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MAGNETIC RESONANCE IMAGING FEATURES OF INFLAMMATORY DEMYELINATING DISEASES OF BRAIN-A CROSS SECTIONAL STUDY IN A TERTIARY CARE CENTRE, NEWDELHI

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Abstract

Background: MRI has been considered as an important radiological non-invasive diagnostic tool in inflammatory demyelinating diseases that helps in early intervention to slow its progression. Lack of data in the current study setting and the fact that, most information on these inflammatory demyelinating disorders come from hospital based cross-sectional studies, this study was conducted.

Aims: To describe the characteristics of inflammatory demyelinating brain lesions on Magnetic Resonance imaging

Methods and Material: A cross sectional study was conducted among fourty clinico-radiologically suspected inflammatory demyelinating diseases i.e. multiple sclerosis (MS), neuromyelitis optica (NMO) and acute disseminated encephalomyelitis (ADEM) in the department of radiodiagnosis in collaboration with the department of neurology, VMMC and Safdarjung hospital, New Delhi. MRI was acquired in different imaging sequences among all the patients and the lesions were described. All the data were expressed in means or proportions based on the type of data and analysis was done using Microsoft Excel.

Results: A total of 24 were having MS, 2 had NMO and 14 had ADEM. Most of the lesions in MS (70.8%) and ADEM (78.6%) were supratentorial. Higher proportions of MS showed hyperintense lesions (84.3% vs 72.7%), contrast enhancement lesions (74.5% vs 54.4%) and false diffusion restriction (76.5% vs 9.1%) compared to ADEM. However, most of the patients with ADEM showed true diffusion restriction (63.6% vs 7.8%) compared to MS.

Conclusions: Hyperintense and contrast enhancement lesions were more common in MS and true diffusion restriction lesions were mostly ADEM lesions.

Keywords: Inflammatory demyelinating disorders, multiple sclerosis (MS), Neuromyelitis optica (NMO), Acute disseminated encephalomyelitis (ADEM)

Introduction

Inflammatory demyelinating diseases are a heterogeneous group of disorders that occur in contrary to the background of the acute or chronic inflammatory processes[1].Such inflammatory demyelinating disorders of central nervous system (CNS) affect brain and the spine[2].Primarily, Multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), acute disseminated encephalomyelitis (ADEM) and myelin oligodendrocytes glycoprotein (MOG) encephalomyelitis form the majority. However, it can also manifest secondary to infections, ischemia, toxins or metabolic disorders[2, 3].

Among all, multiple sclerosis is the most common inflammatory neurological disease affectingyoung adults[4].In 2016, the prevalence of multiple sclerosis was 2.22 million accounting for 10.4% which has increased in 2020 to 2.8 million[4, 5].

An uncommon inflammatory disease of the central nervous system is Neuromyelitis optica spectrum disorder (NMOSD) that manifests clinically as optic neuritis, myelitis, and certain brain and brainstem syndromes. The prevalence is known to vary from 0.5 to 4/100,000 and can be up to 10/100,000 with some reported regional differences. However it is relatively less than MS, ranging from 1 to 2/100,000 in the equatorial region, to 150 to 200/100,000 in Canada and northern part of Europe. According to 2015 IPND criteria, the prevalence among South Indians in Mangalore was noted to be 0.72/100,000[6].

Another inflammatory demyelinating syndrome with encephalopathy is acute disseminated encephalomyelitis (ADEM) that mainly affects young children and mostly a post infection condition. The incidence rates are reported to be 0.07, 0.3, 0.4 and 0.64 per 100,000 children per year in Germany, China, San Diego and Japan respectively[7].

Singhal B reported a prevalence of MS to be 5 to 10 per 100,000 individuals[8]. In a registry based study, conducted in Urban Mangalore, a crude prevalence of MS was noted as 8.3/100,000. Of all demyelinating disorders, Neuromyelitis optica (NMO) and spectrum disorders (NMOS) constituted for 13.9%, with a prevalence being 2.6/100,000[9].

