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CENTRAL MYELIN AND DEMYELINATION

Neurology

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ABSTRACT

INTRODUCTION:CNS demyelinating disorders are common neurological illness that affects the brain. This causes significant disability and mortality if not properly identified and treated. CNS demyelinating diseases includes multiple sclerosis, acute disseminated encephalomyelitis, NMO spectrum disorders and transverse myelits. Here we are reporting a case of central demyelination.

CASE SUMMARY: 44yrs female admitted with subacute onset of weakness of all four limbs, more on left side and sensory disturbance in the form of numbness and tingling in all four limbs, more on left side, associated with urinary urgency and constipation. Patient had right optic neuritis 3 years back. General examination was normal. Vital signs were stable.

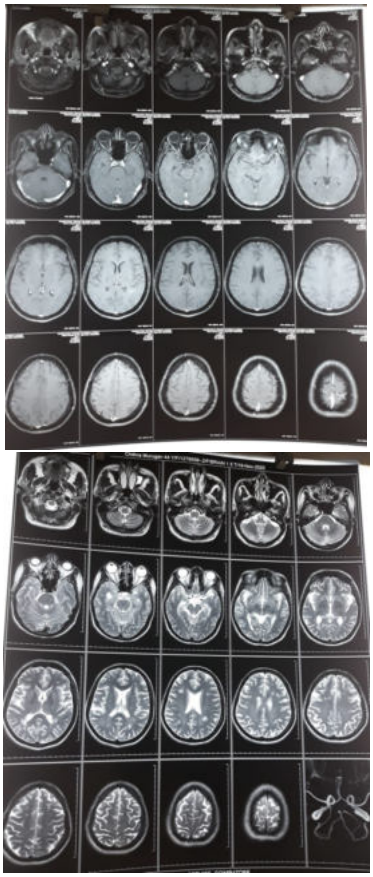
On nervous system examination, patient had decresed visual acuity in right eye, with relative afferent pupillary defect and impaired red green colour vision, fundus was normal. Motor system examination, Patient had normal bulk, increased tone, brisk deep tendon reflexes, power of 4 on right and 4- on left side with extensor planter on both sides. Patient had decresed sensation below C5 spinal cord level, predominantly joint position and vibration sense with positive lhermitte's sign. Other systems were normal. Routine lab investigation ,ECG,CXR were normal. CSF analysis revealed elevated protein of 72mg.

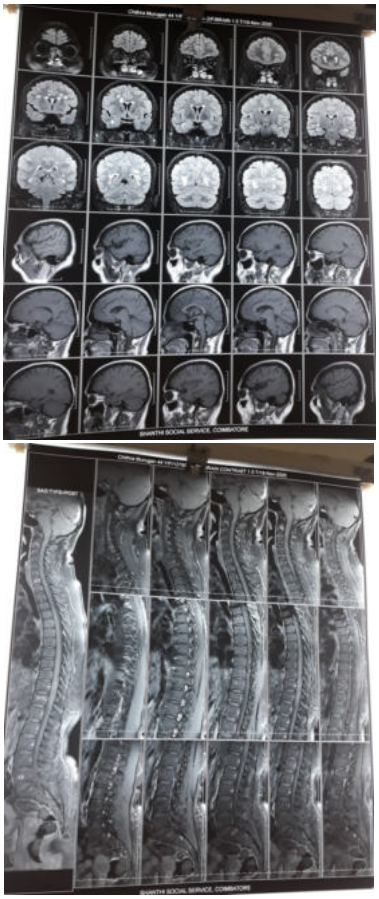
MRI BRAIN WITH WHOLE SPINE SCREENING(contrast) revealed Multiple smallT2/FLAIR hyperintense lesion in bilateral juxta cortical, subcortical(involving the temporal lobes and callososeptal interface), subtle patchy enhancement in the left peritrigonal lesion and in body of corpus callosum. Mild atrophy of cervical cord from C3 to C5 with T2 hyperintense involving both hemicord from C2 to C5 level, focal Hyperintensity subtle contrast enhancement in Dorsal cord at the level of D11, Features suggestive of demyelination likely Multiple Sclerosis.

