Rare presentations of acute acquired demyelinating syndromes (ads) among children: a case series

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Abstract

Acute demyelinating syndromes (ADS) in children presents with neurological symptoms with a pathology involving either single central nervous system (CNS) location (mono focal ADS) or multiple sites (poly focal ADS), with or without encephalopathy. It is a diagnostic dilemma requiring a high index of suspicion. A thorough clinical examination with neuroimaging and cerebrospinal fluid (CSF) analysis is needed for making a diagnosis. Clear cut guidelines regarding long term management and prognosis is lacking. Myelin oligodendrocyte glycoprotein (MOG) antibody must be done in all suspected cases as it helps in prognosticating and counselling parents. Recurrence is rare, recovery is usually complete and most children respond to pulse high dose methylprednisolone injection. In this case series we map out different unique presentations of acute ADS with and without Myelin oligodendrocyte glycoprotein (MOG) antibody positivity among children from a tertiary care hospital in central Kerala, INDIA.

Keywords: Anti-MOG Antibody, Acquired Demyelinating syndromes (ADS), monofocal ADS, polyfocal ADS

Introduction

Acquired demyelinating syndromes (ADS) in children presents with neurological symptoms with a pathology involving either single location (mono focal ADS) or multiple sites (poly focal ADS) in the brain, with or without encephalopathy. The disease is an acute demyelination involving white matter of optic nerve, brain and spinal cord. The clinical presentations of ADS varies from case to case. The incidence of ADS among children is 0.5 to 1.66 per 100,000 children.[1,2] ADS cases among children are like a labyrinth to pediatricians and neurologists which may begin with benign symptoms and later take the unexpected paths. In this series we describe clinico-biochemical and radiological profiles of three cases of ADS from our tertiary hospital.

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Materials & Methods

In this retrospective record review we discuss three cases with ADS who were admitted in the pediatric ward during the month of February 2023. After obtaining institutional ethical committee clearance, the clinical profile, laboratory and imaging results were followed up for a minimum of three months after discharge. Magnetic Resonance Imaging (MRI) brain and spinal cord were performed for all patients with 1.5 T Magnetom vision of Siemens, Germany having a gradient strength of 25 MT/min. The non-contrast enhanced spin echo MRI was used to take axial, coronal, sagittal T1 weighted,T2 weighted spin echo images. The slice thickness in all planes were 5mm.

Results

The present study is a case series of three children diagnosed with ADS by clinical features, biochemical parameters and imaging results. They were followed up for a minimum of 3 months (Table1). The children in our series presented with wide spectrum of clinical features of mono focal ADS to poly focal ADS. All children in our study either had a history of febrile illness in the preceding two weeks or at presentation. The five year old child was immunized in the preceding week and then presented to us with fever and sudden onset of vision loss whereas the one year old child presented with isolated ataxia. The 11 year old boy initially presented with symptoms suggestive of acute gastritis for a week, which eventually progressed to back pain, tremors, ataxia and finally inability to stand without support. This child had poly-symptomatic presentation consisting of motor, sensory and autonomic symptoms. Consciousness were intact in all the three children. None of our patients had seizures. The Cerebrospinal fluid (CSF) analysis showed Myelin oligodendrocyte glycoprotein

(MOG) antibody (ab) positive in two patients. MRI brain and spine was suggestive of demyelination in all cases. All patients received methylprednisolone pulse therapy. Only one child required IVIG (Intravenous immunoglobulin) injection, as clinical outcome after methylprednisolone administration was not satisfactory. All patients had favorable outcome at the time of discharge.

Table 1: Clinical characteristics of cases

Case No.	1	2	3
Age	5years	11 year	1 year
Sex	Female	Male	Female
Clinical presentation	Fever with Vision loss	Fever with pain abdomen and tremors	Fever with Ataxia
Preceding vaccination	No	No	No
MRI findings (Figure 1)	• Multiple flame shapedwhite matter FLAIR hyperintensities seen in bilateral fronto-parietal subcortical white matter,bilateral insular cortex and to lesser extent surrounding the temporal horn of both lateral ventricles. • T2/FLAIR hyperintensities seen in the intracranial prechiasmatic portion of left optic nerve extending into left optic tract.	• Multiple flame shapedwhite matter FLAIR hyperintensities in B/l frontal and temporal lobe subcortical white matter,left cingulate gyrus,B/l cerebellar hemisphere subcortical region,right anterior medulla and retrochiasmatic portion of both optic nerves.	• Areas of confluent T2/FLAIR hyperintensities noted involving the white matter in the periventricular region and deep white matter without any evidence of diffusion restriction-?demyleinayion
CSF Analysis	• WBC-12(Neutrophils8%, Lymphocytic92%) • RBC-nil • Glucose-103 • Protein-45 • Culture-Sterile	• WBC-22 (Neutrophils7%, Lymphocytes93%) • RBC-nil • Glucose-53 • Protein-84 • Culture-Sterile	• WBC -2 • RBC-10 • Glucose-79 • Protein-11 Culture-Sterile
CSF Anti MOG Antibody	Positive	Positive	Negative
Treatment	• IvIg for 5days • Methylprednisolone for 5 days • Prednisolone for 45days	• Methylprednisolone*5 days • Prednisolone*45days	• Methylprednisolone*5 days • Prednisolone*15days
At discharge	• Regained vision • B/L RAPD	• Ataxia Improved • Tremors reduced • Gait improved	• Ataxia resolved • Gait improved
Follow up	Complete resolution of symptoms.	Complete resolution of symptoms.	Complete resolution of symptoms.

