MOTOR NEURON DISEASE.

(Dr. S. Uma Devi)

Commonest degenerative disorder of motor neuron is Motor neuron disease. **Definition:**
MND is a “progressive” (steady and relentless) degenerative disease with clinical signs of lower and upper motor neuron damage in the absence of electrophysiological and imaging evidence of other disease processes that explain the clinical signs.

Degeneration involves
1. upper motor neurons in the motor cortex
2. Corticospinal fibres, cortico bulbar pathways
3. Anterior horn cells of spinal cord
4. Motor cranial nuclei in the brain stem (lower cranial nerves)
Thus there is degeneration of both upper and lower motor neuron. Characteristically Sensory system is never involved.

**Levels of lesion:**
Various levels of motor system may be involved in the spinal cord.
- Cervical, lumbo sacral, thoracic and bulbar.
  Initially specific regions are involved.
  At the end all levels of motor system may be involved.

**Etiology:**
Actual cause not known. several theories exist
90% are sporadic.
10%- Familial ;Autosomal dominant
  Genetic factors determine the susceptibility.
  Onset may be triggered by environmental factors.

**Pathology:**
Macroscopic;
  Degeneration of anterior horn cells of spinal cord and anterior roots
  Degeneration of motor nuclei of cranial nerves,
Microscopic;
  Neurones show ‘spongiosis’, inclusion bodies – Skein like inclusions, bunina bodies vacuolization. Astrocytes present.
  Accumulation of pigmented lipids (lipofuscin) in motor neuron

**Epidemiology:**
Age of onset – between 30 – 60 yrs
Predominantly affects middle aged, mean age of onset 55yrs
(Younger can also be affected)
male;female-1.5:1

Clinical presentation: (mnemonic ABCD)
A. Atrophy: - wasting, weakness, fasciculation (LMN lesion)
B. Hyperactive tendon reflexes.(UMN lesion)
C. Extensor plantar reflex.
D. No sensory changes.

Types of motor Neuron disease:
1. Amyotrophic Lateral sclerosis.
2. Primary lateral sclerosis
3. Progressive muscular atrophy.
4. Brainstem involvement;
   A. Bulbar palsy
   B. Progressive bulbar palsy.

1. Amyotrophic Lateral Sclerosis:
The most common presentation:
-Wasting in the upper limbs and spasticity in the lower limbs.
Synonym: Lou Gehrig's Disease

Progressive muscular atrophy(also called spinal muscular atrophy)
Predominantly or purely lower motor neuron changes.
(Affecting upper and lower limbs)
proximal pattern of progression

Progressive Lateral sclerosis:
Predominantly or purely pyramidal tract degeneration.
(In upper and lower limbs).
Clinically shows progressive UMN signs without LMN signs
PLS may progress to ALS decades later.

Brainstem involvement:
Motor nuclei of Medulla and Pons affected.
   Bulbar palsy: mainly flaccid paralysis of bulbar muscles
   Progressive bulbar; mixed palsy of bulbar muscles (UMN and LMN)
   In many, death occurs before limb involvement.

Evolution of Natural course of the disease
1. PLS, PSB and PMA may eventually evolve into AML and carry same poor prognosis
2. Or may remain in the limited form
   But there is no way to predict the course
   ALS is a fatal disease; median survival is 3-5 yrs

Selectivity of neuronal cell death in MND
Remarkably selectively involves certain neurons only
Sensory system never involved
Cognitive process not involved
Within the motor system also – selectivity occurs
Motor neurons of ocular motility not involved
Neurons of sphincters of bowel and bladder not involved

Symptoms: of Motor disturbances:
Wasting, weakness, stiffness, fasciculations
❖ Wasting of small muscles of the hand, ❖ Weak grip, difficulty in doing specific tasks like turning a key.
❖ Extensor weakness more common than flexors
❖ Floppiness of foot.

Symptoms of bulbar involvement:
In bulbar palsy, disease primarily affects motor nuclei of cranial nerves
Cranial nerves are predominantly affected
❖ Insidious: Difficulty in swallowing, Nasal regurgitation, Nasal speech,
❖ Fibrillation of the tongue, ❖ Wasting of the tongue
Difficulty in chewing, coughing, breathing, talking (dysarthria)
Treatment:
Cricomyotomy may help briefly in swallowing (Crico pharyngeal sphinterotomy)

Signs of bulbar involvement:
• Progressive bulbar:
  Drooping of palate,
  Depressed gag reflex,
  Pooling of saliva in pharynx,
  Weak cough
  Wasted, fibrillating tongue.
• Pseudo bulbar:
  1. Contracted spastic tongue almost immobile tongue.
  2. Emotional lability
     — involuntary excess weeping or laughing (pseudobulbar affect)

cont-------------
Signs of LMN and UMN involvement:

- Atrophy: wasting, weakness, fasciculation (LMN lesion)
- Hyperactive tendon reflexes.
- Extensor plantar reflex.
- Wasting of small muscles of hand (weak grip)
- Floppiness of foot

Key diagnostic features of MND:

- Fasciculation
- Wasting and weakness
- Exaggerated reflexes.
- Combination of upper and lower motor neuron signs.
  (Exaggerated reflexes in the presence of severe muscle wasting.)
- Simultaneous involvement of UMN and LMN
- No sensory changes
- No sphincter disturbances

Onset focal and asymmetrical, but disease becomes symmetrical later

Definite ALS – if 4 sites involved (bulbar, cervical, thoracic, lumbo sacral)

Probable – if 2 sites involved

Possible – if only one site is implicated

Diagnosis of MND is essentially a clinical one.