Magnetic resonance imaging (MRI), a non-invasive technique has been the gold standard imaging technique for the identification of demyelinating lesions[10, 11].Using new MRI diagnostic criteria, multiple sclerosis can be diagnosed among those with clinically isolated syndromes (CIS)[10].CIS is considered the earliest clinical expression of MS and research on such patients may provide new insights which might affect the course and progression of the disease. MRI evidence of dissemination in time and space is considered as a diagnostic criteria as per the International Panel of McDonald and colleagues to let a diagnosis of definite MS in patients with CIS[11].In addition, most of the information about these inflammatory demyelinating disorders come from hospital based cross-sectional studies. Similarly, the current study also adds to the existing data and helps to add to the typical features of various demyelinating disorders of inflammatory origin. Hence the current study was conducted to describe the characteristics of inflammatory demyelinating brain lesions on Magnetic Resonance imaging.

Materials & Methods

This is a cross sectional study conducted among 40 clinico-radiologically suspected cases of inflammatory demyelinating diseases viz., multiple sclerosis, neuro myelitis optica and acute disseminated encephalomyelitis based on revised diagnostic criteria. The study was conducted for a period of two years in the Department of Radiodiagnosis in collaboration with Department of Neurology, VMMC and Safdarjung hospital, New Delhi.

Sampling and sample size

Adopting purposive sampling, a total of 40 cases were selected after considering the average input of the hospital patients with features suggestive of inflammatory demyelinating diseases. The input of such patients varied from 15 to 20 per year and considering the maximum limit of 20, for 2 years, a total of 40 cases were included in this study. Prior to starting the study, clearance for the Institutional Ethics Committee was obtain

Study subjects

All patients who presented with clinico-radiological features suggestive of inflammatory demyelinating diseases comprising Multiple Sclerosis, Neuromyelitis Optica and Acute Disseminated Encephalomyelitis according to revised diagnostic criteria were included in the study, after obtaining written and informed consent from each subject.

Inclusion criteria

All the patients presenting with features suggestive of inflammatory demyelinating diseases according to the McDonald's revised diagnostic criteria were considered.

Exclusion criteria

Patients with acute CNS infections, CNS tuberculosis (known or suspected), neuro-degenerative diseases, hypoxic ischemic encephalopathy or with psychiatric illness and also those with history of head trauma or stroke in the past 6 months were excluded from the study.

Study tools and procedures

1. PHILIPS 1.5 TESLA ACHIEVA machine was used for MRI examination
2. In axial, coronal and sagittal planes, various imaging sequences viz., Fast Spin Echo (FSE) T1 weighted imaging (T1WI), T2 weighted imaging (T2WI) and Fluid attenuated inversion recovery (FLAIR) were done for MR imaging of the brain.
3. In the three orthogonal directions, Diffusion weighted imaging (DWI) sequence with an identical slice thickness of 5mm and position at T1WI, T2WI and T2/ FLAIR imaging, was obtained with a single-shot echo planar spin-echo sequence [b value-1000 sec/mm^3] and a baseline image was also obtained [b value of 0 sec/mm^3]. Using software, the values of Apparent Diffusion Coefficient (ADC) were obtained and ADC maps were generated. The DWI was performed.
4. Followed by DWI imaging, using 0.1 mmol/kg body weight of Gadolinium based contrast agent, contrast enhanced T1 weighted imaging (CE T1WI) was done in axial, coronal and sagittal planes.

5. The demyelinating lesions were initially labelled on T2WI and FLAIR with their sizes being no less than 3 mm for better delineation on CE T1WI and DWI.
6. After labelling, the number, distribution and morphology of demyelinating lesions on T2/FLAIR in the cortical gray matter, white matter, deep gray matter and brainstem were determined in each subject.
7. On CE T1WI such lesions were labelled as enhancing or non-enhancing. Whereas, on DWI and ADC maps, the signal intensity of the lesions were considered as either hyperintense or non-hyperintense (isointense or hypointense) in comparison to the surrounding normal appearing white matter. If any area of perilesional oedema was noted then, they were not evaluated.

Statistical analysis

All the data were collected and entered into Microsoft Excel. The data entry was verified and checked for accuracy. All the continuous variables were presented as mean ± SD and median and the categorical variables were expressed in proportions.

