   - Alexander disease.

***MS (Multiple Sclerosis)-** is an inflammatory demyelinating disease of the Central Nervous System (CNS) due to autoimmune demyelination in genetically susceptible individuals. However, with the advent of multi-echo sequences of MR, even subtle lesions of demyelination can be detected.[4]

***ADEM (Acute Disseminated Encephalomyelitis)**- is an immune-mediated demyelination, which is typically seen 5 days to 2 weeks following a viral illness or immunisation. On MR, lesions are located in the subcortical white matter with asymmetric involvement of both hemispheres with or without brain stem involvement.

Though it predominantly involves the white matter, it can involve the grey white matter as well.

***PML (Progressive Multifocal Leucoencephalopathy)-**
On MRI, bilateral and asymmetric hyperintensities are seen in the subcortical or periventricular white matter of the parieto-occipital region.

***CPM (Central Pontine Myelinolysis)-** is a demyelinating disease found commonly in alcoholics and in systemic disorders with electrolyte abnormalities. MR findings are of high signal intensity on T2WI in the upper and middle central pons and characteristically spares the peripheral pial and ventricular surface. The study done by Laubenberger et al[5] showed that the size of the pontine lesion was not found to correlate with the clinical severity.

***PVL (Periventricular Leucomalacia)**- is due to the ischaemic infarction of the periventricular white matter, the vascular watershed zone in the developing foetus.

It is particularly seen in preterm infants and in perinatal asphyxia.[6] Typical imaging findings include peritrigonal hyperintensities on T2WI, focal ventricular enlargement and irregular, scalloped ventricular contours. White matter volume is reduced and the posterior corpus callosum appears moderately atrophic.

***RPLE**- Reversible posterior leucoencephalopathy (hypertensive leucoencephalopathy). Typical imaging findings include high-signal intensity on long TR sequences in subcortical white matter of occipital, parietal and posterior temporal lobes. Mild mass effect with sulcal effacement is usually seen. The changes are reversible after control of BP.

***ALD (adrenoleukodystrophy)**- The classic MR appearance is the bilateral and symmetrical demyelination of the occipital lobes and the splenium of the corpus callosum. Enhancement of the inflammatory leading edge of demyelination if noted when contrast is administered. Calcification can be seen in the parieto-occipital region.

***MLD (Metachromatic Leukodystrophy)**- is a demyelinating disorder with extensive symmetrical demyelination of the periventricular and subcortical white matter resulting in a butterfly configuration. The demyelination initially spares the subcortical U fibres and the basal ganglia with involvement of the arcuate fibres and the cerebellar white matter in later stage of disease.

***DAI (Diffuse Axonal Injury)-** Most common location is grey white matter interface, corpus callosum and dorsal aspect of upper brainstem.

Aims and Objectives-

- To evaluate the role of MRI as an investigative modality in white matter diseases.
- To document its value in early diagnosis and management.

This was done by studying the MR appearances of various white matter diseases encountered in Viswabharathi Medical College with special reference to multiple sclerosis and correlating it with the clinical presentation. In addition, the most common diseases among them were identified.

*Twenty five clinically-suspected patients (out of total of 400 patients) with demyelination during a period of one year (February 2016 to January 2017) formed the basis of the present study. The patient population consisted of 14 men and 11 women.

All the patients with age-related vascular causes of demyelination were excluded from the study group.

*The MRI scan was performed using a 1.5 Tesla (Signa contour, GE) scanner using standard head coil for the acquisition of images. Axial and sagittal scans were obtained.

Using multi-slice, multi-echo sequences with a slice thickness of 5 mm and at interslice gap of 3 mm.

*The data acquisition was done using a matrix of 256 x 192. For T1W images, pulse sequences used were TR/TE of 440/10 msecs and for T2WI, TR/TE of 2240/90 msecs.

Special sequence like FLAIR (fluid attenuated inversion recovery sequence) were obtained in all cases (TR/TE 10,000/94 msecs).

*Contrast (Gadolinium - DTPA) at dose of 0.1 mmol/kg body weight was given wherever necessary.

