Section: Radiology

Original Research Article

ROLE OF MRI IN PEDIATRIC DEMYELINATING DISORDERS - ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY

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ABSTRACT

Background: The aim of this study is to determine the clinical profile and imaging features of the pediatric acquired demyelinating disorders of the central nervous system.

Materials and Methods: One-year hospital based cross sectional study was done in Department of Radio-diagnosis from January 2021- December 2021. 30 pediatric patients clinically suspected of having demyelination disease were included in the study. The patients were subjected to MRI brain and spine scan. The study population were analysed based on age, gender, clinical history, abnormalities on MRI brain, optic nerve & spine imaging.

Results: Among ADEM on follow up scan complete resolution was seen in 50.00 % cases with minor residuals in 6.25% and no follow up scan was done for 43.75% participants. Among MOGAD on follow up scan, complete resolution was seen in 28.57 % cases but minor & moderate residuals were seen in 14.29% cases each (1) and no follow up scan was done for 3 (42.86 %) participants. Among NMOSD on follow up scan 42.86 % (3) cases showed minor residuals and14.29% (1) showed complete resolution. No follow up scan was done for in 3 (42.86 %) participants.

Conclusion: In our study, the majority (43.33%) were aged between 7 to 12 years with mild female predominance. The most common diagnosis was ADEM (53.33%) followed by equal distribution of MOGAD & NMOSD. ADEM cases showed lesions in bilateral cerebral hemispheres in an asymmetric distribution with predominant supratentorial brain involvement and majority of the cases showed large lesions. In MOGAD cases, brain parenchyma showed predominantly large lesions in supratentorial distribution. Spinal cord lesion was predominantly LETM with statistically significant involvement of the lumbar spinal cord. In NMOSD cases, statistically significant association was seen with area postrema syndrome and periaqueductal grey matter & area postrema lesions on MRI brain. Spinal cord lesions in NMOSD was predominantly LETM with involvement of the cervical and thoracic spinal cord involvement.

Keywords: Pediatric demyelinating disorder, MRI, ADEM, NMOSD, MOGAD.

INTRODUCTION

The acquired demyelinating disorder (ADD) is characterized by the destruction or damage of normally myelinated structures of the central nervous system (CNS) which are immunologically mediated.[1] Acquired demyelinating disorders encountered during childhood include acute disseminated encephalomyelitis (ADEM), neuromyelitis optica spectrum disorder (NMOSD), multiple sclerosis (MS), Clinically isolated syndrome (CIS) and the more recently discovered anti-myelin oligodendrocyte glycoprotein (anti-MOG)–associated encephalomyelitis.[2] The

discovery of antibody-based biomarkers have led to changes in defining criteria of these disorders.[2]
Radiologists play a major role in the diagnosis and differentiation these diseases. There was recent discovery of some key MRI imaging features which can be explained by the pathophysiological basis of these different entities. It helps in identifying magnetic resonance imaging predictors of a particular demyelinating diagnosis in the paediatric population which can have broad implications on treatment of the disease. Radiologists can also use history and biomarkers to improve the interpretation of the MRI imaging. This composite approach improved the understanding, diagnosis, prognosis and treatment of these disease entities.[2]

MATERIAL AND METHODS

A cross-sectional study was conducted in patients clinically suspected of having pediatric demyelinating disorder presenting to the Department of Radio-Diagnosis from 1st January 2021 to 31st December 2021and MRI brain and spine is done. Data was collected by single examiner and recorded in case proforma. Records were maintained and analyzed statistically.