Results

There were a total of 24 subjects with multiple sclerosis and 2 were with neuromyelitis optica and 14 were with acute disseminated encephalomyelitis. Majority of the study subjects with multiple sclerosis were aged more than 30 years with 33.3% of them belonged to 31 to 40 years and 29.2% of them belonged to 41 to 50 years whereas those subjects with neuromyelitis optica, equal proportions were belonging to 21 to 30 and 31 to 40 years age group. However, those with acute disseminated encephalomyelitis half of them i.e. 50.0% belonged to the age group of 10 and under 10 years. [Table-1]

Females predominated among the conditions with multiple sclerosis (70.8%) and 100.0% of females had neuromyelitis optica but it was vice-versa in acute disseminated encephalomyelitis where males predominated (71.4%) the condition. [Table-2]

Most of the lesions in MS (70.8%) and ADEM (78.6%) were supratentorial. But in those with NMO, the lesions in brain were noted only among one of the patients (50.0%). The median number of supratentorial lesions was 14 in MS and it was 10 in ADEM. The infratentorial lesions ranged from a minimum of 0 to a maximum of 4. [Table-3]

The highest proportions of those with frontal (55.6%), parietal lobe (57.2%) and deep gray matter (53.8%) had acute disseminated encephalomyelitis. 100.0% of those with temporal and occipital lobe gray matters had multiple sclerosis and acute disseminated encephalomyelitis respectively. However 69.7% of those with periventricular white matter, 61.7% had subcortical white matter and 73.9% of those with deep white matter had multiple sclerosis. 100.0% of those with Callososeptal Interface had multiple sclerosis and 100.0% of those with infratentorial cerebellar lesions and 60.0% of those with infratentorial brain stem lesions had multiple sclerosis. [Table-4]

Higher proportions of MS showed hyperintense lesions (84.3% vs 72.7%), contrast enhancement lesions (74.5% vs 54.4%) and false diffusion restriction (76.5% vs 9.1%) compared to ADEM. However, most of the patients with ADEM showed true diffusion restriction (63.6% vs 7.8%) and compared to MS. [Table-5]

Table 1: Distribution of the study subjects based on age group

Age group in years	MSn (%)	NMOn (%)	ADEMn (%)	Totaln (%)
≤ 10	01 (4.2)	00 (0.0)	07 (50.0)	08 (20.0)
11- 20	02 (8.3)	00 (0.0)	05 (35.7)	07 (17.5)
21- 30	06 (25.0)	01 (50.0)	02 (14.3)	09 (22.5)
31- 40	08 (33.3)	01 (50.0)	00 (0.0)	09 (22.5)
41-50	07 (29.2)	00 (0.0)	00 (0.0)	07 (17.5)
Total	24 (100.0)	02 (100.0)	14 (100.0)	40 (100.0)

Table 2: Distribution of the study subjects based on gender

Gender (n=40)	MSn (%)	NMOn (%)	ADEMn (%)	Totaln (%)
Males	07 (29.2)	00 (0.0)	10 (71.4)	17 (42.5)
Females	17 (70.8)	02 (100.0)	04 (28.6)	23 (57.5)
Total	24 (100.0)	02 (100.0)	14 (100.0)	40 (100.0)

Table 3: Distribution of the study subjects based on the site of lesions

Site of lesions	MS (n=24) n (%)	NMO (n=2) n (%)	ADEM (n=14) n (%)	Total (n=40) n (%)
No lesions	00 (0.0)	01 (50.0)	00 (0.0)	01 (2.5)
Supratentorial	17 (70.8)	00 (0.0)	11 (78.6)	28 (70.0)
Median no. of supratentorial lesions [Range]	14 [1-34]	-	10 [0-21]	11.5 [0-34]
Infratentorial	00 (0.0)	01 (50.0)	02 (14.3)	03 (7.5)
Median no. of infratentorial lesions [Range]	00 [0-4]	0.5 [0-1]	00 [0-2]	00 [0-4]
Both	07 (29.2)	00 (0.0)	01 (7.1)	08 (20.0)

Table 4: Location of lesions among the different inflammatory demyelinating diseases

Location of lesion	MSn (%)	NMO§n (%)	ADEMn (%)
Supratentorial			
Frontal lobe gray matter (n=9)	04 (44.4)	00 (0.0)	05 (55.6)
Parietal lobe gray matter (n=7)	03 (42.8)	00 (0.0)	04 (57.2)
Temporal lobe gray matter (n=1)	01 (100.0)	00 (0.0)	00 (0.0)
Occipital lobe matter (n=1)	00 (0.0)	00 (0.0)	01 (100.0)
Deep gray matter (n=13)	06 (46.2)	00 (0.0)	07 (53.8)
Periventricular white matter (n=33)	23 (69.7)	00 (0.0)	10 (30.3)
Deep white matter (n=23)	17 (73.9)	00 (0.0)	06 (26.1)
Subcortical white matter (n=34)	21 (61.7)	00 (0.0)	13 (38.3)
Callososeptal Interface (n=15)	15 (100.0)	00 (0.0)	00 (0.0)
Infratentorial			
Cerebellum (n=3)	03 (100.0)	00 (0.0)	00 (0.0)
Brainstem (n=10)	06 (60.0)	01 (10.0)	03 (30.0)
§ NMO one case is excluded as no lesions were seen			

