A CASE OF RECURRENT DEMYELINATION
VIGNESH KUMAR
Department of Pediatrics, KILPAUK MEDICAL COLLEGE AND HOSPITAL

Abstract: Pediatric multiple sclerosis (MS) is a rare chronic demyelinating disorder involving the central nervous system, spinal cord and optic nerve. Multiple sclerosis in children is characterized by a slightly higher preponderance in males versus females and an onset after 6 years of age. Beyond 12 years of age, the male female ratio becomes 1:2. The disease process mainly targets normally formed white matter through an immune mediated mechanism. It is diagnosed when two de-myelinating episodes localize to distinct CNS regions and when the duration of each episode is greater than 24 hours and each episode is separated by an interval of greater than 30 days. High doses of methyl prednisolone are used to treat relapses. Disease modifying agents are used to reduce the frequency of relapses.

Keyword: Demyelinating disorder, MRI, High dose methyl prednisolone

12 year old Porselvi, a girl child, born of non consanguinous parentage, was brought by her mother on the 12th of May 2011 with the history of projectile vomiting, bi-frontal headache without photophobia for half an hour and one episode of left focal seizure which lasted for 10 minutes. She had been apparently normal until ten months ago, when she had been admitted with similar complaints for which she had been provisionally diagnosed to have an acute encephalopathy. Her CT brain showed a hypo-dense lesion in the left frontal lobe. MRI revealed focal altered signals in the left frontal lobe and her EEG showed epileptiform activity. She was discharged with anti-epileptic drugs and advised regular follow-up. On arrival into our hospital, she was oriented but drowsy. Her vitals were stable, and her anthropometric measurements were within normal limits. Her CNS examination was normal, there were no neuro-cutaneous markers, and she had no evidence of meningeal irritation. Other systemic examination was normal. Hematological parameters were normal except for decreased hemoglobin and normocytic, hypochromic anemia. Her blood sugar, renal function tests and liver function tests were normal. Mantoux was negative and ESR was normal. CSF analysis did not show any evidence of infection. A provisional diagnosis of acute encephalopathy was made and she was given supportive care. Since the MRI showed focal altered signals in the peri-ventricular region of the left frontal lobe, head of caudate nucleus, genu of corpus callosum and sub-cortical white matter, the MRI was repeated.

It showed new lesions in the white matter of the supra-tentorial region, bilateral medial thalamus and splenium of corpus callosum. Differential diagnosis of multiple sclerosis, relapsing acute disseminated encephalomyelitis and CNS vasculitis were also entertained.

On further work up, her ANA was weakly positive (1:100 dilution), pure tone audiogram was normal and CSF electrophoresis showed absence of the oligo-clonal band. Ophthalmological evaluation showed no evidence of optic neuritis. She was treated with IV Methyl Prednisolone [30mg/kg/day] for 5 days, followed by oral Prednisolone [1mg/kg/day] for 10 days along with anti-convulsants and iron supplements. She improved and was discharged with advise to come for regular follow-up.

Follow up MRI after 3 months showed well defined, long hyper intense lesion in the right superior frontal gyrus, right corona radiata,right superior temporal gyrus and right side of the pons. Serial MRI pictures of Porselvi

August 2010 May 2011

Focal altered signals noted in left frontal lobe involving the peri-ventricular region, head of caudate nucleus, genu of corpus callosum and sub-cortical white matter

New whitematter lesion in the supratentorial region, bilateral medial thalamus, splenium of the corpus callosum

An Initiative of The Tamil Nadu Dr. M.G.R. Medical University
University Journal of Medicine and Medical Specialties
**Discussion:** Multiple Sclerosis (MS) is a chronic, remitting-relapsing disorder with multiple white matter lesions in the CNS, separated by time and location in the brain. MS also known as “disseminated sclerosis” or “encephalomyelitis disseminata”, is an inflammatory disease in which the fatty myelin sheaths around the axons of the brain and spinal cord are damaged, leading to demyelination and scarring. Disease usually occurs in young adults, and is more common in women. It has a prevalence that ranges between 2 and 150 per 100,000.[2] MS was first described in 1868 by Jean-Martin Charcot. In MS, the body’s own immune system attacks and damages the myelin. When myelin is lost, the axons can no longer effectively conduct signals. MS takes several forms, with new symptoms occurring either in discrete attacks (relapsing forms) or slowly accumulating over time (progressive forms). Between attacks, symptoms may go away completely, but permanent neurological problems often occur, especially as the disease advances. CAUSES: MS is believed to be an immune-mediated disorder mediated by a complex interaction of the individual’s genetics and environmental insults. Damage is believed to be caused by the person’s own immune system attacking the nervous system.