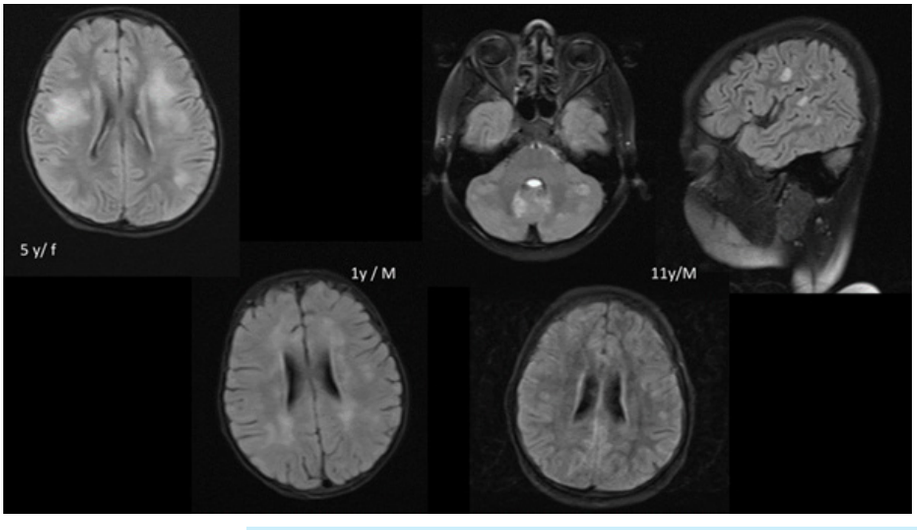

Figure 1: MRI findings of the three children

Discussion

Acquired demyelination of CNS can present as a monophasic illness or as first attack of a chronic inflammatory diseases like multiple Sclerosis (MS) and neuromyelitis optica (NMO).

Monophasic/Acute illnesses:

A.Optic Neuritis (ON)

Any child presenting with acute vision loss should be evaluated for ON. Reduced visual acuity, a central visual field deficit, pain on ocular movements, red color desaturation are some of the clinical features suggestive of ON. Optic disc edema may be present or may be absent as in retrobulbar ON. Abnormalities of optic nerve may be found in neuroimaging studies, visual-evoked potentials (a P100 latency delay might be a typical finding), optical coherence tomography (OCT) may yield quantitative axonal and neuronal loss. Following an episode of ON, approximately 80 to 85% children regain vision. These children have 30% risk of MS in future. Approximately 30% of all cases of pediatric MOG-associated disorders are with optic neuritis.[3] The current studies suggests that children with MOG-positive neuromyelitis optica spectrum disorder (NMOSD) have a lower propensity for relapse and better visual/ motor outcomes.[4]

B. Transverse Myelitis(TM)

The demyelination of spinal cord causes TM. The children often present with sub acute bilateral lower limb weakness, a spinal sensory level weakness and dysfunction of bowel/bladder control. Initially the weakness may be flaccid with hyporeflexia and later hyper-reflexia below the level of lesion. There is a risk of 2% to 8% risk for MS in later life. The children with younger age of onset, complete paraplegia, loss of sphincter control and maximum deficit in 24 hours are associated with poor prognosis.

Children with longitudinally extensive TM (LETM), that is, involvement of 3 or more spinal segments, recurrent TM and TM with ON should be evaluated for NMO.

C. Poly-focal Demyelination

Multiple neurologic symptoms with more than one CNS area being involved are suggestive of poly-focal demyelination. This with encephalopathy (altered consciousness or behavioural changes) with or without seizures is known as acute disseminated encephalomyelitis (ADEM). A recent history of infection and fever is commonly associated. ADEM is more common in young children, and it has a good outcome when treated appropriately.

The other presentations like intranuclear ophthalmoplegia (INO), focal motor deficits, sensory loss/ paresthesias or isolated cerebellar deficits are rarer in children.

