
**A 38 year old man presents to the Neurology outpatient department with a complaint of progressive weakness in his hands and feet.The patient states that these symptoms have slowly progressed over the past few months.Initially, he was unable to manipulate small objects such as picking up a coin or buttoning his shirt.Now he complains of difficulty in grasping a gallon of milk and notices the muscle in his hands twitching.He often trips while walking because he feels he cannot lift his toes up and lacks coordination.In addition he says muscles in his legs occasionally spasm.**

1.What is the most likely diagnosis and why?

Answer-

The most likely diagnosis is Amylotrophic Lateral Sclerosis(ALS). It is the most common progressive motor neuron disease.
The hallmark of this disease is that it presents with both LMN lesion of upper limbs and UMN lesion of lower limbs.

2.What differential diagnosis will you consider here?

Answer-

- Progressive muscular atrophy(LMN lesion only),
- Primary lateral sclerosis(UMN lesion only),
- Stroke (Risk factors should be present, accompanying cranial nerve lesions,Sensory sensations may be impaired) ,
- Gullian barre syndrome (Ascending Paralysis, LMN lesion with diminished reflexes)
- Myasthenia gravis ( weakness increases throughout the day, on repeated use)

3.What is the pathophysiology of this disease and how does it explain the symptoms of the patient?

Answer-

Progressive loss of UMNs and LMNs in brain and spinal cord, involving degeneration of anterior horn cells and corticospinal tract is the pathologic hallmark -involving loss of anterior horn cells in the spinal cord and their brainstem homologues innervating bulbar muscles as well as and death of Corticospinal Motor Neurons which originate in layer 5 of the motor cortex and descend via the pyramidal tract to synapse with LMNs, either directly or indirectly via interneurons).

Neurologic Pathophysiology

ALS patients lack the enzyme “Superoxide Dismutase” which is responsible for digesting the superoxide molecule to produce less damaging Hydrogen peroxide and water molecule.

Weakness results from free radical damage of lower motor neurons in the brainstem motor nuclei and the anterior horn of the spinal cord or even dysfunction of the axons of these neurons as they pass to skeletal muscle, resulting in decrease in the activation of number of muscle fibers through a loss of α/alpha motor neurons or disruption of their connections to muscle.

Loss of γ/gamma motor neurons decreases tension on the muscle spindles, decreasing muscle tone and attenuates the stretch reflexes.

Diseased motor units, especially in anterior horn cell diseases, discharge spontaneously, producing fasciculations - accounting for the muscle twitches.

When α motor neurons or their axons degenerate, the denervated muscle fibers also may discharge spontaneously.

Pathological Symptoms in ALS

Although at its onset ALS may involve selective loss of function of only upper or lower motor neurons, it ultimately causes progressive loss of both categories of motor neurons.

Progression of Symptoms as seen with the patient in this case, is initial involvement of fine motor skill loss, which gradually progressed to dysfunction of major limb muscle groups. Weakness caused by denervation is associated with progressive wasting and atrophy of muscles and, particularly, spontaneous twitching of motor units, or fasciculations, which is noticed when the patient is lifting things.

The disease is progressive explaining the fact that it starts with impairment of fine motor skills (Buttoning of shirt) leading to gross motor deficits such as grasping of the gallon of milk.

The diagnosis is strictly ALS because -

Clinical diagnosis of ALS requires LMN signs in at least two extremities which is seen in this case(Hands) and UMN signs in one region, which here is manifesting as spasm (spasticity) in the legs.

Even in the late stages of the illness, sensory, bowel and bladder, and cognitive functions are preserved. Even when there is severe brainstem disease, ocular motility is spared. And in the given case, patient has NOT presented with any loss of sensation or bowel/bladder dysfuntion or ocular dysfunction.

4.How will you manage this patient?

Answer-

The drug riluzole (100 mg/d) was approved for ALS because it produces a modest lengthening of survival. But no treatment arrests the underlying pathologic process in ALS.

The Drug Edaravone – Approved in 2017 for I.V use ( acts as an antioxidant by digesting the superoxide molecule)

In the absence of a primary therapy for ALS, a variety of rehabilitative aids may substantially assist ALS patients.
Foot-drop splints facilitate ambulation by preventing the need for excessive hip flexion and prevents tripping on a floppy foot.
Finger extension splints can potentiate grip.
Respiratory support may be life-sustaining. For patients electing against long-term ventilation by tracheostomy, positive-pressure ventilation by mouth or nose provides transient (weeks to months) relief from hypercarbia and hypoxia.
For some patients, a Cough Assist Device, producing an artificial cough is extremely beneficial.
It is highly effective in clearing airways and preventing aspiration pneumonia.