RESULTS

Among the study population, the most common diagnosis was ADEM in 53.33% (16) participants followed by equal number of MOGAD and NMOSD cases, accounting for 23.33% (7) participants each (as shown in table 1). Most of the participants (43.33%) was included in the age group of 7-12 years, followed by 1-6 years (33.33%) and 13-18 years (23.3%). The participants showed a slight female predominance with a female: male ratio of 1.3:1. The major clinical symptoms were fever for 18 (60.00%) participants followed by encephalopathy and head ache for 13 (43.33 %) participants each.
Among the study population ADEM cases showed deep white matter lesions in 11 (68.75 %) cases followed by juxta cortical white matter, basal ganglia and thalamus in 8 (50.00 %) cases each. MOGAD group showed equal distribution of deep white matter, thalamus and brain stem lesions accounting for 57.14 % (4) participants each. Among NMOSD the common anatomical locations of the brain lesions were deep white matter, periventricular white matter and brain stem lesions in 4 (57.13 %) participants followed by periaqueductal grey matter, area postrema, thalamus, basal ganglia and cerebellum in 3 (42.86 %) participants each. Involvement of area postrema and periaqueductal grey matter showed statistically significant (p value = 0.0210) association with NMOSD cases as compared to ADEM & MOGAD cases. In ADEM and MOGAD the findings were more common in supratentorial brain parenchyma with a mean value of 3.19 and 3.17 respectively, whereas NMOSD showed relatively equal number of positive of findings involving both the supratentorial & infratentorial brain parenchyma. Majority of the ADEM and MOGAD cases showed large lesions in about 68.75 % and 57.14% participants each. But NMOSD cases showed majority of small lesions (71.43%).
Optic nerve imaging showed equal distribution of unilateral & bilateral optic nerve involvement among ADEM & NMOSD group in 6.25 % & 14.29% cases respectively. Among NMOSD, 42.86 % cases showed optic nerve involvement and all the cases showed bilateral involvement. ADEM & MOGAD cases showed only anterior optic nerve involvement in 12.5% & 28.57 % cases respectively and none of them showed posterior involvement. However, among NMOSD cases, posterior optic nerve involvement was more common (28.57 %) than anterior involvement (14.29 %).
Spinal cord imaging in ADEM group showed, LETM in 12.50 % (2) participants and foal spinal cord lesions in 6.25 % (1) cases. Among MOGAD & NMOSD, the most common type of spinal cord involvement was LETM in 3 (42.86 %) participants and foal spinal cord lesions in 1(14.29 %) participants each. Cervical (18.75 %) spinal cord involvement was more common in ADEM than thoracic (12.50%), lumbar (6.25 %) and conus medullaris (6.25 %) involvement. Among MOGAD cases, majority showed lumbar spinal cord involvement (57.14%) which showed statistical significance (p value= 0.0180). MOGAD also showed thoracic (42.86%), conus medullaris (28.57 %) & cervical (28.57 %) spinal cord involvement. Majority of the NMOSD showed involvement of cervical spinal cord (57.14 %) followed by thoracic (42.86%), lumbar (14.29%) and conus medullaris in (14.29%) involvement.
Among ADEM on follow up scan complete resolution was seen in 50.00 % cases with minor residuals in 6.25% and no follow up scan was done for 43.75% participants. Among MOGAD on follow up scan, complete resolution was seen in 28.57 % cases but minor & moderate residuals were seen in 14.29% cases each (1) and no follow up scan was done for 3 (42.86 %) participants. Among NMOSD on follow up scan 42.86 % (3) cases showed minor residuals and14.29% (1) showed complete resolution. No follow up scan was done for in 3 (42.86 %) participants.

Table 1: Descriptive analysis of diagnosis in the population(N=30)

Diagnosis	Number	percentage
ADEM	16	53.33%
MOGAD	7	23.33%
NMOSD	7	23.33%

Total	30	100.00%

Table 2: Comparison of diagnosis groups with Clinical symptoms

Clinical symptoms	ADEM	%	MOGAD	%	NMOSD	%	Total	%	Chi-square	p-value
Fever	12	75.00	3	42.86	3	42.86	18	60.00	3.2140	0.2000
Seizure	6	37.50	3	42.86	2	28.57	11	36.67	0.3180	0.8530
Encephalopathy	9	56.25	2	28.57	2	28.57	13	43.33	2.3300	0.3120
Visual disturbance	2	12.50	3	42.86	3	42.86	8	26.67	3.5190	0.1720
Limb weakness	3	18.75	4	57.14	3	42.86	10	33.33	3.6030	0.1650
Area postrema syndrome	0	0.00	1	14.29	3	42.86	4	13.33	7.7470	0.0210*
Cerebellar Symptoms	4	25.00	3	42.86	2	28.57	9	30.00	0.7480	0.6880
Head ache	7	43.75	3	42.86	3	42.86	13	43.33	0.0020	0.9990

***p<0.05 indicates significant association**

Table 3: Comparison of diagnosis groups with MRI Brain anatomical location (T2 and FLAIR hyperintensity)

