Chapter 15: An Overview of Multiple Sclerosis (MS) and Neuropsychiatric Disorders

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Introduction

- MS is the most common demyelinating disorder. It is more common in females, with a peak age of onset around 35 years.
- The cause in unknown but is thought to be a cell mediated immune response against myelin components within the CNS signified by auto-reactive lymphocytes which leads to an inflammatory cascade with microglial activation resulting, eventually, in chronic neurodegeneration
- Patients rarely present at the occurrence of the first lesion (plaque) and at the time of presentation there are often already multiple, asymptomatic plaques present.
- Episodes (flares) usually lasts days-weeks but must be at least 24 hours
- The inflammatory lesions are disseminated in space and time (there are multiple lesions in different parts of the CNS and lesions occur at different times)
- It is associated with marked disability due to the chronicity of the disease

Pathophysiology

- MS is marked by focal, demyelinated plaques in the CNS accompanied by varying degrees of inflammation and gliosis.
- Lesions are typically found in: the optic nerve (optic neuritis), spinal cord (UMN and sensory symptoms), brainstem (cranial neuropathies, ophthalmoplegia), cerebellum (gait abnormalities), juxta-cortical and periventricular white matter, and the corpus callosum

Classification

1. Relapsing and Remitting MS (RRMS) is the most common type: it is recognized by periodic symptoms with complete recovery between episodes (early in disease course) but the majority go on to:

2. Secondary Progressive Disease (SPMS): Gradual progression with superimposed acute exacerbations.

a. Primary Progressive MS (PPMS) is less common (10%): Presents with steady progression from the outset with no periods of remission. This subset of patients usually present >50 years

Clinical Picture

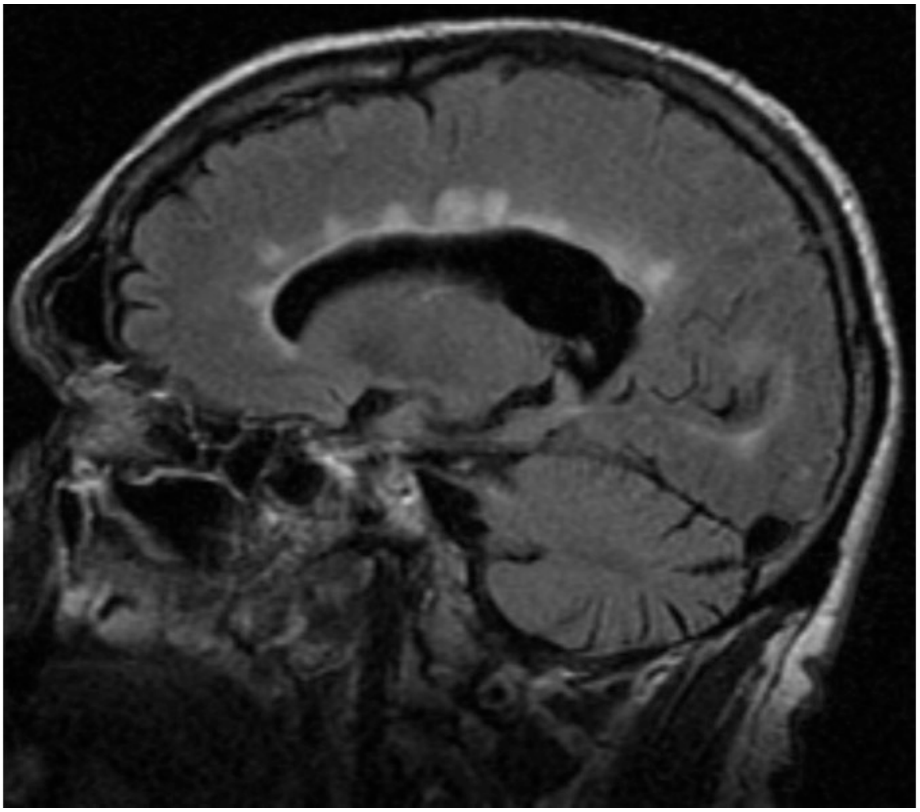
MS is neurological disease in the first instance and presents with variable motor and sensory features. The neuropsychiatric aspects typically follow acute or chronic neurologic disease.

