Spectrum of acute central nervous system demyelinating diseases

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ABSTRACT

Central nervous system(CNS) demyelinative diseases are mainly Multiple Sclerosis, Acute Disseminated Encephalomyelitis (ADEM), Acute hemorrhagic Leucoencephalitis (AHL). Multiple Sclerosis is the most common. A clinically isolated syndrome is the result of a single episode of demyelination in one area of the central nervous system (a monofocal episode) or several areas of the central nervous system (a multifocal episode) which lasts for at least 24 hours. Among the people who are diagnosed with Multiple Sclerosis(MS), 85% experience an initial onset of symptoms or a first attack that is referred to as a clinically isolated syndrome (CIS). Here we are reporting different cases of central nervous system demyelinating diseases presented to Prathima Institute of Medical Sciences(PIMS) with various manifestations. Magnetic Resonance Imaging(MRI) findings have been discussed.

Keywords: Clinically Isolated Syndrome, Multiple Sclerosis, ADEM, AHL, MRI.

INTRODUCTION

Among the CNS demyelinating diseases, Multiple sclerosis is the common. Incidence of MS is two to three times more in women than men. Usual presentation of age is between 15 and 55 years. Typical features of MS include weakness, paraparesis, paresthesia, visual disturbances, diplopia, dysarthria, ataxia. Bowel, bladder and sexual dysfunction are common. Common manifestations of MS are optic neuritis, transverse myelitis, cerebellar ataxia, brainstem syndromes. Devic's neuromyelitis optica (NMO) is an idiopathic inflammatory demyelinating and necrotizing disease characterized by predominant involvement of the optic nerves and spinal cord. NMO characterized by presence of autoantibodies to the aquaporin4 water channel protein located in foot processes of astrocytes. Anti NMO-IgG antibodies has high sensitivity and specificity for NMO. In case of NMO myelopathy tends to be more severe than MS. Acute inflammatory demyelination in a patient, below 10 years of age is more likely to be due to ADEM. It is also known to be postinfectious, postexanthem, postvaccinal encephalomyelitis.

CASE REPORT

Case 1: A 35years old female patient came with complaints of sudden onset of loss of vision in right eye since 1wk followed by loss of vision in left eye. Central nervous system examination shows no motor and sensory deficit. Extraocular movements normal. No other cranial nerve abnormalities found except Optic nerve. Bilateral plantar response flexion. MRI Brain and Orbits with contrast suggestive of B/L Optic Neuritis(fig 1-4). MRI Cervical spine(fig 5) shows no abnormality. Anti Nuclear Antibodies negative. Anti Neuromyelitis Optica(NMO) antibodies negative(1:10titres). CSF for Oligoclonal bands not seen. Visual Evoked Potential (VEP) shows prolonged P100 latency(left>right). She was diagnosed as Bilateral Optic Neuritis(CIS). Patient was initially given methylprednisolone 1gm IV once daily for 5days. After that she was prescribed prednisolone 20mg twice daily, and discontinued in tappering doses. Her vision got improved after 3 months of treatment.

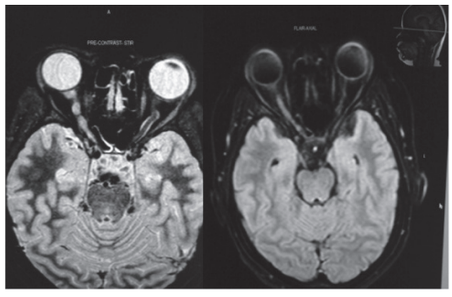

Fig 1&2: MRI Brain shows hyper intensities of bilateral optic nerve on pre contrast STIR, pre contrast FLAIR AXIAL views respectively

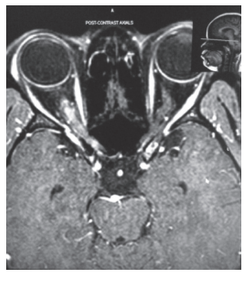

Fig 3: MRI Brain shows bilateral thickened nerve sheath complex with adjacent edema and thickening of optic tract noted, which is showing enhancement after contrast administration.