RESULTS

- Multiple Sclerosis (MS) was the most common white matter disease encountered in this study. Table 1 shows the distribution of the various diseases encountered in Viswabharathi Medical College.
- In MS (36%), majority of the patients were in the third decade of lift with a definite female preponderance (M:F - 1:2). The mean age of onset was 27.6 years. The average age of onset in females was found to be 24 years and 35 years in males.
- The most common symptom noted was visual impairment (77.7%). Table 2 summaries the main presenting complaints of 9 patients with MS.

Diseases	Cases
Multiple sclerosis	9
Acute disseminated encephalomyelitis	5
Progressive multifocal leukoencephalopathy	2
Central pontine myelinolysis	2
Radiation injury	1
Leukodystrophies	2
Periventricular leukomalacia	1
Diffuse axonal injury	1
Reversible posterior leukoencephalopathy	1
Motor neuron disease	1

Table 1. Distribution of White Matter Diseases

Symptoms	Cases	Percentage
Visual loss	7	77.7
Weakness	4	44.4
Sensory loss	2	22.0
Ataxia	1	11.0
Seizures	1	11.0
Facial palsy	1	11.0

Table 2. Presenting Complaints of MS

Most of the patients had more than one problem.

*Five patients of Acute Disseminated Encephalomyelitis (ADEM) were evaluated by MRI (20%), all having a history of fever prior to the onset of clinical symptoms.

The age group varied through a wide range of 6 to 52 years, of which, three were adults and two children. The most common clinical symptoms were altered consciousness (60%), followed by motor symptoms and urinary retention (40% each).

Majority of the lesions in this study were located in the cerebral white matter (100%) with asymmetric and patchy involvement, followed by brain stem involvement (40%).

Spinal cord and cerebellar involvement were noted in one patient each. Thalamic involvement was seen in one case and added to the specificity of diagnosis. On steroid therapy, majority showed clinical improvement.

*Progressive Multifocal Leukoencephalopathy (PML) accounted for two patients (8%).

One of them was male and another female and both of them were HIV positive with a mean age of onset of 27 years. Both the patients presented with motor symptoms in the form of hemiparesis and one patient had cerebellar signs in addition. On MR, one patient showed patchy hypointense lesions on T1WI in subcortical white matter of right occipital and parietal lobe, which were hyperintense on T2WI and FLAIR sequences.

Second patient showed bilateral symmetrical hyperintensities on T2 and FLAIR sequences in periventricular region. The lesions were focal with no mass effect or cortical atrophy.

*There were two patients of Central Pontine Myelinolysis (CPM) (8%) in this study. Both the patients were males with the mean age of presentation at 35 years. One of them had definite predisposing factors like hyponatraemia and the other patient was alcoholic. Both the patients showed extra pontine involvement in addition to the characteristic involvement of central pons.

*One case of Periventricular Leucomalacia - (PVL)- (4%) was studied. Patient is an 8-year-old female child presented with history of preterm delivery and both asphyxia with microcephaly. At present, the patient has presented with mental retardation and seizures. MRI showed loss of white matter volume and bilateral symmetrical hyperintensity of the periventricular white matter especially of the periatrial region.

There was scalloping of ventricular margins, however, there was no evidence of hydrocephalus.

*One classical case of Adrenoleukodystrophy (ALD) was studied (4%), the child being a 10-year-old boy presented with headache and seizures of one year duration with black.

Discoloration of skin- On MRI, there was hyperintensity on T2WI in the periatrial region spanning the corpus callosum and brainstem (PONS) region.

*One case of Metachromatic Leukodystrophy (MLD) was studied (4%). The patient is 14-year-old male presented with difficulty in walking, seizure and abnormal speech. MRI shows hyperintensity on T2WI in bilateral symmetrical periventricular white matter involving posterior limb of internal capsule and body of corpus callosum. Subtle hypointensity on T2WI in basal ganglia region noted suggesting hemosiderin deposition.

One case of reversible posterior leukoencephalopathy-RPLE- (hypertensive encephalopathy) was studied. Patient is 15-year-old male, known case of crescentic glomerulonephritis and hypertension on treatment with steroids for last 4 months.

