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Original Research Article

An Observational Study Assessing Acquired Demyelinating Diseases in Children: A Retrospective Study

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Abstract

Aim: The aim of the present study was to assess the acquired demyelinating diseases in children.

Methods: The present study was conducted in the Department of Pediatrics, Patna medical College and Hospital, Patna, Bihar, India for the period of 1 year. A total of 50 patients were enrolled in the study.

Results: Of these, 33 (66%) cases were of acquired demyelinating encephalomyelitis (ADEM), 10 (20%) of transverse myelitis (TM), 5 (10%) of neuromyelitis optica (NMO), 1 (2%) of optic neuritis (ON) and 1 (2%) of multiple sclerosis (MS). The mean age of presentation was 7.7 years (range: 2-12 years). Of 50 cases, 24 (48%) were male and 26 (52%) females. History of preceding illness was present as upper respiratory infection /acute febrile illness and mean duration between preceding events and onset of symptoms was 7.24±2.9 days. All patients diagnosed with ADEM had encephalopathy. Areas involved in descending order of frequency were subcortical white matter, basal ganglia, thalamus, brainstem, cerebellum and spinal cord involvement.

Conclusion: Children presenting with new, subacute focal neurological deficits with history of some preceding event and in absence of trauma, metabolic derangements, or structural abnormalities should be suspected of having acquired CNS demyelination. These patients should be investigated with CSF analysis, serum antibodies and neuroimaging. ADEM is the most common among ADS. Early diagnosis and management with steroid therapy improves outcome in most of the patients.

Keywords: Pediatric demyelinating disorders, ADEM, Transverse myelitis, MOG

Introduction

Acquired demyelinating syndromes (ADS) can be defined as syndromes resulting in single (monofocal) or multiple (polyfocal) lesions originating in the central nervous system (CNS) caused by inflammatory demyelination. Monophasic events may be classified as (1) clinically isolated syndrome (CIS), characterized by monofocal or polyfocal deficits without encephalopathy, or (2) acute disseminated encephalomyelitis (ADEM), characterized by polyfocal deficits and encephalopathy. Recurrent disorders include pediatric multiple sclerosis (MS), neuromyelitis optica spectrum disorders (NMOSD), and serum antibodies to myelin oligodendrocyte glycoprotein (MOG)-associated demyelination. [1]

Optic neuritis (ON) is characterized by inflammation of the optic nerve. It may present as an isolated condition or can be associated with variety of other immune-mediated CNS or systemic disorders. [2] Mean age of onset ranges from 9 to 12 years of age with an approximate 1.5:1 female-to-male ratio. [3] Its incidence is 1–5 per 100,000/year.3 Between 13% and 36% of children with an initial episode of ON are eventually diagnosed with MS. [4]

Clinical Features Common clinical features of ON include periorbital pain or headache made worse by eye movement, subacute decrease in visual acuity (VA), abnormal color vision, reduced low-contrast letter acuity, and visual field (VF) defects. Physical examination at the time of an acute event will reveal a relative afferent pupillary defect (RAPD) in unilateral cases. Initial visual acuity can range from 20/40 or better to no light perception. Close to 60% of children have a VA of 20/200 or worse. [5] Inflammation of the optic nerve head (papillitis) is reported in up to 64% of cases of ON in children. [6] Bilateral ON and papillitis at onset are seen in 72% of children younger than 10 years of age, in comparison to older children.[5] The absence of pain and presence of retinal exudates, retinal

hemorrhages, severe disk swelling, and lack of response to treatment suggest alternative diagnosis

MRI of the CNS is critical in the accurate diagnosis and classification of an acquired demyelinating syndrome. MRI should be obtained with gadolinium contrast and should include the area of the CNS that is impacted (eg, MRI of the brain and orbits for an optic neuritis, MRI of the spinal cord for those with a myelitis presentation). Imaging outside the area affected can also yield important prognostic information. In children presenting with acute transverse myelitis, lesions within the brain bode a significant future risk for relapse and ultimate MS diagnosis. [7]

