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Case Report

Rare presentations of Acute Acquired Demyelinating Syndromes (ADS) Among Children: A Case Series.

Jeffy Joy.K *[1], Rose Xavier [2], Ebin Jose*[3], Vinod Jacob Cheriyan [4]

1. Department of Paediatrics, Jubilee Mission Medical College & Research Institute, Thrissur, Kerala.

***Correspondence to:** Jeffy Joy.K, Department of Paediatrics, Jubilee Mission Medical College and Research Institute, Thrissur, Kerala, India.

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Abstract

Acquired 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.In this case series we map out different unique presentations of acute ADS with and without Myelin oligodendrocyte glycoprotein (MOG) antibody among children from a tertiary 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 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.

Materials and Methods

In this retrospective record review we discuss three cases with ADS who were admitted in pediatric ward of Jubilee mission medical college and research Institute, Thrissur, Kerala, INDIA during the month of February 2023.The clinical profile, laboratory and imaging results were followed up for a minimum of three months after discharge from hospital. 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. One child had immunization history in preceding week and presented to us with fever and sudden onset of vision loss whereas another child presented with isolated ataxia. The third 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 were suggestive of demyelination in all cases. All patients received methylprednisolone pulse therapy. Only one child required IVIG, as clincal outcome after methylprednisolone therapy was not satisfactory. All patients had favourable outcome by the time of discharge.

Case No.	Age	Sex	Clinical presentation	Preceding vaccination	MRI findings	CSF Analysis	CSF Anti MOG Antibody	Treatment	At discharge	Follow up
1	*5years*	*Female*	*Fever with Vision loss*	*No*	● *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*	● *WBC-12(Neutrophils 8%,Lymphocytic 92%)* ● *RBC-nil* ● *Glucose-103* ● *Protein-45* ● *Culture-Sterile*	*Positive*	● *IvIg* 5days* ● *Methylprednisolone* 5days* ● *Prednisolone *45days*	● *Regained vision* ● *B/L RAP D*	*Complete resolution of symptoms.*

					portion of left optic nerve extending into left optic tract.					
2	*11 year*	*Male*	*Fever with pain abdomen and tremors*	*No*	● *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.*	● *WBC - 22(Neutrophils 7%,Lymphocytes93%)* ● *RBC-nil* ● *Glucose-53* ● *Protein-84* ● *Culture-Sterile*	*Positive*	● *Methylprednisolone* 5 days* ● *Prednisolone* 45days*	● *Ataxia Improved* ● *Tremors reduced* ● *Gait improved*	*Complete resolution of symptoms.*
3	*1 year*	*Female*	*Fever with Ataxia*	*No*	● *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*	*WBC -2 RBC-10 Glucose-79 Protein-11 Culture-Sterile*	*Negative*	● *Methylprednisolone* 5 days* ● *Prednisolone* 15days*	● *Ataxia resolved* ● *Gait improved*	*Complete resolution of symptoms.*

Table1: Clinical characteristics of cases

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 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 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 subacute 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 involved are suggestive of poly-focal demyelination. This can be with encephalopathy (altered consciousness or behavioural changes) known as acute disseminated encephalomyelitis (ADEM). A recent history of infection and fever are commonly

associated. Although ADEM is more common in young children, it has good outcome.

ADS also have rare presentations like intranuclear ophthalmoplegia(INO), focal motor deficits, sensory loss/paresthesias or isolated cerebellar deficits among children.

The pediatric population with ADS manifest with distinct clinical ,biochemical and radiological findings and should be thoroughly investigated with history probing for potential preceding factors like infections or vaccines, travelling, insect/tick bites, rashes, recent trauma/injury. The physical examination focusing on nervous system, blood/CSF tests including MOG, Aquaporin-4(AQP4) IgG antibodies and advanced neuroimaging techniques aids at confirming diagnosis and also to predict prognosis of disease for followup.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 1)(3).They suggest that MOG-ab testing along with AQP4-ab testing in the blood, and with CSF analysis for oligoclonal bands (OCB). This is different from previous suggested protocols of MOGab antibody testing where MOG-abs tested only in atypical MS presentations (6,5). However,the interpretation of typical MS can differ between clinicians. MOG-ab positivity should result in patient referral to a centre of expertise for further management. Additionally, previously suggested protocols advised to only test NMOSD patients for MOG-abs if they were tested negative for AQP4-abs (6,7).