Presently, patient has vertigo and 2 episodes of GTCS, 3 days back. BP 170/110 mmHg.

MRI reveals hyperintensity on T2 and FLAIR sequences in subcortical white matter region of bilateral (left more than right) occipital lobes. Diffusion WI do not show any hyperintensity suggesting that the lesion is not infarct.

*One case of Diffuse Axonal Injury (DAI) was studied (4%)- 21-year-old male presented with head injury with sudden transient loss of consciousness. Initial CT scan was normal. MRI showed hyperintense foci on T2WI in grey white matter interface of left temporal region, splenium of corpus callosum and right basal ganglia. T1W images were unremarkable.

*One case of radiation injury was studied (4%)- MR appearance of radiation injury depends upon duration of radiation. MRI showed diffuse hyperintensities in bilateral centrum semiovale on T2WI, which was hypointense on T1WI associated cerebral atrophy was also noted.

*One case of motor neuron disease was studied (4%)- A 35-year-old male presented with weakness of upper and lower limb with atrophy of upper limb muscles (hand).

No evidence of respiratory symptoms. MRI showed classical hyperintensity in white matter tracts (extending from posterior limb of internal capsule and cerebral peduncles) on T2WI and FLAIR sequence.

Case 1- Multiple Sclerosis

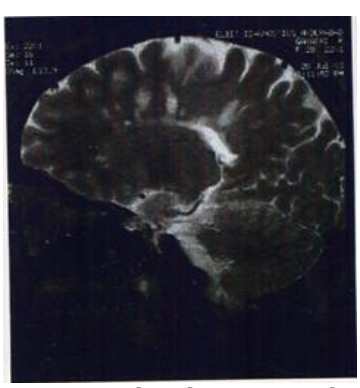