Transverse myelitis (TM) includes a pathobiologically heterogeneous syndrome characterized by acute or subacute spinal cord dysfunction resulting in paresis, a sensory level, and autonomic (bladder, bowel, and sexual) impairment below the level of the lesion. [8,9] In 2004, discovery of a pathogenic NMO-associated IgG antibody, targeting the water channel membrane protein aquaporin-4 (AQP4), was an important milestone in differentiating NMO from MS. [10] After varying forms of clinical presentation were described for the disease, the term NMO spectrum disorder (NMOSD) was introduced in 2007. [11] The myelin oligodendrocyte glycoprotein is one of several proteins produced by oligodendrocytes, which are the myelin-forming cells of the CNS. Together with others: myelin basic protein (MBP), proteolipid protein (PLP) and myelin-associated glycoprotein (MAG), MOG is an essential component of the oligodendrocyte surface membranes; these glycoproteins have fundamental roles in the formation, maintenance and disintegration of myelin sheaths. [12]

The aim of the present study was to assess the acquired demyelinating diseases in children.

Materials and Methods

The present study was conducted in the Department of Pediatrics, Patna medical College and Hospital, Patna, Bihar, India for the period of 1 year. A total of 50 patients were enrolled in the study. The aim of the present study was to assess the acquired demyelinating diseases in children.

Inclusion Criteria

All children in the age group between 1 year to 12 years who present with clinical, radiological, and immunological features of acquired demyelinating disorders were included in the study.

Exclusion Criteria

Parents/ guardians not willing to give written informed consent to enroll their child in the study were excluded from the study.

The study was initiated only after institutional ethics committee permission was obtained. The study was performed in accordance with the ethical principles specified in the declaration of Helsinki and as per the guidelines of good clinical practice.

Statistical Analysis

After data collection, data entry was done in a Microsoft Excel sheet. Data analysis was done with the help of statistical software GraphPad InStat.v3.0 .Data were presented in tables as well as figures, wherever needed descriptive statistics were used to note down the distribution of patients based on age, gender, patient history details, and other findings. A p value of less than 0.05 was considered significant wherever applicable.

Brief Methodology Details

After enrollment, demographic details such as age, sex and socioeconomic status were noted in the predesigned proforma. Patient details were noted as follows-Detailed patient history, complete physical and neurological examination and laboratory investigations-Routine blood (CBC, liver and renal function test), serum antibodies for MOG and AQP-4 and MRI (brain/spine) scan. CSF ANTIBODY gone to outside lab for testing due to unavailability in PMCH.

The diagnosis of ADS was based on the acute onset of neurologic signs and symptoms together with brain MRI evidence of multifocal, hyperintense lesions on T2- weighted according to IPMSSG 2010 criterion.

Results

Table 1: Frequency distribution of age groups with acquired demyelinating diseases

Age groups(Years)	ADEM	TM	NMO	MS	ON	Total (%)
1 to 4	7	2	0	0	0	9 (18)
5 to 8	14	2	1	0	0	17 (34)
9 to 12	12	6	4	1	1	24 (48)
Total	33	10	5	1	1	50 (100)
Mean ± SD	7.04±3.09	8.5±3.34	9.16±2.3	12	12	7.7±3.07

Of these, 33 (66%) cases were of acquired demyelinating encephalomyelitis (ADEM), 10 (20%) of transverse myelitis (TM), 5 (10%) of neuromyelitis optica (NMO), 1 (2%) of optic neuritis (ON) and 1 (2%) of multiple sclerosis (MS). The mean age of presentation was 7.7 years (range: 2-12 years).

Table 2: Frequency distribution of gender of patients with acquired demyelinating diseases

Gender	ADEM	TM	NMO	MS	ON	Total (%)
Male	21	2	0	0	1	24 (48)
Female	12	8	5	1	0	26 (52)
Total	33	10	5	1	1	50 (100)

Of 50 cases, 24 (48%) were male and 26 (52%) females.

Table 3: Clinical features of pediatric demyelinating disorders

Clinical features	ADEM, (n=33)	TM, (n=10)	NMO, (n=5)	ON, (n=1)	MS, (n=1)
Encephalopathy	33	-	1	-	-
Seizures	8	-	-	-	-
Fever	6	-	-	-	-
Visual disturbances	-	-	5	1	-
Unilateral	-	-	-	1	-
Bilateral	-	-	5	-	-
Limb weakness	17	10	5	-	1
Hemiparesis	5	-	-	-	-
Paraparesis	2	8	5	-	-
Quadriparesis	10	3	-	-	1
Cerebellar signs	9	-	-	-	-
Sensory involvement	-	10	2	-	-
Meningism	18	-	-	-	-
Bowel and bladder involvement	4	10	2	-	-
Recurrent history	4	-	-	-	1

History of preceding illness was present as upper respiratory infection /acute febrile illness and mean duration between preceding events and onset of symptoms was 7.24±2.9 days. All patients diagnosed with ADEM had encephalopathy.