- Clinical picture is variable and depends on the plaque location
- At the onset of disease the clinical picture is often vague with complaints such as lack of energy, headache, depression, aches in the limbs etc.
- Early in the disease course, one of the most common symptoms is unilateral optic neuritis with loss of vision in the effected eye and pain on eye movement. Further eye signs include oculomotor disorders such as diplopia, nystagmus and abnormal smooth pursuit movements. Trigeminal neuralgia may be an early symptom in young people
- Spinal cord lesions present with motor symptoms such as spasticity and weakness. Lesions of the ascending tracts present with sensory symptoms such as numbness, tingling, pins and needles, impaired vibration sense, impaired proprioception and patchy areas of decreased sensation.
- Cerebellar involvement presents with incoordination, gait abnormalities, slurred speech, tremor and dysmetria
- Pain is common and may be paroxysmal or persistent and is often described as an icy cold or burning sensation
- Other general features include: severe fatigue, Lhermitte's sign, Urinary incontinence and sexual dysfunction and Neuropsychiatric symptoms

Special Investigations

- No lab finding is pathognomonic
- CSF is often abnormal; mild lymphocytosis, increased IgG, oligoclonal bands
- Abnormal Visual Evoked Potential (VEP)
- Imaging is the gold standard for diagnosing MS
    - CTB is not sensitive but may show atrophy in longstanding disease
    - MRI is the imaging investigation of choice, FLAIR will show hyperintense, ovoid, periventricular white matter lesions typically radiating from the corpus callosum but can also be seen in the brainstem and spinal cord

Figure 1: Dawson’s fingers on FLAIR



Case courtesy of Prof Frank Gaillard, Radiopaedia.org

Neuropsychiatric Complications of MS

1. Cognitive impairment / Disorders

Dementia (major neurocognitive disorder) is uncommon but some degree of cognitive impairment on neuropsychological testing is common (up to 70% of patients), even at onset. The degree of cognitive decline correlates with diffuse white matter disease and plaque burden. It is important to screen for, and treat depression in patients with cognitive symptoms as this may contribute to the deficits.

Deficits are commonly seen in “subcortical” domains such as Attention, problem-solving, processing speed, fluency and working memory. There are no conclusive data supporting the use of cholinesterase inhibitors for the treatment of cognitive symptoms, however, one small open label study has shown modest benefit

Delirium is rare but may occur occasionally due to acute cerebral lesions. Exclude other causes of delirium such as medication side-effects

2. Depression

Lifetime prevalence in persons with MS is 50%. The aetiology is a complex interaction of structural and functional abnormalities of the limbic circuits as well as the response to living with a chronic, disabling illness and possible side-effects of immunosuppressant medications.

SSRIs are considered first line treatment for depression, however, TCAs or SNRIs could be helpful for depression with prominent pain symptoms. ECT is relatively contraindicated as it may lead to deterioration.

Linked to depression and mood disorders is the “Pseudobulbar Affect (PBA)”. It is common in advanced disease where the cerebro-pontine-cerebellar pathways are involved. It presents with laughing or crying in the absence of affective disorder (felt mood state). It can lead to embarrassment and distress and can be difficult to treat. Small trials have been published suggesting a value for the use of SSRIs, quinine + dextromethorphan (10mg+20mg) and carbamazepine.

3. Mania

Presents as an euphoric mania. It is associated with increased plaque burden and mostly accompanied by cognitive symptoms. May be associated with the use of corticosteroids. Treatment as per standard protocols for mania

4. Psychosis

It is uncommon and normally the result of high dose corticosteroids.

References

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