MRI Brain	ADEM	%	MOGAD	%	NMOSD	%	Total	%	Chi-square	p-value
Cortical grey matter	5	31.25	2	28.57	0	0.00	7	23.33	2.7980	0.2470
Juxta cortical white matter	8	50.00	3	42.86	0	0.00	11	36.67	5.3930	0.0670
Deep white matter	11	68.75	4	57.14	4	57.14	19	63.33	0.4330	0.8050
Periventricular white matter	6	37.50	2	28.57	4	57.14	12	40.00	1.2800	0.5270
Periaqueductal grey matter	0	0.00	1	14.29	3	42.86	4	13.33	7.7470	0.0210*
Corpus callosum	3	18.75	3	42.86	2	28.57	8	26.67	1.4640	0.4810
Thalamus	8	50.00	4	57.14	3	42.86	15	50.00	0.2860	0.8670
Basal ganglia	8	50.00	3	42.86	3	42.86	14	46.67	0.1530	0.9260
Brain stem	7	43.75	4	57.14	4	57.14	15	50.00	0.5360	0.7650
Area postrema	0	0.00	1	14.29	3	42.86	4	13.33	7.7470	0.0210*
Cerebellum	6	37.50	3	42.86	3	42.86	12	40.00	0.0890	0.9560

***p<0.05 indicates significant association**

Table 4: Comparison of diagnosis groups with Spinal cord segment involved

Spinal cord segment involved	ADEM	%	MOGAD	%	NMOSD	%	Total	%	Chi-square	p-value
Cervical	3	18.75	2	28.57	4	57.14	9	30.00	3.4270	0.1800
Thoracic	2	12.50	3	42.86	3	42.86	8	26.67	3.5190	0.1720
Lumbar	1	6.25	4	57.14	1	14.29	6	20.00	8.0690	0.0180*
Conus medullaris	1	6.25	2	28.57	1	14.29	4	13.33	2.1070	0.3490

***p<0.05**

DISCUSSION

In this study all pediatric patients with clinical features suggestive of acute demyelinating disorder who underwent MRI brain and spine imaging were included. All MOG antibody positive cases were considered as MOGAD. All NMO antibody positive cases and other cases fulfilling the new diagnostic criteria of NMOSD (2015),[3] was considered as NMOSD. All demyelinating cases seronegative for NMO or MOG antibodies and presenting with polyfocal deficits in the presence of encephalopathy and was considered as ADEM.

In the present study of 30 cases of paediatric acquired demyelinating disorders, the most common diagnosis was ADEM in 16 (53.33%) cases followed by MOGAD & NMOSD, which accounted for 7 (23.33%) cases each. Similarly, in a study by Salma Zouari mallouli,[4] showed that the most common acquired demyelinating disorder in the paediatric age group was ADEM (36%), followed by CIS (24%), MS (19%), NMOSD (7%) and MOGAD (2%)

ADEM

In this study of 30 cases of paediatric acquired demyelinating disorders, majority of the cases (53.33%) were ADEM. The mean age of presentation in the ADEM group was 6.88 ± 4.05 years, ranges from 1 year to 13 years. Similar age distribution was noted in a previous study by Vykuntaraju K5 where the mean age of presentation was 5.5 years (ranges from 9 months–15 years). The study showed equal distribution of males and females, with a male: female ratio of 1:1.

In ADEM group the most common clinical presentation was fever (75.00%) followed by encephalopathy (56.25%) and head ache (43.75%). Similarly, in a study by Vykuntaraju K,[5] the commonest symptom was fever (80%), encephalopathy (53.3%) and seizure (40%). Encephalopathy which is one important criteria for the diagnosing ADEM, was found in 56.25 % patients in this study.

MRI brain showed demyelination in the form of T2 & FLAIR hyperintensities in the supratentorial and infratentorial brain parenchyma. ADEM showed lesions in bilateral cerebral hemispheres in an asymmetric distribution. Supratentorial brain

involvement was 4 times as compared to infratentorial brain involvement. Majority of the cases showed large lesions (68.75%) with size >2 cm. The most common location involved was deep white matter (68.75%) followed by juxta cortical white matter (50%), thalamus (50%), basal ganglia (50%), brain stem (43.75%), cerebellum (37.5%), periventricular white matter (37.5%) and cortical grey matter (31.25%) cases. None of the ADEM cases showed peri aqueductal grey matter or area postrema involvement. This was similar to the observations in a study by Alpert et.al,[6] in 2009 where most common site of brain lesions were deep white matter (68%), cerebellum (50%), basal ganglia (43%), brain stem (41%), juxta cortical white matter (21%) and periventricular white matter (18%).

Only 2 (12.5%) cases of the ADEM group showed optic nerve involvement which was anterior in both cases, however one patient showed unilateral involvement while the other one showed bilateral involvement. 3 ADEM cases showed spinal cord involvement which was LETM in 2 (12.5%) patients and focal lesion was seen in one patient. All the 3 (18.7%) cases showed cervical spinal cord involvement, where as thoracic involvement was seen in 2 (12.5%) cases and lumbar and conus medullaris involvement was seen in 1 (6.2%) case each. Similarly in a study by Matthias Baumann et-al,[7] the most common site spinal cord involvement was in the cervical (73%) region, followed by thoracic (54%), lumbar (35%) and conus medullaris (27%).