Table 5: Features of inflammatory demyelinating diseases on MRI

MRI appearances	Diagnosis	
	MS(n=51)	ADEM(n=22)
Hyperintense on DWI		
Present	43 (84.3)	16 (72.7)
Absent	08 (15.7)	06 (27.3)
Contrast Enhancement		
Present	38 (74.5)	12 (54.5)
Absent	13 (25.5)	10 (45.5)
True Diffusion Restriction		
Present	04 (7.8)	14 (63.6)
Absent	47 (92.2)	08 (36.4)
False Diffusion Restriction		
Present	39 (76.5)	02 (9.1)
Absent	12 (23.5)	20 (90.9)

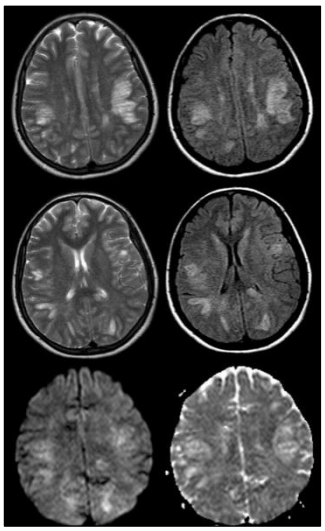


Fig 1: Bilateral, asymmetric, multiple, large T2/FLAIR hyperintensities predominantly involving subcortical white matter of bilateral frontoparietal lobes in a clinically diagnosed case of ADEM

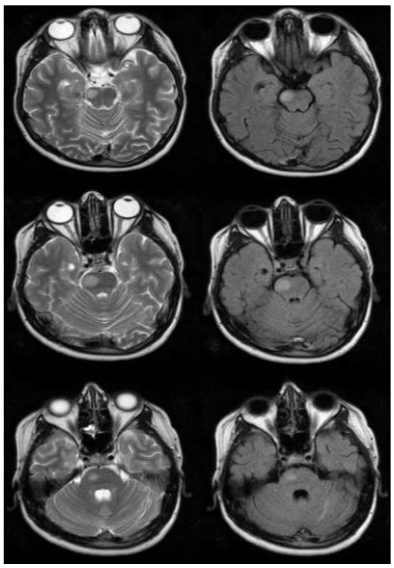
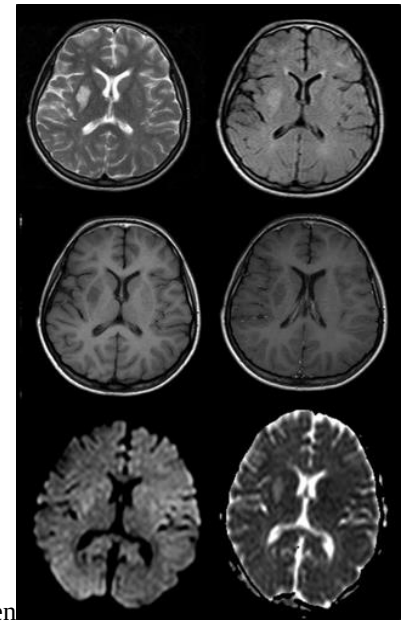


Fig 2: Brainstem lesion in ADEM, wherein a well-defined T2/FLAIR hyperintensity involving the right ventral



ons is seen

Fig 3: Basal ganglia involvement in a case of ADEM

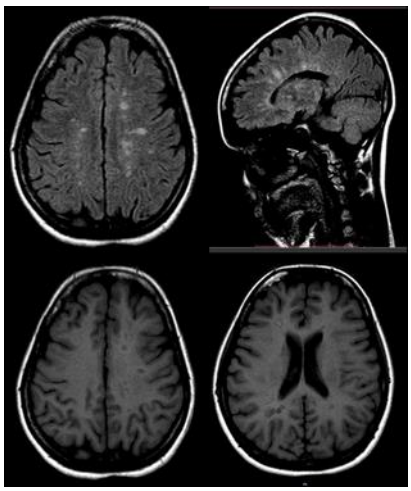


Fig 4: FLAIR and T1 weighted images depicting Dawson's fingers and T1 black holes respectively, in a patient with Multiple sclerosis

