

Case Report

Mills hemiparetic or hemiplegic variant of amyotrophic lateral sclerosis

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ABSTRACT

Mills hemiplegic variant of Amyotrophic lateral sclerosis (ALS) is a gradually progressive, spastic ascending or descending hemiparesis or hemiplegia without any sensory involvement. Authors presented a 47 years old female with history of gradually progressive left sided wasting of muscles including the tongue, left hemiparesis along with dysarthria and fasciculation's of tongue and left sided muscles with left sided cortico-spinal tract signs of 2 years duration. There were no sensory as well as bowel bladder involvement. Her cognition was intact. Relevant blood and CSF examinations were within normal limit. MRI Brain and whole spine were unremarkable. Nerve conduction study was essentially normal. Electromyography(EMG) showed chronic denervation potentials which is in accordance to Revised El Escorial criteria, 2015 for the diagnosis of this extremely uncommon entity- Mills hemiplegic variant of ALS. The major challenge in diagnosis of this disease entity is to exclude other diseases/disorders that may mimic its symptomatology.

Keywords: Amyotrophic lateral sclerosis, Electromyography, Lower motor neuron, Mills syndrome, Revised El Escorial criteria, Upper motor neuron

INTRODUCTION

The general term Motor neuron disease designates a group of degenerative disorders of motor neurons in spinal cord, brainstem and motor cortex, manifested clinically by muscular weakness, atrophy and corticospinal tract signs in varying combinations.¹

Customarily motor neuron disease is subdivided into several subtypes on the basis of the grouping of symptoms and signs. The most frequent form, in which amyotrophy and hyperreflexia are combined, where there is denervation atrophy and weakness of muscles is termed as Amyotrophic lateral sclerosis (ALS).^{1,2} There are many patterns of neuromuscular involvement. In one type of pattern of ALS, involvement of arm and leg are affected on the same side, first with spasticity and then

with some degree of amyotrophy; this has been called Mills hemiplegic variant of ALS or Mills syndrome.¹

This extremely uncommon syndrome of gradually progressive, with UMN predominant ascending or descending hemiparesis or hemiplegia, with no significant sensory impairment was first described by American Neurologist Charles Karsner Mills (1845-1930) in 1900, which several cases were reported later. However, after diagnostic tests and radiological imaging study improvements, the number of reports has shortened.

A possible explanation for this shortage is the identification of other diseases that could mimic the clinical picture.²⁻⁴ Currently, this uncommon entity has an uncertain nosological status, since it is described based

on symptomatology, clinical examination and assisted by ancillary investigations to exclude other diseases/disorders that may mimic it.⁴

CASE REPORT

A 47 years old right handed female presented with gradually progressive ascending left hemiparesis and wasting of left sided limb muscles including the small muscles of limbs and tongue with dysarthria for 2 years duration. Along with, there were also history of rippling of muscles in the left sided limbs occasionally. There were no similar history in the family and any bowel or bowel incontinence.

Clinical examination showed intact cognition (Mini mental status examination-24/30) but with dysarthria with left sided spastic hemiparesis (Ashworth scale-3/5), hyperreflexia of left sided deep tendon reflexes with left sided positive Hoffmann and Babinski responses along with fasciculation in the left lower limb. The clinical examination on the right side was essentially normal.

Vasculitic profile including Antiphospholipid antibody, serum electrophoresis, VDRL, CSF analysis were normal. MRI Brain was normal and MRI whole spine showed mild intervertebral disc bulges at C3-C4, C6-C7, L3-L4, L4-L5 levels which seems unlikely to contribute to the symptomatology (Figures 1,2) .

Nerve conduction study was essentially normal. EMG study showed chronic denervation potentials in left Biceps, left Vastus lateralis, left Gastrocnemius, left Paravertebral muscles in accordance to Revised El Escorial criteria, 2015 for the diagnosis. (Figures 3,4,5 and 6). She was prescribed with antiglutamate agent Riluzole -100mg daily.

During the follow up evaluation after 8 months later, Neurological examination revealed the same left hemiparesis with increased wasting of left sided limb muscles with increased muscle fasciculations without any deterioration of cognition or any increase in spasticity in accordance with the Ashworth scale of 3/5.