On follow up MRI, majority of the ADEM cases showed complete resolution (50%) and in 1 case, minor residuals were seen, however follow up MRI was not done in 43.3 % of the cases.

MOGAD

In our study of 30 cases of paediatric demyelinating disorders, 7 (23.33%) cases had the diagnosis of MOGAD. The mean age of presentation in the MOGAD group was 10 ± 4.0 years, ranging from 3 years to 15 years and showed female predominance with a female: male ratio of 1.33:1.

In MOGAD the most common presenting feature was limb weakness (57.14%) followed by fever, seizure, visual disturbance, cerebellar symptoms, headache. Area postrema syndrome was seen in 1 (14.29%) case. In a study by M Baumann et-al,[8] the most common clinical presentation among MOG antibody positive MOGAD was altered consciousness (89.5%) followed by limb weakness (52.6%), cerebellar (52.6%) signs and optic neuritis (15.8%), however in our study, altered sensorium was seen in only 2 (28.57%) cases.

On MRI Brain study, MOGAD group showed equal distribution of deep white matter, thalamus and brain stem lesions in 57.14 % (4) participants each, followed by basal ganglia, cerebellar and corpus callosal lesions. Cortical grey matter and juxta cortical white matter lesions were seen in 28.5% and 48.2% cases respectively. Although periaqueductal grey matter and area postrema lesions are specific for NMOSD cases, in our study one MOGAD case (14.29%) showed these lesions. Similarly in a study by Sara Salama et al,[9] 7% of the MOG antibody disease showed area postrema involvement and 57% cases showed cortical/juxta cortical involvement.

In our study MOGAD cases showed supratentorial distribution of the lesions more than infratentorial lesions in the ratio of 1.9:1. MOGAD cases showed more number of large lesions (57.14%) as compared to small lesions (42.8%). Optic nerve involvement was seen in 2 (28.5%) cases of MOGAD which showed involvement of the anterior segment in both cases, however one had unilateral involvement while the other showed bilateral involvement. 4 (57.15%) cases of MOGAD showed spinal cord involvement, among which 3 cases had LETM and 1 case showed focal spinal cord lesion. All of them showed involvement of the lumbar spinal cord with a statistically significant p value (0.0180) (as shown in table 4), thoracic involvement was seen in 3 (42.8%) cases and conus meduallaris and cervical spinal cord involvement was seen in 2 (28.5%) cases each.

4 (57.15 %) out of the 7 MOGAD cases had follow up MRI which showed, minor residuals in 3 cases (42.8%) and complete resolution in 1 case (14.29%)

NMOSD

In our study of 30 cases of paediatric demyelinating disorders, 7 (23.33%) cases had the diagnosis of NMOSD. The mean age of presentation in the NMOSD group was 11.57 ± 6.63 years, ranging from 1 year to 18 years and showed female predominance with a female: male ratio of 2.5: 1. Similarly in a study by E. Bulut 10 the mean age of presentation in the NMOSD group was 10.3 ± 5.6 years and showed female predominance with a female: male ratio of 2.3:1.

Among NMOSD cases, the commonest presenting complaint was fever, visual disturbance, limb weakness, area postrema syndrome and head ache for 3 (42.86%) cases each followed by seizure, encephalopathy and cerebellar symptoms in 2 (28.57%) cases each. For area postrema syndrome p value was statistically significant with NMOSD as compared to ADEM & MOGAD cases (as shown in table 2).

On MRI Brain NMOSD group showed equal distribution of deep white matter, brain stem and periventricular white matter lesions in 57.14 % (4) participants each, followed by periaqueductal grey matter, area postrema, thalamus, basal ganglia and cerebellar lesions. Periaqueductal grey matter and area postrema lesions which are specific for NMOSD cases was seen in 42.8% cases in our study with statistically significant p value (as shown in table 3). Cortical grey matter and juxta cortical white matter lesions were not seen in NMOSD cases. Similarly in a study by Sara Salama et al,[9] 50% of the NMOSD cases showed area postrema involvement and none of the cases showed cortical/juxta cortical involvement.