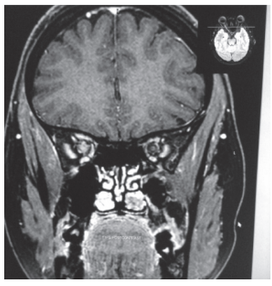

Fig 4: MRI T1FS coronal sequence showing enhancement of bilateral optic nerves after contrast.

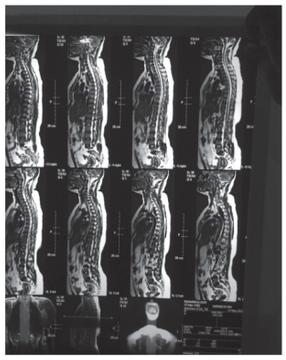

Fig 5: MRI cervical spine shows no abnormality.

Case 2: A 31 years old male patient came with complaints of tingling and numbness of left half of face since 3days, sudden in onset. Central nervous system examination normal except tingling and numbness of left half of face. No motor deficit. Bilateral plantar response flexion. MRI Brain with contrast(Fig 6-11) shows T2 hyper intense lesion noted at left lateral pons at the origin of the left trigeminal nerve which is enhancing on contrast. S/O Demyelination. Anti Nuclear Antibodies negative. Anti Neuromyelitis Optica(NMO) antibodies negative(1:10 titres) . CSF for Oligoclonal bands not seen . VEP shows prolonged P100 latency (right>left), suggestive of anterior visual pathway defect. EEG shows normal study. He was diagnosed as Trigeminal Neuropathy , Root entry Demyelination(CIS). He was started on low dose steroid (prednisolone 20mg twice daily). His symptoms were improved and doing well.

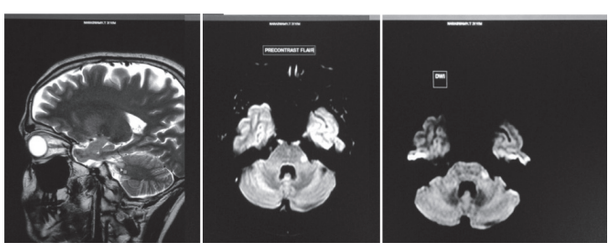

Fig 6,7&8: MRI Brain shows hyperintensities at left lateral part of pons at the origin of the trigeminal nerve on pre contrast T2 sagittal view, pre contrast FLAIR and pre contrast DWI sequences respectively.

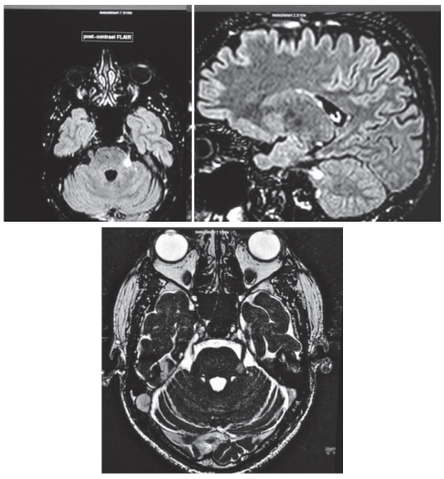

Fig 9,10,11: MRI Brain shows hyper intense lesion noted at left lateral part of pons at the origin of trigeminal nerve which is enhancing after contrast administration on post contrast FLAIR axial and sagittal views. Fig 11: MRI Cranial nerve sequence showing left trigeminal nerve root entry demyelination respectively.