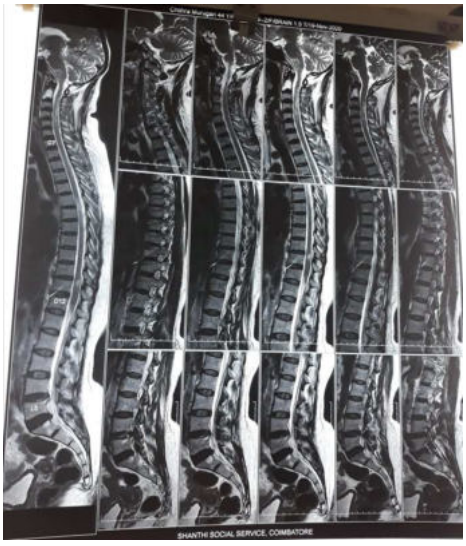
KEYWORDS

Central myelin, Demyelination, Multiple Sclerosis.

NEUROIMAGING – MULTIPLE SCLEROSIS







DISCUSSION

Myelin is a word coined by Rudolph Virchow in 1854. Myelin is a lipid rich substance present around the axons and helps to conduct the action potential along the axon. Myelin is formed in the central nervous system by the oligodendrocyte and in the peripheral nervous system by schwann cells. Each myelin sheath is formed by concentric wrapping of the oligodendrocyte or schwann cell. Myelin helps in saltatory conduction in which the action potential jumps from one node of Ranvier to another until it reaches the axon. The insulating role of myelin is essential for normal motor function, sensory function and cognition.(1,2)

Myelination is most important process which helps in neuronal interaction during brain development differentiating oligodendrocyte and axon. Oligodendrocyte plasticity and myelin remodelling is the major step in the repair of demyelination.(1,2)

White matter of the brain is made up of myelinated axons also called as tracts. White matter affects learning and brain functions through modulating the distribution of action potential and acts as a coordinating communication between different brain regions.(3)

Demyelinating disease is any disease of nervous system in which the myelin sheath of the neurons is getting damaged results in the impaired conduction of signals in the affected nerves. This impairment in the conduction results in deficiency in sensory, motor, cognition and other functions in the brain. Demyelinating disease can be caused by genetics, microbiome, autoimmune disease and other unknown factors.(4)

CENTRAL DEMYELINATING DISORDERS

MULTIPLE SCLEROSIS

Multiple Sclerosis was first described my Jean-martin Charcot in 1868. The name multiple sclerosis means numerous glial scars which developes on the white matter of the brain and spinal cord.

The name multiple sclerosis refers to the scars (sclerae – better known as plaques or lesions) that form in the nervous system. These lesions most commonly affect the white matter in the optic nerve, brain stem, basal ganglia, and spinal cord, or white matter tracts close to the lateral ventricles. The function of white matter cells is to carry signals between grey matter areas, where the processing is done, and the rest of the body. The peripheral nervous system is rarely involved.

Multiple Sclerosis also known as encephalomyelitis disseminate is a demyelination disease of central myelin. Damage to central myelin results in impaired motor ,sensory, cognitive and psychiatric functions. The common symptoms include double vision, diminished vision, muscle weakness, sensory disturbance and incoordination.

The condition begins in 85% of cases as a clinically isolated syndrome (CIS) over a number of days with 45% having motor or sensory problems, 20% having optic neuritis, and 10% having symptoms related to brainstem dysfunction, while the remaining 25% have more than one of the previous difficulties. The course of symptoms occurs in two main patterns initially: either as episodes of sudden worsening that last a few days to months (called relapses, exacerbations, bouts, attacks, or flare-ups) followed by improvement (85% of cases) or as a gradual worsening over time without periods of recovery (10–15% of cases). A combination of these two patterns may also occur or people may start in a relapsing and remitting course that then becomes progressive later on.

Relapses are usually not predictable, occurring without warning. Exacerbations rarely occur more frequently than twice per year. Some relapses, however, are preceded by common triggers and they occur more frequently during spring and summer. Similarly, viral infections such as the common cold, influenza, or gastroenteritis increase their risk. Stress may also trigger an attack. Women with MS who become pregnant experience fewer relapses; however, during the first months after delivery the risk increases. Overall, pregnancy does not seem to influence long-term disability. Many events have been found not to affect relapse rates including vaccination, breast feeding, physical trauma, and Uhthoff's phenomenon.

Multiple sclerosis is typically diagnosed based on the presenting signs and symptoms, in combination with supporting medical imaging and laboratory testing. It can be difficult to confirm, especially early on, since the signs and symptoms may be similar to those of other medical problems. The McDonald criteria, which focus on clinical, laboratory, and radiologic evidence of lesions at different times and in different areas, is the most commonly used method of diagnosis with the Schumacher and Poser criteria being of mostly historical significance.

Types:

1. Clinically isolated syndrome (CIS)
2. Relapsing-remitting MS (RRMS)
3. Primary progressive MS (PPMS)
4. Secondary progressive MS (SPMS)

Variants

Atypical variants of MS have been described; these include tumefactive multiple sclerosis, Balo concentric sclerosis, Schilder's diffuse sclerosis, and Marburg multiple sclerosis. There is debate on whether they are MS variants or different diseases. Some diseases previously considered MS variants like Devic's disease are now considered outside the MS spectrum.

Acute attacks

During symptomatic attacks, administration of high doses of intravenous corticosteroids, such as methylprednisolone, is the usual therapy, with oral corticosteroids seeming to have a similar efficacy and safety profile. Although effective in the short term for relieving symptoms, corticosteroid treatments do not appear to have a significant impact on long-term recovery. The long term benefit is unclear in optic neuritis as of 2020. The consequences of severe attacks that do not respond to corticosteroids might be treatable by plasmapheresis.

Disease-modifying treatments

Relapsing remitting multiple sclerosis

As of 2020, multiple disease-modifying medications are approved by regulatory agencies for relapsing-remitting multiple sclerosis (RRMS). They are interferon beta-1a, interferon beta-1b, glatiramer acetate, mitoxantrone, natalizumab, fingolimod, teriflunomide, dimethyl fumarate, alemtuzumab, ocrelizumab, siponimod, cladribine, and ozanimod.(5,11)

NMO SPECTRUM DISORDERS

Neuromyelitis optica (NMO) is an etiologically heterogeneous syndrome characterized by acute inflammation of the optic nerve (optic neuritis, ON) and the spinal cord (myelitis). ON and myelitis can occur either simultaneously or successively and a relapsing disease course is common, especially in untreated patients. In more than 80% of cases, NMO is caused by immunoglobulin G autoantibodies to aquaporin 4 (anti-AQP4), the most abundant water channel protein in the central nervous system. A subset of anti-AQP4-negative cases is associated with antibodies to myelin oligodendrocyte glycoprotein (anti-MOG). Rarely, NMO may occur in the context of other autoimmune diseases (e.g. connective tissue disorders, paraneoplastic syndromes) or infectious diseases. In some cases, the etiology remains unknown (idiopathic NMO).

The main symptoms of NMO are temporary or, especially if not treated

in time, permanent loss of vision and spinal cord function. Optic neuritis may lead to varying degrees as visual impairment with decreased visual acuity, although visual field defects, or loss of color vision may occur in isolation or prior to formal loss of visual acuity. Spinal cord dysfunction can lead to muscle weakness, reduced sensation, or loss of bladder and bowel control as well as erectile dysfunction. Other symptoms typically associated NMOSD include respiratory insufficiency due to lesions in the brainstem or upper cervical spinal cord, vomiting or hiccups caused by lesions in area postrema of the medulla oblongata, and pain as well as tonic spasms. Additional brain lesions are common but often asymptomatic (though cognitive deficits as well as depression may be underdiagnosed sequalae); lesions may also affect the diencephalon (mostly in anti-AQP4-positive NMO).(6)

ACUTE DEMYELINATING ENCEPHALOMYELITIS

Acute disseminated encephalomyelitis (ADEM),or acute demyelinating encephalomyelitis is a rare autoimmune disease marked by a sudden, widespread attack of inflammation in the brain and spinal cord. ADEM attacks the nerves of the central nervous system and damages their myelin insulation, which as a result, destroys the white matter. It is often triggered by a viral infection or (very rarely) non specific vaccinations. ADEM is one of the possible cause of anti-MOG associated encephalomyelitis.

The possible theories are,

- Viral infections include influenza virus, dengue, retrovirus, measles, mumps, rubella, varicella zoster, Epstein Barr virus, cytomegalovirus, herpes simplex virus, hepatitis A, Cossacks virus and COVID 19. Bacterial infections include Mycoplasma pneumoniae, Cordelia burgdoferi, leptospira and beta hemolytic streptococci.
- Exposure to Vaccines: The only vaccine proven related to ARE is the Sample form of the rabies vaccine, but hepatitis B, pertussis, diphtheria, measles, mumps, rubella, pneumococcus, varicella, influenza, Japanese encephalitis, and polio vaccines have all been implicated.
- In rare cases, ADEM seems to follow from organ transplantation.

It affects about 8 per 1,000,000 people per year. Although it occurs in all ages, most reported cases are in children and adolescent, with average age around 5 to 8 years old. The disease affects males and females almost equally. ADAM shows seasonal variation with higher incidence in winter and spring months which may coincide with higher viral infections during these months. The mortality rate may be as high as 5%, however full recovery is seen in 50 to 75% of the cases with increase survival rates up to 70 to 90% with figures including minor residual disability. The average time to recover from ADEM flare-ups is one to six months.

ADEM produces multiple inflammatory lesions in the brain and spinal cord, particularly in the white matter. Usually these are found in the subcortical and central white matter and cortical gray-white junction of both cerebral hemisphere, cerebellum, brainstem, and spinal cord, but periventricular white matter and gray matter of the cortex, thalamic and basal ganglia may also be involved. When a person has more than one demyelinating episode of ADEM, the disease is called recurrent disseminated encephalomyelitis or multiphasic disseminated encephalomyelitis.

ADEM has an abrupt onset and a monophasic course. Symptoms usually begin 1-3 weeks after infection. Major symptoms include fever, headache, nausea and vomiting, confusion, vision impairment, drowsiness, seizures and coma. Although initially the symptoms are usually mild, they worsen rapidly over the course of hours to days, with average time to maximum severity being about four and half days. Additional symptoms include hemiparesis, paraparesis and cranial nerve palsies.(8,9)

TRANSVERSE MYELITIS

Transverse myelits is a rare neurological condition in which the spinal cord is inflamed. Transverse implies that the inflammation extends horizontally across the spinal cord. Partial transverse myelits are termed sometimes used to specify inflammation that only affects part of the width of the spinal cord. TM is characterised by weakness and numbness of the limbs, deficits in sensation and motor skills, dysfunctional urethral anal sphincter activities and dysfunction of the autonomic nervous system that can lead to episode of high blood pressure. Signs and symptoms vary according to the affected level of the spinal cord. The underlying cause of TM is unknown. The spinal cord inflammation seen in TM has been associated with various infections, immune system disorders or damage to nerve fibres by loss of myelin. As opposed to leukomyelitis which affects only the white matter, it affects the entire cross-section of the spinal cord.(10)

This patient sensorium was normal. Since the patient was illiterate complete cognition examination was not done. She was oriented to the environment. She had upper motor neuron type of weakness of all four limbs with sensory distrbance below cervical region with disturbed bladder and bowel function, she gave past history of visual disturbance in right eye, possibility of optic spinal myelits. CSF protein was elevated suggestive of neuroinflammation. On MRI imaging patient had neuritis plaques in juxtacortical, subcortical, corpus callosum, cervical cord and dorsal cord.

Since this patient had normal sensorium, relapsing course, past history of optic neuritis ADEM was excluded. Since this patient had juxta cortical, subcortical, neuritis plaques and anti aquaporin 4 negative state, NMO spectrum disorder was excluded. In the presence of features of neuro demyelination with neuritis plaques in juxtacortical, subcortical, corpus callosum, cervical cord and dorsal cord with clinical manifestation of upper motor neuron type of quadriparesis with optic neuritis possibility of multiple sclerosis is considered. Patient was treated with intravenous Methylprednisolone followed by oral steroids. Patient showed improvement and has been kept on Interferon therapy to prevent relapses.(5,7,11)

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