**GENETICS:**

The risk of acquiring MS is higher in relatives of a person with the disease than in the general population. The disease has an overall familial recurrence rate of 20%. The group of genes in chromosome 6 that serves as the major histo-compatibility complex (MHC) in human increases the probability of MS. The most consistent finding is the association between multiple sclerosis and alleles of the MHC defined as DR15 and DQ6.[3]

**ENVIRONMENTAL FACTORS:**

MS is believed to be more common in people who live in temperate regions, who have vitamin D deficiency, and who have reduced exposure to sunlight exposure. Smoking is also a risk factor.[4],[5] [6]

**INFECTIONS:**

Viral infections that have been attributed to causing MS are herpes, Epstein-barr virus, Measles, Mumps and Rubella.[7]

**PATHOPHYSIOLOGY:**

MS is a dys-regulation of the T and B lymphocytes resulting in inflammation, axonal de-myelination, axonal loss, and regeneration within the white and grey matter.

**Lesions:**

MS destroys oligodendrocytes, the cells responsible for creating and maintaining a fatty layer viz myelin sheath. The latter helps the neurons to carry electrical signals (action potentials). When myelin is lost, the neuron can no longer effectively conduct electrical signals. A repair process, called re-myelination, takes place in the early phases of the disease. However, the oligodendrocytes cannot completely rebuild the cell’s myelin sheath. Repeated attacks lead to successively fewer effective re-myelination, until a scar-like plaque is built up around the damaged axons.

**Inflammation:**

Apart from demyelination, the other pathologic hallmark of the disease is inflammation. The inflammatory process is caused by T cells that gain entry into the brain via disruptions in the blood–brain barrier.

The T cells recognize myelin as foreign and attack it as if it were an invading virus. This triggers inflammatory processes, stimulating other immune cells and soluble factors like cytokines and antibodies. Further leakage occurs in the blood–brain barrier, which in turn causes a number of other damaging effects such as swelling, activation of macrophages, and more activation of cytokines and other destructive proteins. Blood–brain barrier breakdown:

**Clinical manifestations:**

Neurological symptoms include sensory loss, paresthesia, muscle weakness in the form of hemiparesis or paraparesis, ataxia, vertigo, dysarthria, dysphagia, optic neuritis and cognitive impairment.

**DIAGNOSIS:**

Multiple sclerosis can be difficult to diagnose since its signs and symptoms may be similar to other medical problems. Historically, the Schumacher and Poser criteria has been popular. McDonald criteria focuses on clinical, laboratory, radiologic data of the dissemination of MS lesions in time and space. Clinical data alone is not sufficient for a diagnosis of MS. MRI of the brain may exhibit discrete T2 lesion in the cerebral white matter, periventricular regions, brainstem, cerebellum, and juxta-cortical and deep grey matter. MRI of the spine shows partial width cord lesion restricted to 1-2 spin e segments. CSF may be normal or exhibit mild pleocytosis. Oligoclonal bands demonstrated in the electrophoresis of the CSF sample, increases the likelihood of MS. However, it may be negative in 10-60% of paediatric MS patients.[14]

**PROGRESSION OF MS SUB-TYPES:**

Several subtypes, or patterns of progression, have been described:

1. Relapsing remitting,
2. Secondary progressive,
3. Primary progressive,
4. Progressive relapsing.

**MANAGEMENT:**

Although there is no known cure for multiple sclerosis, several therapies have proven helpful.

**Acute attacks**

Symptomatic attacks are treated with Methylprednisolone (30 mg/kg/day) for 5 days. Subsequently it is tapered. [1]

**Disease modifying agents:**

Disease modifying agents that are approved by the FDA are interferon beta-1a, interferon beta-1b, glatiramer acetate, mitoxantrone, natalizumab, fingolimod and teriflunomide. No treatment has been proven to modify the course of primary progressive MS.[15],[16] Treatment of progressive MS is more difficult than relapsing-remitting MS. Mitoxantrone has shown positive effects in those with secondary progressive and progressive relapsing courses. It is moderately effective in reducing the progression of the disease and the frequency of relapses in short-term follow-up.[17]

**PROGNOSIS:**

Female gender, relapsing-remitting subtype, optic neuritis or sensory symptoms at onset, few attacks in the initial years and especially early age at onset, are associated with a better course.

---

September 2011

Well defined long hyper intense lesions in right superior frontal gyrus right corona radiata, right superior temporal gyrus and right side of the Pons

**Lesions:**

The periventricular regions in both hemispheres show hyperintense lesions, in the left and right parietal perisylvian, and right temporal regions.

**CNS Lesions:**

The T2 axial MRI of the brain shows hyperintense lesions in the right parietal and left frontal regions. The right parietal lesion is surrounded by a hypointense ring.

**MRI of the Brain Stem:**

In the T2 sagittal MRI of the brain stem, multiple hyperintense lesions are seen, predominantly in the right side.

**Diagnosis of Multiple Sclerosis:**

The diagnosis of multiple sclerosis is based on the clinical history, physical examination, and neuroimaging studies. MRI of the brain and spinal cord are damaged, leading to demyelination and scarring.

**DISCUSSION:**

Multiple sclerosis is a chronic, remitting-relapsing disorder with multiple white matter lesions in the CNS, separated by time and location in the brain. MS is a dys-regulation of the T and B lymphocytes resulting in inflammation, axonal de-myelination, axonal loss, and regeneration within the white and grey matter. MS is believed to be more common in people who live in temperate regions, who have vitamin D deficiency, and who have reduced exposure to sunlight exposure. Smoking is also a risk factor.

