Motor Neurone Disease (MND)

Synonyms: Amyotrophic lateral sclerosis (ALS), Lou Gehrig's disease (after US baseball player), Charcot's disease, Charcot's syndrome, Charcot's sclerosis.

Description

Spectrum of degenerative motor diseases affecting both UMN & LMNs (motor cranial nuclei & anterior horn cells of the spinal cord). LMN signs usually predominate. Cause is not conclusively known (?mitochondrial dysfunction causing oxidative stress in motor neurones). No known cure.

Epidemiology

Incidence 5-10 cases per 100,000 population.

Tends to affect people in the fourth to seventh decades, with familial cases usually occurring at the younger end of the spectrum and sporadic cases affecting older people.

Presentation

Symptoms

Patients or their families often notice problems occurring in one or more of the patterns below:

- Bulbar onset – difficulty eating, drooling, dysarthria, dysphonia, pulmonary aspiration.
- Limb weakness – usually upper limbs but can affect legs (e.g. foot drop or gait anomaly)
- Fasciculations of the muscles of the limbs, or of the tongue, may be a presenting feature.
- Rarer features:
    - Pain or sensory disturbance is uncommon
    - Symptoms due to impaired respiratory muscle function usually occur late
    - Some patients with pseudo-bulbar palsy may have 'emotional incontinence', an over-reaction to sad or funny events that they are aware of as being abnormal.
    - Cognitive impairment is not common but can affect some patients with bulbar palsy.

Signs

- Lower motor neurone dysfunction in the limbs manifests as weakness, atrophy, fasciculations and hyporeflexia. The thighs are often a site of marked fasciculation.
- Upper motor neurone dysfunction manifests as weakness predominating in the arm extensors and leg flexors with evidence of hypertonia, hyper-reflexia and upgoing plantar responses; the bulbar muscles may also show spasticity with an exaggerated jaw jerk.
- Ocular, sensory or autonomic dysregulation signs are usually late features of the disease.

Differential Diagnosis

The differential diagnosis is vast & includes:

- Diabetic amyotrophy
- Guillan-Barré syndrome
- Post-polio syndrome
- Myasthenia gravis or Lambert-Eaton syndrome
- Peripheral nerve lesions, e.g. diabetic
- Thyrotoxicosis with assoc myopathy
- Radiculopathy or myelopathy
- Spinal cord tumours
- Cerebrovascular disease and stroke
- Polymyositis or dermatomyositis
- Glioma of brainstem
- HIV-associated neuro-/myopathy
- Lyme disease
- Spinal muscular atrophy
- Hereditary polyneuropathies, e.g. Charcot-Marie-Tooth syndrome
- Focal muscular atrophies (monomelic amyotrophy)
- Post-radiation myeloplexopathy
- Viral plexopathies
- Tay-Sachs disease (adult form)
- Multifocal motor neuropathy with conduction block

Investigations

No definitive diagnostic tests. The following may be done during work-up:

- EMG and nerve-conduction studies shoe characteristic pattern
- CT and/or MRI of the brain and spinal cord are useful in excluding other pathologies
- Blood tests to exclude other conditions such as vitamin B_{12} and folate levels, HIV serology, Lyme disease serology, creatine kinase assay, serum protein electrophoresis, anti-GM1 antibodies (multifocal motor neuropathy with conduction block), urinary hexosaminidase-A assay (Tay-Sachs), etc.
- Muscle biopsy may be considered to exclude or diagnose myopathic conditions.

Management

Non-drug

- General palliative care.
- A multidisciplinary approach involving GP, primary-care nurses, OT, physios, speech therapists, dieticians, home care workers, hospital physicians and neurologists, etc.
- PEG, tracheostomy, specialised communication & mobility devices may be required.

Drug treatments

- **Riluzole** (a neuroprotective glutamate-release inhibitor) is the only drug of proven (but modest) disease-modifying efficacy. It may extend lifespan by about 2 months.
- Other supportive Mx for Cx of the disease, for example:
    - Muscle cramps & spasticity - **diazepam**, **baclofen**, **tizanidine**, **phenytoin** & **quinine**.
    - Pain – analgesics
    - Respiratory distress and the sensation of choking - opioids but SE resp depression.
    - Respiratory failure: NIV & invasive respiratory support
    - Drooling - anticholinergics such as **hyoscine**.
    - Depression - antidepressants
    - Treatment of infections (pneumonias, UTIs) - ABx
    - Constipation – aperients
    - Mobility devices

Complications

- Respiratory failure and death
- Pneumonia due to infection or aspiration
- Urinary tract infections
- Constipation
- Spasticity and cramping of muscles
- Depression
- Loss of speech as a means of communication
- Immobility and attendant disability
- Complications of immobility such as skin infections/bedsores and ulcers
- Cognitive deterioration is rare but is seen occasionally.

Prognosis

MND is usually a rapidly progressive and fatal disease.
Median survival is 3–5 years. A subset (10–20%, male, early limb onset) may have longer survival
Death usually occurs due to respiratory failure or pneumonia due to hypoventilation.