Figure 1: MRI brain images (T1, T2, GRE, DWI sequences respectively) of normal brain parenchyma.



Figure 2: MRI of spine of non-specific changes (Intervertebral disc bulges at C4-C5, C6- C7, L3-L4, L4-L5).

Routine blood investigations were within normal limit. Screening for HIV, HTLV-I and II, Vitamin B12,

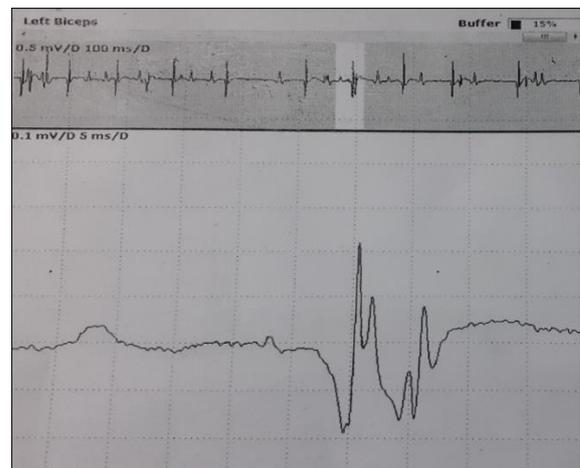


Figure 3: Evidences of chronic denervation potentials in left biceps muscle.

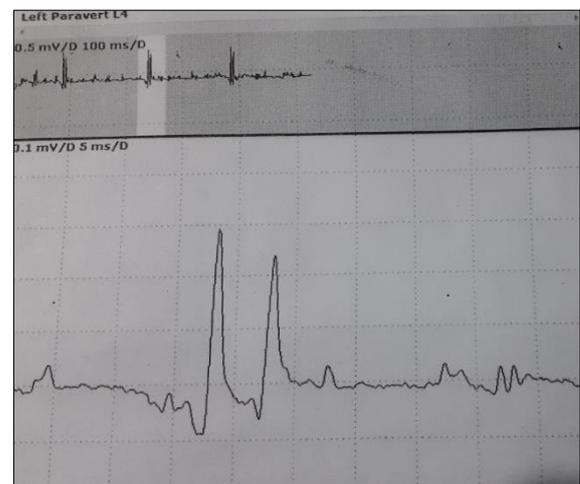


Figure 4: Evidences of chronic denervation potentials in paravertebral muscles.



Figure 5: Evidences of chronic denervation potentials in left vastus lateralis muscle.

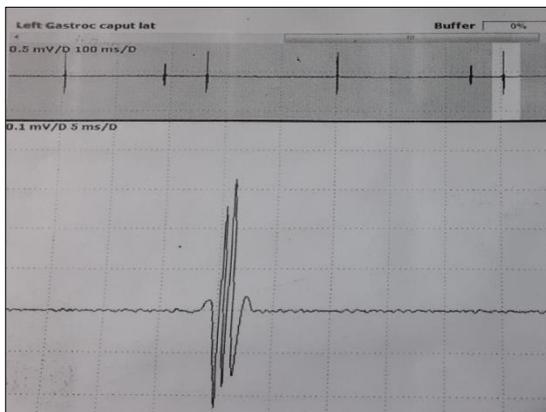


Figure 6: Evidences of chronic denervation in left gastrocnemius muscle.

A repeat Nerve conduction study revealed normal study. EMG repeat study showed presence of chronic denervation potentials in left biceps, left vastus lateralis, left gastrocnemius and involvement of bilateral paravertebral muscles whereas during the initial visit she had only unilateral left sided involvement.