Table 4: Radiological findings of pediatric demyelinating disorders

Radiological findings	ADEM, (n=33)	LETM, (n=10)	NMO, (n=5)	ON, (n=1)	MS, (n=1)
Areas involved					
Cerebral cortex	30	-	1	-	1
Thalamus	18	-	1	-	-
Brainstem	14	-	2	-	-
Cerebellum	10	-	1	-	1
Spine	2	10	5	-	-
Optic nerve	-	-	5	1	-
Contrast enhancement	7	-	1	-	1

Areas involved in descending order of frequency were subcortical white matter, basal ganglia, thalamus, brainstem, cerebellum and spinal cord involvement.

Discussion

Acquired demyelinating diseases (ADS) constitute a heterogeneous group of central nervous system disorders of autoimmune origin and cause significant physical and cognitive disabilities. The spectrum includes monophasic, multiphasic, and progressive disorders ranging from highly localized forms to multifocal or diffuse variants. [13] Monophasic events may be classified as clinically isolated syndrome (CIS), characterized by monofocal or polyfocal deficits without encephalopathy or acute disseminated encephalomyelitis (ADEM), characterized by polyfocal deficits and encephalopathy. [14] Recurrent disorders include multiple sclerosis (MS), neuromyelitis optica spectrum disorders (NMOSD) and serum antibodies to myelin oligodendrocyte glycoprotein (MOG)- associated demyelination. [15] International pediatric multiple sclerosis study group (IPMSSG) has proposed the criteria for pediatric multiple sclerosis and immune-mediated

central nervous system demyelinating disorders for diagnosis and research purpose. [16]

Of these, 33 (66%) cases were of acquired demyelinating encephalomyelitis (ADEM), 10 (20%) of transverse myelitis (TM), 5 (10%) of neuromyelitis optica (NMO), 1 (2%) of optic neuritis (ON) and 1 (2%) of multiple sclerosis (MS). The mean age of presentation was 7.7 years (range: 2-12 years). ADEM was the most common acquired demyelinating disorder in our study with mean age of presentation being 7 years which was similar to 5.5 and 6.14 years seen in other similar pediatric studies done by Torisu H, Singhi PD et al. [17,18] Although some studies have reported equal sex distribution. [14] Most common presentation in ADEM patients was encephalopathy with multifocal motor deficit and meningism similar to other studies. [17-19]

Of 50 cases, 24 (48%) were male and 26 (52%) females. History of preceding illness was present as upper respiratory infection /acute febrile illness and mean duration between preceding events and onset of symptoms was 7.24±2.9 days. All patients diagnosed with ADEM had encephalopathy. Areas involved in descending order of frequency were subcortical white matter, basal ganglia, thalamus, brainstem, cerebellum and spinal cord involvement. MRI is highly sensitive in detecting white matter abnormalities and investigation of choice for demyelinating disorders. ADEM present with multiple hyperintense bilateral, asymmetric patchy and poorly marginated lesions on T2 weighted and FLAIR images on MRI. ADEM lesions typically involve the subcortical and central white matter and cortical gray white matter junction. Most of patients in our study present with subcortical white matter and brainstem involvement with occasional spinal cord involvement. Deep grey matter lesions involving basal ganglia and thalamus 54% which is similar to studies showing 49% to 60%. [17,20] Most of the patients responded well to the pulse dose of steroids on 3 month follow up.

Conclusion

Children presenting with new, subacute focal neurological deficits with history of some preceding event and in absence of trauma, metabolic derangements, or structural abnormalities should be suspected of having acquired CNS demyelination. These patients should be investigated with CSF analysis, serum antibodies and neuroimaging. ADEM is the most common among ADS. Early diagnosis and management with steroid therapy improves outcome in most of the patients.

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