There is no specific diagnostic test. Diagnosed by process of elimination –
Elimination of similar diseases by investigations; in early stages - in doubt –
review every year.

Mode of death -
Commonest - respiratory paralysis

Rare form of ALS
Familial ALS (FALS)
e.g. SODI
  Kennedy syndrome

Differential Diagnosis;

- For UMN lesion:
  1. compressive spinal cord lesion (cervical, cervicomedullary junction)
  2. Space occupying lesion
  3. Multiple sclerosis

- For LMN type:
  1. Infection of anterior horn cells - e.g. polio
  2. Radiculopathy, plexopathy, peripheral neuropathy myopathy –
     Differentiated by clinical exam
  3. Monoclonal gammopathy
4. **Multi focal motor neuropathy with conduction block.**
Both 3 and 4 may show pure motor syndromes; differentiation is by ENMG.
5. A pure motor neuropathy may occur in Hodgkin's
6. **Post polio syndrome:** a condition affecting polio survivors, decades after their recovery from poliomyelitis

**Conditions causing LMN signs in upper limb and UMN signs in lower limb**
1. Amyotrophic lateral sclerosis
2. Syphilitic amyotrophy
3. Syringomyelia, hematomyelia
4. Hypertrophic pachymeningitis
5. Cervical arachnoiditis
6. Cervical spondylosis
7. Extramedullary cord compression at cervical region
8. Multiple sclerosis
9. Nutritional amyotrophy

Conditions **causing UMN bulbar palsy**
Brain stem lesions
Syrinx, stroke, degenerative and demyelinating conditions
LMN bulbar signs_Cranial nerve palsies

**Investigations:**
1. ENMG.
2. Muscle biopsy shows histological changes of denervation.
3. Myelogram
4. MRI to exclude high cervical lesion.
5. If tongue fibrillation present, CSF exam advised to rule out neurosyphilis.
6. Serum creatinine kinase is slightly raised but never to high levels as in muscular dystrophies.
7. CSF is normal in MND.

1. Changes found in ENMG: in cases of MND:
   1. chronic partial denervation,
   2. Abnormal spontaneous activity in the resting muscles,
   3. Reduction in number of motor units under voluntary control
   (For definite diagnosis changes must be found in at least 3 extremities)
   motor conduction velocity is usually normal

**Treatment:**
- No cure or standard treatment
- **Drug** – Riluzole- 50 mg oral twice a day
- prolongs life by 2-3 mths; does not relieve symptoms.
It is a Sodium channel blocker
Inhibits the release of glutamate
Also has other neuro protective features
Minocycline- being tried and also COX2 inhibitors

**Symptomatic therapy:**
- For spasticity – muscle relaxants-beclofen, benzodiazepines, tizanidine.
- To reduce excess salivation- atropine, glycopyrollate, amitryptiline.
- For cramps- quinine, phenetoin
- To relieve pain – NSAIDS
- For sleep disturbance- tranquilizers, antidepressants
- To control drooling-anticholinergic
- In advanced stages – morphine for pain and musculoskeletal abnormalities

**Supportive therapy:**
To improve posture and help in joint stiffness, muscle atrophy, swallowing difficulty.
- Physio therapy, to prevent contractures
- Speech therapy
- Occupational therapy
- Rehabilitation therapy

**Assist devices:**
- Braces or walker to improve mobility, orthotics, speech synthesizers, wheel chairs
- Foot drop splints-prevent tripping
- Finger extension splints Potentiate grip
- Nasopharyngeal tube or semiliquid diet for severe bulbar involvement
- For respiratory weakness–Non invasive respiratory support/full ventilatory support

**Surgical:**
1. Crico pharyngo myotomy in severe bulbar involvement or Gastrostomy
2. Tracheostomy if respiratory muscles are involved severely.

**Prognosis:**
Most cases ALS progress quickly, fatal in 2-5 yrs.
Bulbar involvement has poorest prognosis
PLS may progress slowly.
Usual mode of death – respiratory failure due to weakness of ventilatory muscles or respiratory infection

**Definition and difference**

**Fasciculation:**
Involuntary contraction or twitching of groups of muscle fibers

**Fibrillation:**
Fine rapid twitching of individual muscle fiber with no movement of the muscle as a whole.
 e.g fibrillations occur in tongue muscles in bulbar palsy.

**Conditions causing fasiculations**
1. Motor neuron disease
2. Syringomyelia
3. Cervical spondylosis
4. Primary muscular atrophy
5. Peroneal muscular atrophy
6. Poliomyelitis (when muscles are actively wasting)
7. Thyrotoxic myopathy
8. Carcinomatous myopathy
9. Organophosphorous poisoning
10. Benign