Multiple Sclerosis (MS)

Introduction

Cell-mediated autoimmune condition characterised by recurrent episodes of CNS demyelinating inflammation. Multiple areas of scar tissue form along neurons resulting in impaired movement and sensation. Genetics & viral infections (?EBV) may be important in cause and relapses.

Classification

There are different patterns of multiple sclerosis (MS):

- Relapsing/remitting MS: 80% of people at onset.
- Secondary progressive MS: follows relapsing/remitting MS in ~50% within first 10yrs.
- Primary progressive MS: 15-20% of people at onset.

Epidemiology

- MS usually starts in early adult life.
- ~1 in 1,000 population. Caucasians have the highest risk.
- Female to male ratio is 3:2.
- Family history, 4% with 1° relative with MS. Overall 20% have an affected relative.

Diagnosis

- Clinical evidence of lesions separated in time and space without alternative explanation.
- Investigations (MRI, evoked potentials) desirable (essential if clinical evidence lacking).

Presentation

Wide range of symptoms and signs. Worsen with ↑body temp. The most common features are:

- **Visual:** Very common. Esp. optic neuritis (30%).
- **Eye movements:** Symmetrical horiz jerking nystagmus, diplopia, VIn palsy, gaze palsy
- **Facial weakness:** Bell's palsy, trigeminal neuralgia, or paroxysmal dysarthria and ataxia
- **Hearing and balance:** Deafness, vertigo, ataxia and headache.
- **Cognitive symptoms:** Visual and auditory inattention, loss of memory more than language.
- **Psychological symptoms:** Depression, rarely psychotic symptoms
- **Taste and smell:** Quite commonly subtly altered.
- **Unpleasant sensations:** Lhermitte's phenomenon, tightness, burning or tearing pain
- **Paraesthesiae/numbness:** Particularly in the legs, perineum and genitalia with altered sphincter function. Transverse myelitis may cause a severe acute episode of this.
- **Autonomic system:** incontinence (urinanry>faecal), impotence, poor thermoregulation
- **Other symptoms:** Horner's syndrome, arrhythmia, weight loss, SIADH.

Differential diagnosis

- Hereditary spastic paraplegia: mimics familial MS, or other inherited diseases
- Cerebral SLE
- Sarcoidosis.
- AIDs, Lyme disease, GBS, neurosyphilis, or neuromyelitis optica.

Investigations

Electrophysiology: Visual evoked potential studies should be the first choice.
MRI scan: 95% patients have periventricular lesions and over 90% show discrete white matter abnormalities. Can also see areas of focal demyelination as plaques in optic nerve, brainstem and spinal cord. Contrast can distinguish active/inactive inflammatory plaques.
Lumbar puncture/CSF: ↑protein with ↑Ig with oligoclonal bands.

Management

General support: Multidisciplinary, medical, family, social, psychological for a chronic condition.

Relapse management

Steroids: **methylprednisolone** 500mg daily x 5d PO or IV. Give omeprazole or ranitidine. Avoid use of steroids >3 times/yr, or for >3wks at a time. **Azathioprine** may spare steroids.

Symptom management

Fatigue: Treat underlying causes,general advice (exercise), consider **amantadine**.
Pain: Analgesia (consider **carbamazepine**, **gabapentin**, **amitriptyline**), TENS
Visual and communication: **Gabapentin** may help nystagmus.
Spasticity and spasms: **Baclofen**, **gabapentin**, **clonazepam**, or **dantrolene**. IM botulinum toxin.
Urgency or urge incontinence: **Oxybutynin**, **desmopressin**. Self-/long term catheterisation.
Bowel problems: May require routine use of suppositories or enemas.
Swallowing difficulties: NG or even percutaneous endoscopic gastrostomy (PEG) tubes.
Emotional lability: Antidepressant medication, CBT or short-term BDZ
Sexual dysfunction: Erectile dysfunction needs full assessment. Sildenafil may be used.
Other considerations: Influenza immunization. Reflexology, massage, & linoleic acid may help.

Disease modifying therapy

Generally used for relapsing, remitting MS (≥2 attacks over the previous 2-3yrs) and still able to walk 100m unaided. Not all respond and some deteriorate. About 30-40% relapse reduction. Side-effects include a flu-like ague for 24 hours after the injection

Interferon beta-1a or 1b *(SC, IM)*

- Interferon beta-1b also licensed for secondary progressive multiple sclerosis.
- It is given SC or IM between 1-4 times a week.
- Women on disease modifying therapy must stop Rx 12mo before trying to conceive.

Glatiramer acetate *(SC)* - It is designed to mimic the effects of the main proteins in myelin.

- It is given daily by subcutaneous injection.
- Other SE: Injection site reactions, sporadic, short-lived chest tightness and SOB.

Also used:

Cannabinoids: Good evidence lacking. Anecdotally help spasticity, tremor, pain, bladder probs.

Emerging therapies

Natalizumab: Recombinant humanised monoclonal Ab, Monthly IV. 68% relapse reduction. ?Risk of progressive multifocal leukoencephalopathy (PML).
CAMPATH-1H: Destroys T cells. IV daily for 5 days. Once a year. 90% reduction in aggressive MS. No reduction in long term disability in secondary progressive MS.
Mitoxantrone: Cytotoxic immunosuppressant. Monthly infusion. 70-90% reduction in very active MS relapses. Possible risk of cardiotoxicity and late leukaemia.
Other possible therapies: Statins, laquinimod, teriflunomide, fingolimod

Prognosis

- ~25% patients have a non-disabling form of MS.
- 5% patients have frequently recurring relapses without recovery rapidly causing disability and early death.
- Up to 15% patients are severely disabled within a short period.
- Episode rates initially ~1.5/year with recovery being slower than onset.
- Secondary progressive MS tends to affect those systems previously involved in relapsing-remitting stage.
- The risk of relapse decreases during pregnancy, and increases transiently postpartum.