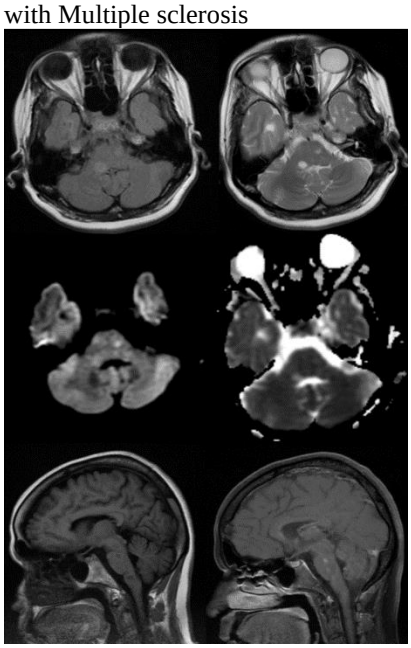


Fig 5: Brain stem involvement in multiple sclerosis

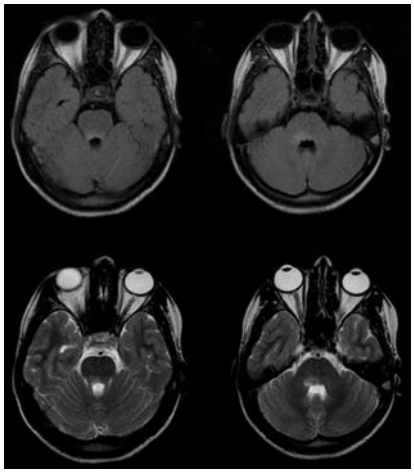


Fig 6: Axial T2/FLAIR images showing small, well defined hyperintensity in the tegmentum of pons in a known case of neuromyelitis optica

Discussion

The pathognomonic radiological signs in demyelinating diseases of central nervous system can be greatly visualized and appreciated on magnetic resonance imaging (MRI) sequences as it is a sensitive tool. Describing the presentations of such CNS demyelinating diseases and also describing such important pathognomonic features in our set up becomes important to add to the data in a larger setting which helps to improve the precision of the diagnosis[2, 3, 12].

Rao TMV and Prasad UG in their study on clinical profile of patients with demyelinating diseases had documented multiple sclerosis in 24% of the subjects and 22% of them had ADEM. However, neuromyelitis optica was noted in 4% of the subjects and the findings are in line with the current study findings with 60.0% having multiple sclerosis, 35.0% had acute disseminated encephalomyelitis and 5.0% had neuromyelitis optica except for the proportions which were higher in our study findings as there were other inflammatory conditions like, demyelinating transverse myelitis and secondary demyelination which were noted in their study[13].

In another study setting, Papais-Alvarenga RM *et al*., have noted the main disease categories i.e. multiple sclerosis among 76.9%, neuromyelitis optica among 11.8%, other NMO syndromes among 6.5%, clinically isolated syndrome among 3.5%, acute disseminated encephalomyelitis among 1.0% and acute encephalopathy in 0.4%[14].

Papais-Alvarenga RM *et al*., noted that except in ADEM, the inflammatory demyelinating diseases occurred between 20 and 39 years old and Xiaong CH *et al.*, reported, that ADEM mainly occurs in children younger than 10 years old and similarly in this study we have documented similar results[14, 15].Papais-Alvarenga RM *et al*., also found female predomination in all the main categories like multiple sclerosis, neuromyelitis optica and acute disseminated encephalomyelitis. Optica

The current study was in correspondence to the findings on gender except for the acute disseminated encephalomyelitis where male predominance was recorded in this study[14]. Xiaong CH *et al*., have found no difference in the incidence of ADEM with gender[15].The differences may be due to the different study settings.