Unique clinical, biochemical and radiological findings are present in children with ADS. History regarding preceding factors like infections or vaccines, travelling, insect/tick bites, rashes, recent trauma/ injury should be taken. Physical examination should focus on nervous system examination and neurologic deficits, blood/ CSF tests should include MOG, Aquaporin-4(AQP4) IgG (Immunoglobulin G) antibodies and neuroimaging should be done for confirming the diagnosis and also to predict prognosis of disease on follow up. The Pediatric European Collaborative Consensus recommends "on testing all children presenting with demyelinating or encephalitic event with abnormalities on brain and/ or spinal MRI" (Fig 2),[3] with MOG-ab and AQP4-ab testing in the blood, and with CSF analysis for oligoclonal bands (OCB). This is different from previous protocols of MOGab antibody testing where MOG-abs is tested only in atypical MS presentations.[5,6] Also, previously suggested protocols advised to only test NMOSD patients for MOG-abs if they were tested negative for AQP4-abs.[6,7] Since the interpretation of typical MS can differ between clinicians, the above tests need to be done in all patients with suspected ADS. Should the child become MOG-ab positive then the patient should be referred to a centre with expertise for further management.

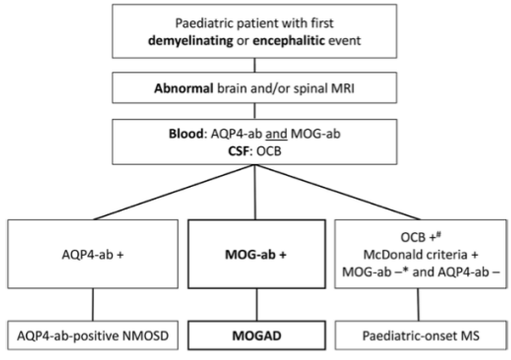

Figure2:Paediatric European Collaborative Consensus recommendation on MOG-ab testing (in an accredited laboratory) in paediatric patients.

Up to 90% of paediatric-onset MS patients have OCB specific to the CSF.8

* A minor proportion of paediatric-onset MS patients have MOG-abs (mostly low titre/weak positive CBA test result which rapidly declines during follow-up). However, presence of MOG-abs should result in patient referral to a centre of expertise for further management.

AQP4-ab :aquaporin-4 antibody, CBA :cell-based assay, CSF :cerebrospinal fluid, NMOSD :neuromyelitis optica spectrum disorders, MOG-ab :myelin oligodendrocyte glycoprotein antibody, MOGAD :MOG-ab-associated disorders, MRI :magnetic resonance imaging, MS :multiple sclerosis, OCB : oligoclonal bands, + : positive, - :negative.

MOG is a surface protein of myelin expressed exclusively in the CNS. At the time of initial onset of acquired demyelinating syndrome, Anti-MOG antibodies are detected in one-third of all children diagnosed with ADS.[9] The MOG-associated demyelination is more common in children (0.31 per 100,000) with a relatively equal sex ratio, particularly in younger children.[10] The MOG-associated demyelination most commonly includes ADEM and optic neuritis; the less common ones are acute transverse myelitis, non-ADEM encephalitis, AQP4-negative NMOSD, and brainstem syndromes.[3] The younger children with MOG-associated demyelination present with ADEM spectrum disorders, whereas older children (>11 years of age) tend to manifest with optic neuritis.[9] In pediatric

patients NMOSD-like phenotypes with MOG-antibodies are more common than AQP4-antibody positive NMOSD.11The children who remain seropositive during follow-up have increased risk for relapse when compared with those children who became seronegative.9 MOG-abs are found five times more often than AQP4-abs among pediatric patients ,especially those presenting with simultaneous ON and LETM. Thus MOG-abs should be tested only in an accredited laboratory, in order to avoid false positive or false negative test results.[12]

The children with mild symptoms, not impairing daily function, needs ongoing monitoring and reassurance. The intravenous (IV) corticosteroids are considered first-line treatment in ADS.[13] The steroids works by modification of cytokine responses, also reduces T-cell activation and acts by reducing blood–brain barrier permeability that, in turn, limits extravasation of immune cells into the CNS. The steroids facilitates apoptosis of activated immune cells.[14] Intravenous methyl prednisolone is administered at doses of 20–30 mg/kg/day (up to 1 g/day) for 3–5 days. Children not responding to steroids are given IvIg and rarely monoclonal antibodies like Rituximab.[15] Oral prednisone, starting at 1 mg/kg/day and tapered over 1–4 weeks, is considered for patients with incomplete resolution of symptoms after IV treatment.

In our case series, only one child required intravenous immunoglobulin (IvIg) for complete resolution of symptoms. The MRI findings in the one year old child was not typical of ADS due to probable age appropriate incomplete myelination. This child needs to be kept under observation for further evolution of symptoms as the child grows. On three months follow up, there was complete resolution of symptoms and MRI findings.

Conclusion

Majority of ADS have good neurological outcome if diagnosed and treated appropriately. Apart from typical presentations of acute ADS, rare and atypical presentations ranging from vague symptoms to life threatening episodes should be evaluated for ADS. Without a high index of suspicion of treating paediatrician and neurologist these cases could be missed. MOG-antibody positivity is useful for counselling families about relapse risk and possible treatment options.

Consent

The authors confirm that caregivers of their patients were fully informed and they agreed to report these cases.
Permission has been obtained from the authors to reproduce figure 1 after including the appropriate references for the figure

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Conflict of Interest
None declared.

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