Case 3: A 20years old female patient came with complaints of numbness of right side of neck followed by right half of the body since 1wk. There is history of decreased sensations of touch and temperature on the right half of the body since 4days. History of weakness of right upper limb followed by right lower limb since 3days, progressive in nature. Weakness progressed to left upper limb and lower limb. Central nervous system examination shows- Higher mental functions normal. Motor system shows 0/5 power on right side, 3/5 power on left side. Decreased sensations of touch and temperature present on right side. Deep tendon reflexes exaggerated. No bowel and bladder incontenence. Bilateral plantar response flexion. MRI brain(Fig 12) and spinal cord(Fig 13) shows T2/STIR hyperintensity in the medulla and cervical cord , extending upto C6-C7 level, causing enlargement of the cervical cord with no enhancement post contrast administration. Suggestive of Longitudinally Extensive Transverse Myelitis. Further investigations showed Anti Nuclear Antibodies positive. Anti NMO(Aquaporin 4) antibodies strongly positive. CSF for oligoclonal bands not seen. She was diagnosed as Neuromyelitis Optica(Devic's Disease). Initially she was treated with intravenous methyl prednisolone 1gm once daily for 5days. Then she was prescribed Azathioprine 50mg once daily. Low dose steroid prednisolone 20mg twice daily, discontinued slowly over 6months. Patient is doing well.

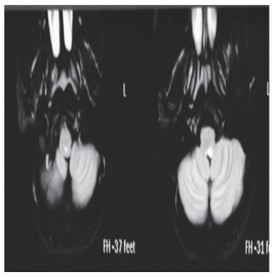

Fig 12: MRI Brain FLAIR shows hyperintensities present in the medulla.

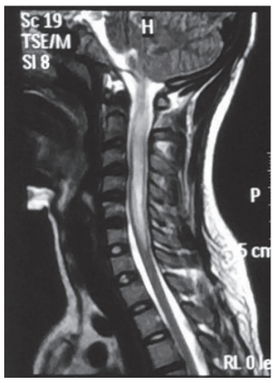

Fig 13: MRI spinal cord shows T2 hyperintensities starting in the medulla and extending to cervical cord C6-C7 level.

Case 4: A 18 months old child brought to the paediatric department with complaints of seizures , one episode, generalised tonic clonic type. History of recent vaccination. History of low grade fever since 2 days. Seizure involving both upper and lower limbs, associated with uprolling of eye balls. Not associated with deviation of mouth, bowel and bladder incontenence. Central nervous system examination showed child is conscious, coherant. Motor system examination showed decreased tone , power of 2/5 in all the 4 limbs. Deep tendon reflexes were normal. Bilateral plantar response flexion. No signs of meningeal irritation. MRI brain showed T2/ FLAIR hyper intensity noted in bilateral putamen , bilateral thalami(Fig 14,15). He was diagnosed as Acute Disseminating Encephalomyelitis. He was started on antiepileptics, antivirals and high dose corticosteroids. He was improved and doing well.

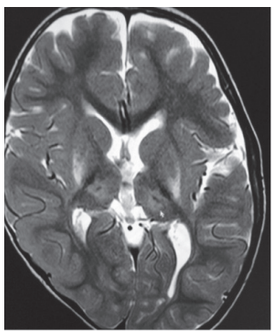

Fig 14: MRI brain shows T2 hyper intensities at bilateral putamen and bilateral thalami

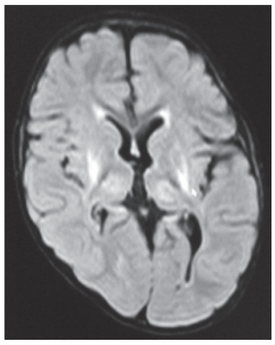

Fig 15: MRI brain shows FLAIR hyper intensities at bilateral putamen and bilateral thalami.