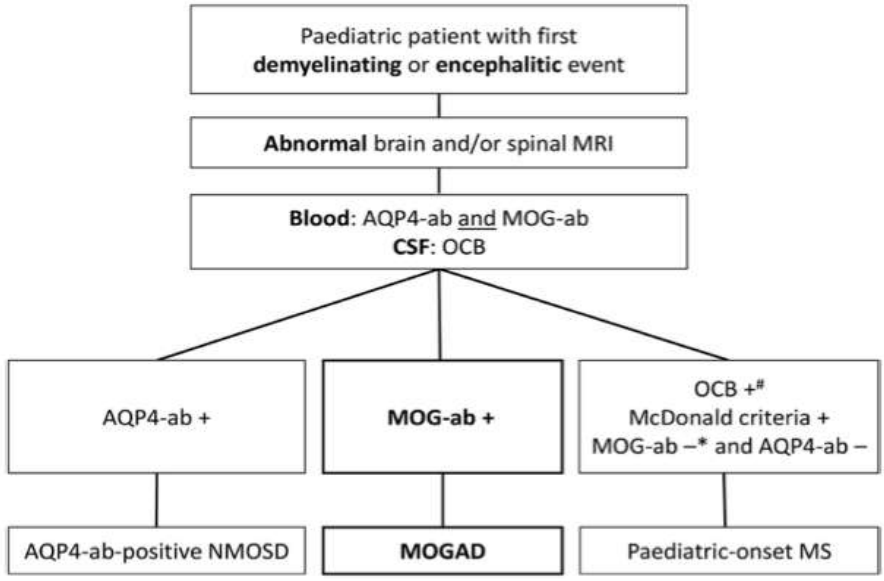

Figure 1

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 protein expressed exclusively in the CNS on the surface of myelin. Anti-MOG antibodies are detected in one-third of all children at the time of initial onset of acquired demyelinating syndrome(9).The incidence of MOG-associated demyelination is higher in children (0.31 per 100,000) and occurs with a relatively equal sex ratio, particularly in younger children(10).The clinical presentation of children with MOG-associated demyelination most commonly includes ADEM and optic neuritis; less common are acute transverse myelitis, AQP4-negative NMOSD, non-ADEM encephalitis, and brainstem syndromes(3). The phenotype of MOG-associated demyelination is somewhat age dependent, with younger children presenting 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(11).The 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 (LE)TM.It is of utmost importance that MOG-abs are tested only in an accredited laboratory, in order to avoid false positive or false negative test results and due to challenges in MOG-ab laboratory testing(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). The IV methyl prednisolone at doses of 20–30 mg/kg/day (up to 1 g/day) for 3–5 days is preferred treatment. 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 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, complete resolution of symptoms and MRI findings.

Conclusion

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 these cases could be missed. MOG-antibody positivity is useful for counselling families about relapse risk and possible treatment options.

Reference

1. Sophie M. Duignan, Cheryl A. Hemingway Paediatric acquired demyelinating syndromes;Paediatrics and Child Health Volume 29, Issue 11, November 2019, Pages 468-475.

2. A. Langer-Gould, MD, PhD, J.L. Zhang, MS, J. Chung, MS, Y. Yeung, MD, E. Waubant, MD, PhD, and J. Yao, MS Incidence of acquired CNS demyelinating syndromes in a multiethnic cohort of children;Neurology. 2011 Sep 20; 77(12): 1143–1148. doi: 10.1212/WNL.0b013e31822facdd

3. Bruijstens AL, Lechner C, Flet-Berliac L, et al. E.U. paediatric MOG consortium consensus: Part 1 - classification of clinical phenotypes of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. Eur J Paediatr Neurol2020; 29:2–13. doi: 10.1016/j.ejpn.2020.10.006

4.Lechner C, Baumann M, Hennes EM, et al. Antibodies to MOG and AQP4 in children with neuromyelitis optica and limited forms of the disease. J Neurol Neurosurg Psychiatry 2016; 87(8):897–905. doi: 10.1136/jnnp-2015-311743.

5. C. Lechner, M. Breu, E.-M. Wendel, B. Kornek, K. Schanda, M. Baumann, et al., Epidemiology of pediatric NMOSD in Germany and Austria, Front. Neurol. 11 (415) (2020).

6. M. Pagany, M. Jagodic, A. Schubart, D. Pham-Dinh, C. Bachelin, A.B. van Evercooren, et al., Myelin oligodendrocyte glycoprotein is expressed in the peripheral nervous system of rodents and primates, Neurosci. Lett. 350 (3) (2003) 165e168.

7. Y. Hacohen, K. Mankad, W.K. Chong, F. Barkhof, A. Vincent, M. Lim, et al., Diagnostic algorithm for relapsing acquired demyelinating syndromes in children, Neurology 89 (3) (2017) 269e278.

8. D. Pohl, K. Rostasy, H. Reiber, F. Hanefeld, CSF characteristics in early-onset multiple sclerosis, Neurology 63 (10) (2004) 1966e1967.

9. Waters P, Fadda G, Woodhall M, et al. Serial anti-myelin oligodendrocyte glycoprotein antibody analyses and outcomes in children with demyelinating syndromes. JAMA Neurol 2020; 77(1):82–93. doi: 10.1001/jamaneurol.2019.294

10. de Mol C, Wong Y, Pelt E, et al. The clinical spectrum and incidence of anti-MOG-associated acquired demyelinating syndromes in children and adults. Mult Scler 2020;26(7): 806–814. doi:10.1177/1352458519845112

11. C.Lechner,M.Breu,E.M.Wendel,B.Kornek,K.Schanda,M.Baumann,et al.Epidemiology of pediatric NMOSD in Germany and Austria.Frontiers in Neurology 11,415,2020.

12. Thaís. Armangue, Marco Capobianco, et al., E.U. paediatric MOG consortium consensus: Part 3 - Biomarkers of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders, Eur. J. Paediatr. Neurol. 21 (2020) 22e31.

13.Chitnis T, Tenembaum S, Banwell B, et al. Consensus statement: evaluation of new and existing therapeutics for pediatric multiple sclerosis. Mult Scler. 2012;18:116–127. doi: 10.1177/1352458511430704.

14. Sloka JS, Stefanelli M. The mechanism of action of methylprednisolone in the treatment of multiple sclerosis. Mult Scler. 2005;11:425–432. doi: 10.1191/1352458505ms1190oa.