DISCUSSION

ALS is a devastating neurodegenerative disorder primarily affects motor neurons. The cardinal feature of this disorder is the presence of a combination of UMN and LMN involvement, either simultaneous or sequential with inexorable progression.⁵

The incidence of ALS is 2-4/1,00,000 and the prevalence is 6/1,00,000. The onset is typically in sixth decade (ranging 20-90 years, average age of onset-63 years). In India, the age of onset occurs almost a decade earlier and published natural history studies have shown about 50% of the patients dying within 30 months of disease onset.⁵ In this disease, the anterior horn cells of the spinal cord as well as the pyramidal fibres, which control the spinal

cord are affected. The reason behind this is unknown technically; it has been thought that reactive astrogliosis and microglial activation may play a role in causing it.⁶

There are no definitive diagnostic tests and diagnosis rests on clinical, EMG and is vital to rule out the mimics. There are no good biomarkers for the disease in distinguishing subtypes and there is blurring of the boundary between diagnosis and phenotypes. Thus, ALS is a spectrum disorder including progressive bulbar palsy, pseudo-bulbar palsy, Primary lateral sclerosis (PLS), Progressive muscular atrophy (PMA) and its other regional variants.^{5,6}

The Mills variant of ALS is extremely uncommon and typically has a slowly progressive course than the aggressive form of classical generalised ALS.^{5,6}

In Mills original cases, described 12 decades ago, different disorders such as Multiple sclerosis, Syphilis, and Parkinsonism probably were included besides ALS, just because in those days, investigative diagnostic armamentarium was not sophisticated as much as we have it now a days.

One study done on eight patients with suspected Mills syndrome reported that the clinical course was slowly progressive, with motor deficiency, unilateral pyramidal signs (or bilateral with asymmetry), without bulbar signs, fasciculations or sensory deficit. Only three of those patients were diagnosed as Mills syndrome. Other cases mimicking Mills syndrome were diagnosed as primary lateral sclerosis, myelitis of unknown origin, progressive primary multiple sclerosis, and antiphospholipid syndrome. The main arguments for final diagnosis were brought by electrophysiology, brain and spinal MRI scan.^{2,3}

Revised El Escorial diagnostic criteria for the diagnosis of ALS, 2015 which states that presence of-

- Signs of lower motor neuron degeneration by clinical, electrophysiologic or neuropathologic examination.
- Signs of UMN degeneration by clinical examination.
- Progression of symptoms or signs over 6 months as demonstrated by spread within a region or other spinal regions.

Diagnosis of ALS is suggested by the absence of-

- Electrophysiologic or pathologic evidence of other disease processes.
- Neuroimaging evidence of other disease processes.

This Revised El Escorial diagnostic criteria, 2015 has been categorized according to diagnostic categories like clinically definite, clinically probable, clinically probable-laboratory supported, clinically possible

depending upon the presence of the diagnostic criteria in different permutations and combinations.^{7,8}

Our patient, presented with slowly progressive unilateral symptoms and signs (both UMN and LMN) with progression of symptoms and signs during the subsequent visit. Clinical examination showed unilateral limb weaknesses as well as muscle and tongue wasting, fasciculations, spasticity with brisk reflexes and extensor Babinski response as well as supported by the ancilliary investigations.

Therefore, patient can be accommodated in the clinically probable-laboratory supported category according to the diagnostic El Escorial criteria, 2015.

Several other studies reported that, patients may have dementia {specifically Fronto-temporal dementia (FTD)}, dysphagia and bulbar involvement, sudomotor as well as gastrointestinal dysregulation.⁹ Also some studies state that it is uncertain if the hemiplegic variant of ALS (Mills Syndrome) is a variant of ALS, PLS, or FTD/ALS. Some even consider it as a form of corticobasal degeneration.¹⁰

CONCLUSION

So it may be considered that the Mills hemiparetic or hemiplegic variant of ALS could be all the variants of motor neuron disease spectrum (ALS, PLS or UMN-ALS, UMN+LMN-ALS) in a hemiplegic, or asymmetrical pattern of involvement. A syndrome is a collective of symptoms and signs that could have many etiologies. Therefore, Mills hemiplegic variant of ALS may be conceptualised as a motor neuron syndrome with a hemiparetic or hemiplegic or markedly asymmetrical pattern of involvement, not like a different disease entity.

Therefore, this extremely uncommon with an uncertain nosology and interesting clinical entity needs further research to arrive at a meaningful conclusion.

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