DISCUSSION

The manifestations of CIS depends on the site of demyelination. 1) Transverse Myelitis occurs when there is demyelination across both sides of one level or segment of the spinal cord. The onset may be sudden - developing over one to two hours, or more gradual – developing over one to two weeks. The symptoms depend on the area of involvement. Common symptoms include muscle weakness, abnormal sensations in the toes and feet, bowel and bladder incontenence. L'hermitte's sign, a symptom that is described as an electric shock like sensation down the shoulders and back and, less commonly down the anterior thighs, on flexion of the neck, is also associated with lesions at the top of the spinal cord. 2)Optic Neuritis is caused by demyelination of the optic nerve. It can occur suddenly or over a period of hours. It manifests as visual disturbances such as blurred vision or sight loss and pain behind the eyeball. Colour vision can also be severely effected. 3)A brainstem syndrome occurs when there is demyelination of nerves found in the brainstem. Symptoms include nausea, vomiting, vertigo, facial pain or numbness, dysarthria and diplopia, but symptoms will vary depending on the specific areas affected. Evidences suggest that people with clinically isolated syndrome have a less than 50% risk of developing MS within five years of experiencing their initial symptoms[1]. Studies suggest that optic neuritis is associated with a lower risk of developing MS and better long-term outcome than other types of clinically isolated syndromes[1]. Isolated sensory symptoms like numbness, tingling, or visual impairment, are thought to be associated with a lower risk of developing MS compared to the presence of symptoms suggestive of motor system involvement which are associated with a higher risk[1]. Presence of oligoclonal IgG bands in the cerebro spinal fluid(CSF) is currently the most widely used test for the confirmation of the diagnosis. More than 90 percent of cases will show oligoclonal bands in CSF of patients with MS[2]. According to Moulin and coworkers and others[2,3] presence of CSF for oligoclonal bands predicts chronic relapsing courseand requires long term therapy with interferons. Another marker for disease conversion is the presence of serum antibodies against myelin basic protein (MBP) and/or myelin

oligodendrocyte glycoprotein (MOG). Recent studies suggest that the presence of these antibodies in patients with CIS was associated with early disease conversion, whereas their absence suggest that patients would remain disease-free for several years[4]. Evidences suggest that initiating treatment early in the course of MS will become effective. Early initiation of disease modifying treatment(Interferons) after a clinically isolated syndrome delays the onset of MS5,[6,7,8]. In case of neuromyelitis Optica which is more often severe form of disease than clinically isolated syndrome. Neuromyelitis optica (NMO; Devic's disease) is an aggressive inflammatory disorder characterized by recurrent attacks of Optic Neuritis and myelitis[9]. NMO is more frequent in women than men (>3:1), typically begins in childhood or early adulthood but can arise at any age. Attacks of ON can be bilateral (rare in MS) or unilateral; myelitis can be severe and transverse (rare in MS) and is typically longitudinally extensive, involving three or more contiguous vertebral segments rather than MS which is focal. Presence of Anti NMO Antobodies(aquaporin4) in CSF is characteristic. Recurrence rate is higher and recurrence interval is shorter in Neuromyelitis Optica than Clinally Isolated syndrome. Acute attacks of NMO are usually treated with high-dose glucocorticoids (solumedrol 1 -2 g/d for 5-1 0 days followed by a prednisone taper). Plasma exchange has also been used empirically for acute episodes those who fail to respond to glucocorticoids. Prophylaxis against relapses is recommended for most patients using one of the following regimens: mycophenylate mofetil (250 mg bid gradually increasing to 1000 mg bid); B cell depletion with anti-CD20 monoclonal antibody (rituximab); or a combination of glucocorticoids (500 mg IV methylprednisolone daily for 5 days; then oral prednisone 1 mg/kg per day for 2 months,followed by slow taper) plus azathioprine (2 mg/kg per day started on week 3). Use of Interferon-ß is ineffective and may increase the risk of NMO relapses[9]. In case of Acute Disseminated Encephalomyelitis which is usually follows antecedent infection and immunization more common in children. The hallmark of ADEM is the presence of small foci of periventricular inflammation and demyelination in contrast to large demyelinating lesions typical of MS. Measles virus is the most common. Neurological symptoms include headache, meningismus and lethargy progressing to coma. Seizures are common. Corticosteroids given early in the course of the onset of neurologic symptoms may modify the severity of the disease. Plasma exchange and intravenous immune globulin have also been successful in fulminant cases[9].

CONCLUSION

Here we are reporting different cases of central nervous system demyelinating diseases with various manifestations. Likelyhood of developing clinically isolated syndromes into MS were discussed. The disease severity and the treatment response were explained in view of central nervous system demyelinating diseases. Since these demyelinating diseases are characterised by relapsing and remitting exacerbations, the petients will be followed up periodically to see if they progress or resolve.

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