In our study NMOSD cases showed equal distribution of lesions in the supratentorial and infratentorial brain parenchyma in the ratio of 1.07: 1 cases respectively. NMOSD cases showed more number of small lesions (71.43 %) as compared to small lesions (28.57 %). Optic nerve involvement was seen in 3 (42.8 %) cases of NMOSD which showed bilateral involvement in all the 3 cases. Posterior segment involvement was more common as it was seen in 2 (28.57%) cases as compared to anterior involvement in 1 case (14.29%). 4 (57.15%) cases of NMOSD showed spinal cord involvement, among which 3 cases had LETM and 1 case showed focal spinal cord lesion. Most of the cases showed cervical and thoracic involvement, 57.15 % and 42.8% cases respectively. Lumbar and conus medullaris involvement was seen only in 1 (14.29%) case each. Similarly in a study by M. Baumaann,[8] the most common site of involvement was cervical spinal cord followed by thoracic, lumbar and conus medullaris.

4 (57.15 %) out of the 7 cases of NMOSD had follow up MRI, which showed complete resolution in 2 cases (28.57%), minor residuals and moderate residuals in 1 (14.28%) case each.

ANNEXURE III MRI IMAGES

IMAGE 1: ADEM 10 year old male patient- Axial FLAIR weighted brain image showing hyperintensities along the periventricular, deep white matter, cortical and juxta cortical white matter

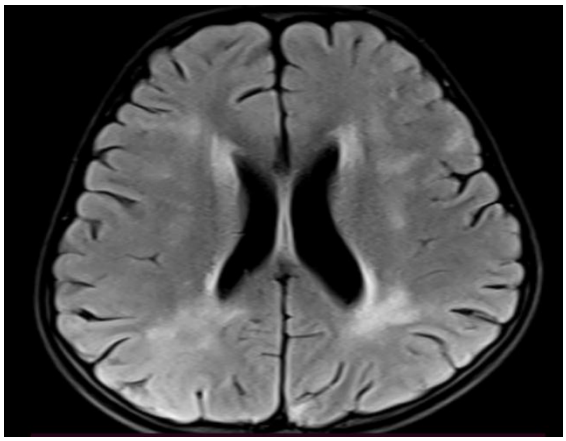


IMAGE 2: NMOSD 13 year old male patient - Sagittal FLAIR weighted spine image showing hyperintensities along the cervical spinal cord

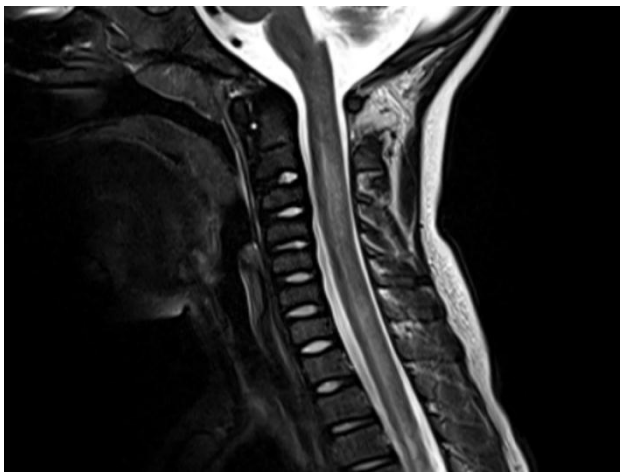
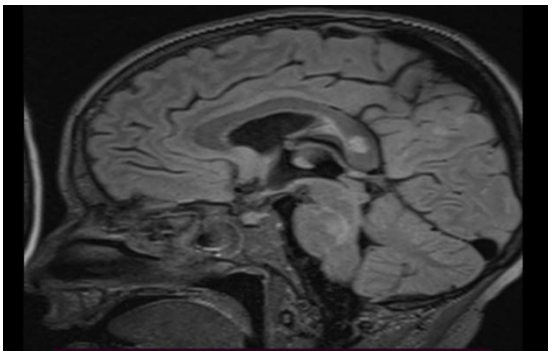


IMAGE 3: MOGAD 12 year old male patient - Axial T2 weighted image showing T2 hyperintensities noted involving the bilateral centrum semiovale and subcortical white matter



CONCLUSION

In our study of 30 patients, the majority (43.33%) were aged between 7 to 12 years. Mild female predominance was noted with a female: male ratio of 1.3:1. The most common diagnosis was ADEM in16 (53.33%) cases followed by equal distribution of MOGAD & NMOSD

ADEM cases showed lesions in bilateral cerebral hemispheres with predominant supratentorial brain involvement and majority of the cases had large lesions. In MOGAD cases, brain parenchyma showed predominantly large lesions in supratentorial distribution. Spinal cord lesion was predominantly LETM with statistically significant involvement of the lumbar spinal cord. In NMOSD cases, statistically significant association was seen with periaqueductal grey matter & area postrema lesions on MRI brain. Spinal cord lesions in NMOSD was predominantly LETM with involvement of the cervical and thoracic spinal cord.

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