Figure 1. T2W1 Showing Dawson's Fingers

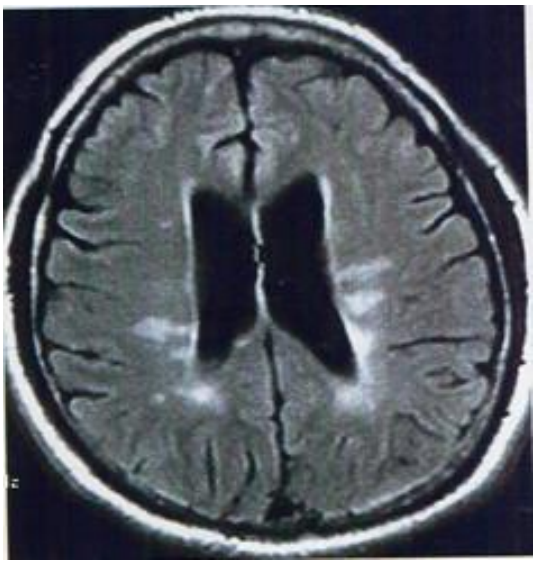

Figure 2. FLAIR Image- Lesions are Perpendicular to Ventricle

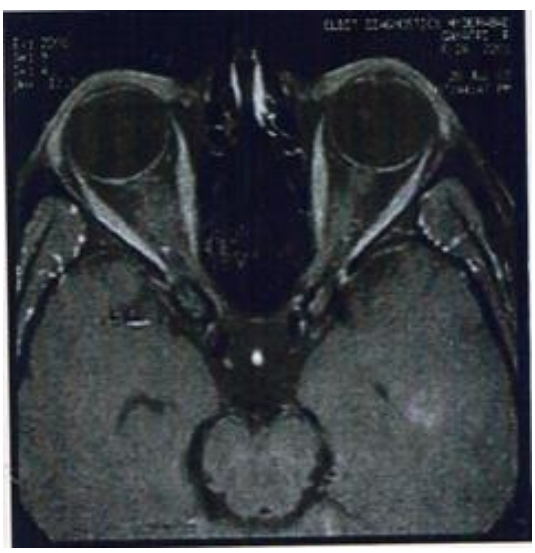

Figure 3. T1 Post Contrast shows Ring Enhancement

Case 2- Acute Disseminated Encephalomyelitis

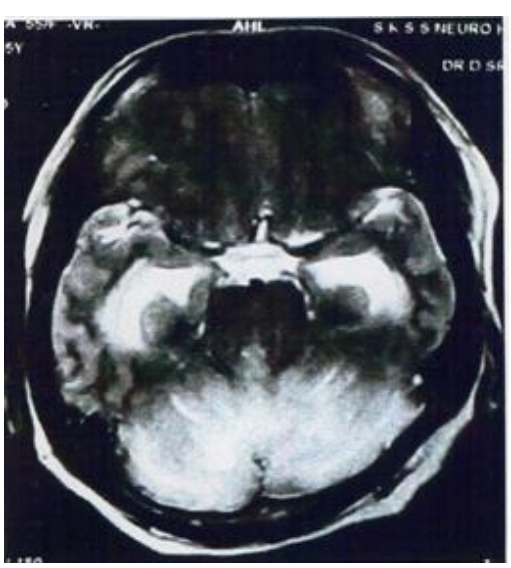

Figure 1. FLAIR Sequence - Bilateral Cerebellar Involvement

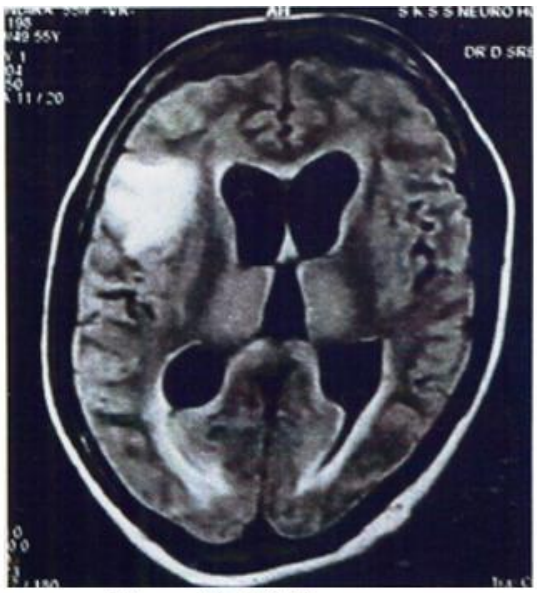

Figure 2. Flair Sequence- Involvement of Right Frontal Region

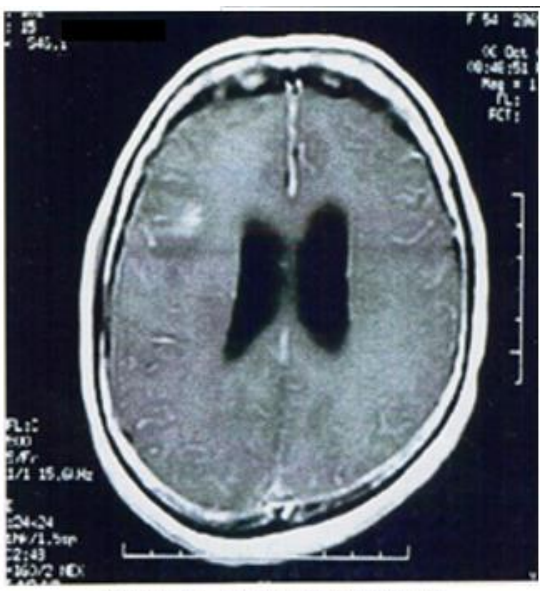

Figure 3. T1 Post Contrast- Enhancement of the Lesion

Case 3- Adrenoleukodystrophy

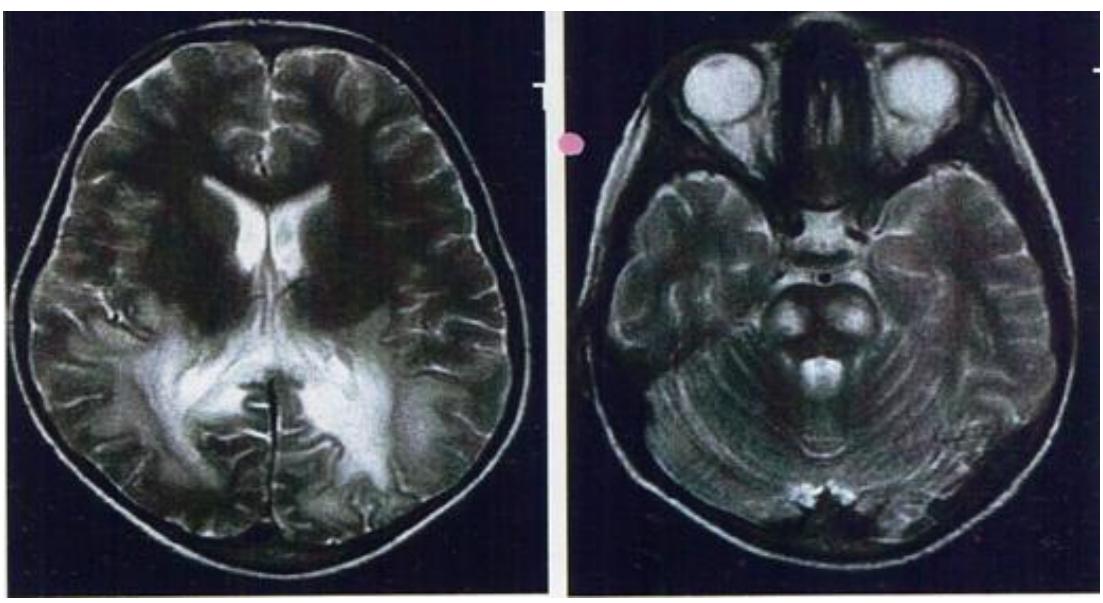

Figure 1 and 2. T2W1- Involvement of Bilateral Symmetrical Peritrigonal White Matter and Pons

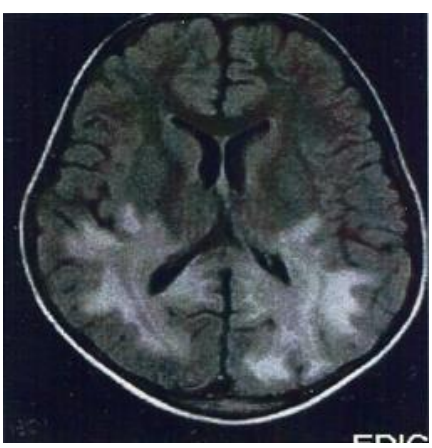

Figure 3. FLAIR Sequence- Involvement of Bilateral Symmetrical Peritrigonal White Matter

DISCUSSION

The advent of MRS has revolutionised the concept of understanding of white matter diseases.

MRI is considered far superior to CT and the imaging modality of choice in white matter diseases. Though CT was used previously for cranial imaging in these conditions, it was not able to detect subtle lesions especially in stages of clinical inactivity[7] and not ideal in posterior fossa imaging due to the beam hardening artifacts produced. MR scores over CT in all the above aspects.

MRI is a non-invasive modality with multiplanar imaging capability and has a very high sensitivity for demyelinating foci due to its excellent grey white matter resolution.

It was found that FLAIR sequences had a better sensitivity for subtle demyelinating foci especially those with periventricular locations thus correlating with the study done by Ashikaga R et al.[8]

The most common site of lesion in this study was the periventricular area. Fazekas et al[9] and Jena AN et al[10] have also noted the periventricular area as the commonest location.

This study showed 82% involvement of callososeptal interface, which corresponds with prospective study conducted by Gean-Marton et al[11] who found that 92% of MS patients demonstrated involvement of callososeptal interface and concluded involvement was specific for MS.

CONCLUSION

*MRI due to its excellent grey white matter resolution is very sensitive in detecting subtle demyelination. The sensitivity being still further enhanced by FLAIR sequences.

*MRI in correlation with the clinical signs and symptoms is an ideal modality in early diagnosis of white matter diseases.

*It also helps in the early institution of therapy so that the curable conditions among them can be treated.

*Confirmation by brain biopsy thus is not essential in all patients except in indeterminate conditions.

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