In the current study, MRI scan of the brain showed involvement of supratentorial sites viz., frontal, parietal, temporal lobe gray matter, deep gray matter, periventricular white matter, deep white matter, subcortical white matter and infratentorial sites of cerebellum and brainstem. It also showed involvement of Callososeptal interface in MS cases. Gowda VK *et al*., demonstrated multiple demyelinating plaques in supratentorial, infratentorial regions, corpus callosum, cerebellum, brainstem on MRI in MS. 100.0% of those with Callososeptal Interface had multiple sclerosis in this study. Similarly Miki Y recorded this type of lesion in more than half of MS patients[3].The present study also observed the involvement of frontal lobe, parietal lobe, occipital lobe, deep gray matter, periventricular white matter, deep white matter, subcortical white matter and infratentorial brain stem involvement in ADEM. However Gowda VK *et al*., showed involvement of deep and subcortical white matter and supratentorial lesions most commonly with occasional involvement of gray matter and spinal cord[16].

Most of the lesions in MS (70.8%) and ADEM (78.6%) were supratentorial. But in those with NMO, the lesions in brain were noted only among one of the patients (50.0%) which was infratentorially located. However,

according to Miki Y, brain lesions were noted in 43 to 70% in patients with NMOSD, at the onset of disease and it was noted to increase with the duration of disease. The dorsal brainstem lesions of NMOSD were seen in 7 to 46% of patients[3].NMO was previously considered as a disease without brain involvement for a longtime, but brain MRI abnormalities seem to exist in a significant proportion of around 50 to 85% of patients. However, in the current study, 50.0% were with no noted MRI abnormalities and rest had infratentorial lesions. Filippi M *et al*., in their practical guidelines on assessment of lesions in MS, it has been described that the lesions can occur in any CNS region, compared to other disorders which cause the lesions in the white matter and they tend to affect specific regions of white matter, such as periventricular and juxtacortical white matter, the corpus callosum, the pons and the cerebellum in the infratentorial areas and the cervical segment of spinal cord[17].NMOSD lesions are noted to typically locate to infratentorial regions[17].Dale RC and Branson JA have spotted that in spite that the white matter is classically involved in both multiple sclerosis and ADEM, the gray matter is frequently said to be involved in ADEM[18].Similarly, Zhang L *et al*., in their study among adults have noted relatively higher proportion to have gray matter lesions compared to other demyelinating diseases[19].

The number of lesions are said to be higher in ADEM than those typically seen with MS.However, the median number of supratentorial lesions was 14 in MS and it was 10 in ADEM where it was slightly higher in MS and the difference may be due to less number of ADEM cases or also difference in the location of the lesions or type of MRI sequence[20].As mentioned earlier, NMOSD have typically located to infratentorial lesions[18]and cortical lesions are rarely seen in NMOSD[2].

Majority of the multiple sclerosis (84.3%) and acute disseminated encephalomyelitis (72.7%) subjects showed hyperintense lesions on DWI sequence of MRI. The active lesions in MS appear hyper-intense because of increase in the blood brain barrier permeability on CE-T1W1 and the use of DWI also shows the active lesions as hyper-intense signals and Radwan MEM and Aboshaera KO foundfourty lesions as hyper-intense on DWI-b1000 which had significant link to seemed as enhancement on contrast enhanced T1WI (100.0%) which indicate the activity of the disease and 74.5% of those with multiple sclerosis and 54.5% of those with acute disseminated encephalomyelitis showed contrast enhancement and 84.3% of those in MS and 72.7% in ADEM were hyperintense in DWI. However all the hyperintense lesions on DWI appeared as enhanced lesion on CET1W1 similar to theirs as Radwan MEM and Aboshaera KO[21].Kamr WH *et al*., reported diffusion restriction among 45.7% and 63.6% showed diffusion restriction in the present study[22].Balashov KE and Lindzen E have reported that selected cases of acute demyelinating lesions exhibiting restricted diffusion in MS which might be suspected as a new variant as described by Markoula S *et al*.[23, 24].

Conclusion

In our study we identified the age, sex distribution among various inflammatory demyelinating diseases and characterized the brain lesions with respect to their location, number, morphology, contrast enhancement and diffusion restriction. This might help in better understanding of the condition and further differentiation of inflammatory demyelinating diseases from one another.

Majority of the lesions in ADEM were identified in subcortical white matter and most of the lesions were found to be poorly marginated. Lesions in the deep grey matter were found in greater proportion in ADEM compared to MS. Brain lesions in MS were relatively well defined with predominant involvement of periventricular white matter. Higher proportions of MS showed hyperintense lesions (84.3% vs 72.7%), contrast enhancement lesions (74.5% vs 54.4%) compared to ADEM. However, most of the patients with ADEM showed true diffusion restriction (63.6% vs 7.8%) compared to MS.

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