**GENETICS:**

The risk of acquiring MS is higher in relatives of a person with the disease than in the general population. The disease has an overall familial recurrence rate of 20%. The group of genes in chromosome 6 that serves as the major histo-compatibility complex (MHC) in human increases the probability of MS. The most consistent finding is the association between multiple sclerosis and alleles of the MHC defined as DR15 and DQ6.

**ENVIRONMENTAL FACTORS:**

MS is believed to be more common in people who live in temperate regions, who have vitamin D deficiency, and who have reduced exposure to sunlight exposure. Smoking is also a risk factor.

**INFECTIONS:**

Viral infections that have been attributed to causing MS are herpes, Epstein-barr virus, Measles, Mumps and Rubella.

**PATHOPHYSIOLOGY:**

MS is a dys-regulation of the T and B lymphocytes resulting in inflammation, axonal de-myelination, axonal loss, and regeneration within the white and grey matter.

**Lesions:**

MS destroys oligodendrocytes, the cells responsible for creating and maintaining a fatty layer viz myelin sheath. The latter helps the neurons to carry electrical signals (action potentials). When myelin is lost, the neuron can no longer effectively conduct electrical signals. A repair process, called re-myelination, takes place in the early phases of the disease. However, the oligodendrocytes cannot completely rebuild the cell’s myelin sheath. Repeated attacks lead to successively fewer effective re-myelination, until a scar-like plaque is built up around the damaged axons.

**Inflammation:**

Apart from demyelination, the other pathologic hallmark of the disease is inflammation. The inflammatory process is caused by T cells that gain entry into the brain via disruptions in the blood–brain barrier.

The T cells recognize myelin as foreign and attack it as if it were an invading virus. This triggers inflammatory processes, stimulating other immune cells and soluble factors like cytokines and antibodies. Further leakage occurs in the blood–brain barrier, which in turn causes a number of other damaging effects such as swelling, activation of macrophages, and more activation of cytokines and other destructive proteins. Blood–brain barrier breakdown:

**Clinical manifestations:**

Neurological symptoms include sensory loss, paresthesia, muscle weakness in the form of hemiparesis or paraparesis, ataxia, vertigo, dysarthria, dysphagia, optic neuritis and cognitive impairment.

**DIAGNOSIS:**

Multiple sclerosis can be difficult to diagnose since its signs and symptoms may be similar to other medical problems. Historically, the Schumacher and Poser criteria has been popular. McDonald criteria focuses on clinical, laboratory, radiologic data of the dissemination of MS lesions in time and space. Clinical data alone is not sufficient for a diagnosis of MS. MRI of the brain may exhibit discrete T2 lesion in the cerebral white matter, periventricular regions, brainstem, cerebellum, and juxta-cortical and deep grey matter. MRI of the spine shows partial width cord lesion restricted to 1-2 spine segments. CSF may be normal or exhibit mild pleocytosis. Oligoclonal bands demonstrated in the electrophoresis of the CSF sample, increases the likelihood of MS. However, it may be negative in 10-60% of paediatric MS patients.

**PROGRESSION OF MS SUB-TYPES:**

Several subtypes, or patterns of progression, have been described:

1. Relapsing remitting,
2. Secondary progressive,
3. Primary progressive,
4. Progressive relapsing.

**MANAGEMENT:**

Although there is no known cure for multiple sclerosis, several therapies have proven helpful.

**Acute attacks**

Symptomatic attacks are treated with Methylprednisolone (30 mg/kg/day) for 5 days. Subsequently it is tapered.

**Disease modifying agents:**

Disease modifying agents that are approved by the FDA are interferon beta-1a, interferon beta-1b, glatiramer acetate, mitoxantrone, natalizumab, fingolimod and teriflunomide. No treatment has been proven to modify the course of primary progressive MS. Treatment of progressive MS is more difficult than relapsing-remitting MS. Mitoxantrone has shown positive effects in those with secondary progressive and progressive relapsing courses. It is moderately effective in reducing the progression of the disease and the frequency of relapses in short-term follow-up.

**PROGNOSIS:**

Female gender, relapsing-remitting subtype, optic neuritis or sensory symptoms at onset, few attacks in the initial years and especially early age at onset, are associated with a better course.

---

An Initiative of The Tamil Nadu Dr. M.G.R. Medical University
University Journal of Medicine and Medical Specialities
The life expectancy of people with MS is 5 to 10 years lower than that of unaffected people.

Conclusions

Ø Symptoms of Multiple Sclerosis can involve almost any neurologic function. Diagnostic evaluation should include a thorough history, neurologic examination, MRI and CSF analysis.
Ø Therapy can decrease inflammation and progression of disability.
Ø Early diagnosis regular follow-up and treatment are of key to effective disease control since treatment is difficult if the patient has progressed into the later stages of MS.

REFERENCES: