Multiple Sclerosis

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Objectives:

- **Not given yet**

References:
Slides - Black
Doctor's notes - Red
Step up / davidson - Blue
Extra explanation - Grey

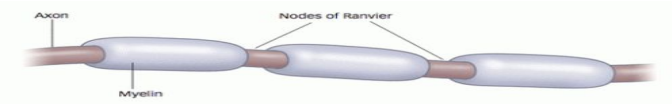
Optional:

11:5 min

Editing file

Introduction:

Mylien is A lipid dense layer that surrounds the axon of the neuron. Insulates the axon and allows continuous propagation of the electrical impulse.
Schwann cells produce the myelin sheath in peripheral nervous system (PNS) neurons. while Oligodendrocytes in central nervous system (CNS).



1-Multiple sclerosis

Defanation

Chronic autoimmune disorder of CNS (brain and spinal cord) white matter resulting multifocal demyelination of axons (plaques) and sometimes damage of axons

Epidemiology:

- **Peak age 15 to 45 (mainly between 20-30s)**
- **More common Female than male and more**
- **More common in 1st degree relive and monozygotic twins**
- **More Common in north america and Europe , rare in tropical country .**
- **More common in people who born and his / her mother had vit-D deficiency .**

The pathological **hallmark of MS** is **FOCAL DEMYELINATED PLAQUES**

Note: MS more common North America and Europe due lack of sunlights which will result Vit-D deficiency in .

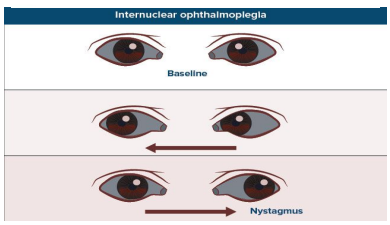
Pathophysiology

Multi Environmental factors (Lack of exposure to sunlight + Vit-D deficiency + Epstein-Bar virus (EBV) + smoking + obesity in children) + Genetic factors (HLA-DR 2 typing, interleukin receptors 2 & 7, CLEC16A (C-type lectin domain family 16 member A) and CD226 genes)→ T lymphocyte + B cell produce Antibody to attack CNS myelin sheath

- **EBV has molecular mimicry of CNS myelin antigen → proinflammatory cytokines (interferon) → T cell and b cell Activated**
- **Obesity → Leptin increases the proliferation of auto-aggressive cells responsible for myelin damage.**

Clinical features:

Relapsing and remission of neurological symptoms. Based on site of demyelination:



1- optic nerve → optic neuritis that characterized by (look to image)
A- monoclour visual loss (eg: blurred vision, reduced perception to red color)
B- pain on movement of eye
C-Black spot in center (central scotoma)
D- decreased pupillary reaction to light

2-Medial longitudinal fasciculus → internuclear ophthalmoplegia characterized by
A-Addiction defect
B- Horizontal nystagmus
C- Diplopia

3-Cerebellum → Ataxia , slurred speech (زي اللي شارب خمر) , intention tremor . oscillopsia

4-Brainstem → diplopia , vertigo , dysphagia and nystagmus

Cognitive function loss (eg:Memory) is a late sign of the disease

5- spinal cord (spinothalamic and posterior columns) → numbness , pins and needle

6-pyramidal tract (upper motor neuron) → spasticity , weakness , paraparesis, hemiparesis , quadriparesis and loss control of bladder

7- Autonomic nervous system → constipation and impotence

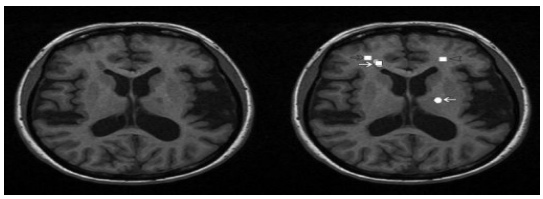
8- cerebrum → memory loss , personality change , emotional lability , anxiety and depression

9-Neuropathic Pain: due to hyperesthesia and trigeminal neuralgia

10- Lhermitte's sign: flexion of neck causes electric shock sensation down back into limbs indicating cervical cord lesion.
11- Uhthoff's phenomenon: neurological dysfunction, stereotyped(same attacks), Less than 24 h, reversible and related to fluctuations in axonal conduction properties due to increasing body temperature "worsening of symptoms (classically optic neuritis) in heat".
12-Transverse myelitis: a general term for spinal cord inflammation.

Course

- **Clinically silent** : known as benign or stable
- **Relapsing/remitting** (most common): exacerbations followed by remissions
- **Secondary progressive:** gradual worsening of symptoms after a long duration of relapsing/remitting
- **Primary progressive :** steady progressive disease that appears later in life (after 40 yrs of age) + tends to have less visual and motor axonal involvement.



Investigation

1- MRI of brain and spinal cord : shows plaques especially in periventricular area and brainstem (see the difference between right and left one)
2- Lumbar puncture and CSF Gel electrophoresis → oligoclonal igG bands
3- Electrophysiological test (Evoked potential test) of visual ,auditory and somatosensory

1-MRI is best initial and the most accurate test
2- CT scan can't shows plaques
3- oligoclonal igG bands not specific for MS patient , but ti present in 95% of cases .

How to diagnose

26.53 The Macdonald criteria for the diagnosis of multiple sclerosis (2011)[1]

Clinical presentation[2]	Additional evidence required for diagnosis of MS
Two or more attacks with either Objective clinical evidence of at least 2 lesions *or* Objective clinical evidence of 1 attack with reasonable evidence (on clinical history) of at least 1 prior attack	None
Two or more attacks with objective clinical evidence of 1 lesion	Dissemination in 'space' demonstrated by MRI ≥ 1 lesion in at least 2 of the MS-typical regions[3] (multiple lesions in different sites) *or* Await further clinical attack at different anatomical site
One attack with objective clinical evidence of ≥ 2 lesions	Dissemination in 'time' demonstrated by Evolving MRI showing combined enhancing (new) and non-enhancing (old) lesions *or* New T2 or enhancing lesion on repeat MRI *or* Await further (second) clinical attack at different anatomical site
One attack with clinical evidence of only 1 lesion (clinically isolated syndrome)	Dissemination in 'space' demonstrated by ≥ 1 T2 lesion in at least 2 MS-typical regions *or* Dissemination in 'time', demonstrated by simultaneous enhancing and non-enhancing lesions *or* New T2 or enhancing lesions on repeat MRI *or* Await further (second) clinical attack
Insidious neurological progression suggestive	1 yr of progression plus 2 of the following:

Mangement

- **Acute Exacerbation** → High dose steroids
  - If not respond (rare) → Plasma exchange
- **drugs prevent the relapse and progression (Disease modifying treatment):**

❑ Glatiramer
❑ Beta interferon
❑ Fingolimod
❑ Fumarate
❑ Teriflunomide
❑ Laquinimod
❑ Cladribine
❑ Mitoxantrone and Natalizumab are for aggressive MS

- **Symptomatic therapy :**

❑ Belafonte or dantrolene for muscle spasticity
❑ carbamazepine or gabapentin
❑ Treat depression

MS Relapse or Attack

- Typical of CNS acute inflammatory demyelinating lesion
- Lasting **at least 24 hours**
- NOT associated with fever(as Uhthoff's phenomena) OR infection

2- Neuromyelitis optica (Devic's disease)

General Features

More common in females (9:1) and in **Asian and African** population. Mean age is 10 years
Affects mainly the optic nerve and the spinal cord. and it ‘s More severe attacks than in MS.

Pathology:

A- Astrocytopathy.
B- Targets aquaporin 4 (a water channel) rich areas.
C- Vasculocentric deposition of immunoglobulin and complement.

Neuromyelitis optica
Neuromyelitis = spinal cord inflammation
+
optica = optic nerve inflammation
So, it loves to attack spinal cord & optic nerve. And rarely the brain

Treatment:

Acute relapses: → steroids or plasma exchange.
Relapses prevention: chronic immunosuppression with azathioprine, mycophenolate mefetil, cyclophosphamide.

MS treatment may worsen NMO

3-Acute disseminated encephalomyelitis

General Features

CNS inflammatory demyelination disease. Usually a monophasic illness (no relapses).
Frequently preceded by **vaccination** or **infection**. More common in children. Usually **a monophasic illness** (no relapses).

Pathology

Widespread white and grey matter perivenous –around veins– “sleeves” of inflammation and demyelination.(Axons are rarely spared)

Symptoms

Encephalopathy (lethargy, stupor and coma).
Multifocal neurological deficit (visual symptoms, ataxia, TM)May fluctuate over a 3 months period.

Treatment

Steroids, plasma exchange and IV immunoglobulins.

MS vs NMO

Differentiating between Devic's disease and multiple sclerosis		
	Devic's disease	Multiple sclerosis
Distribution of symptoms and signs	Restricted to the optic nerves and spinal cord	Any white-matter track
Attack severity	Usually severe	Usually mild
Head MRI	Usually normal/non-specific changes	Multiple periventricular white-matter lesions
Cord MRI	Longitudinally extensive central necrotic lesions	Multiple small peripheral lesions
CSF cells	Pleocytosis during attacks	Rarely > 25 white cells
Oligoclonal bands	Usually absent	Usually present
Permanent disability	Usually attack-related	Usually in late progressive phase
Female patients	80 – 90%	60-70%
Coexisting autoimmunity	Frequent (30-40%)	Less common
Serum neuromyelitus optica antibody	Present	Absent
Modified from Weinshenket et al		

MS vs ADEM

Features	ADEM	MS
Antecedent events	**Infections or vaccination**	**No recognize antecedent infections or vaccinations**
Clinical characteristics	**Meningism. stupor, focal signs**	**Focal signs**
Course	**No progressive monophasic**	**Relapsing and remitting or progressive**
Recovery	**Recovery is rapid and often complete**	**Trcovery variable, may be rapid and complete**

MCQ's

Q1: A 23-year-old woman complains that her right leg has become progressively stiff and clumsy over the last couple of weeks. She is worried as she has not been able to go to work for the last 4 days. On examination, tone is increased and there is a catch at the knee. She has six beats of clonus and an upgoing plantar. Power is reduced to 3-4/5 in the right leg flexors. There is no sensory involvement and the rest of the neurological exam is normal other than a pale disc on ophthalmoscopy. On further questioning, she admits that she has had two episodes of blurred vision in her right eye in the last two years. Each lasted a couple of weeks from which she fully recovered. What is the most appropriate initial treatment?
A. A non-steroidal anti-inflammatory drug (NSAID)
B. Interferon-beta
C. Bed rest
D. Methotrexate
E. A course of oral steroids

Q2: A 34-year-old female flight attendant presents with a recurring, sharp pain radiating from her left ear to her mouth. She describes the pain as intense but intermittent, precipitated by cold, light touch, and chewing. Neurologic examination is normal. A tentative diagnosis of trigeminal neuralgia is made, and carbamazepine is prescribed. She returns 6 weeks later complaining of the same pain on both sides of her face and a new onset of urinary incontinence, which of the following is the most likely diagnosis?
(A) Acoustic neuroma
(B) Amyotrophic lateral sclerosis
(C) Bell palsy
(D) Multiple sclerosis
(E) Myasthenia gravis

Q3: A 32-year-old woman is referred to a neurologist for evaluation of unsteady gait and numbness in the right foot. Examination reveals weakness of the right lower extremity with muscle spasticity and decreased vibratory sensation. MRI studies show cerebral and spinal cord changes suspicious for demyelinating lesions. A lumbar puncture is performed for examination of CSF. Which of the following CSF findings would be most consistent with a diagnosis of demyelinating disorder?
(A) Elevated protein with marked lymphocytosis
(B) Elevated protein with normal cell count
(c) Marked neutrophilic leukocytosis with reduced glucose
(D) Mildly increased protein with oligoclonal IgG bands
(E) Normal protein with mild lymphocytosis

Answers: 1.E, 2.D, 3.D

Thank you

If you have any question please contact with us at:
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