FROM UNILATERAL LIMB WEAKNESS TO GAIT INSTABILITY AND INVOLUNTARY MOVEMENTS – A UNIQUE CASE OF HEMIPLEGIC VARIANT OF AMYOTROPHIC LATERAL SCLEROSIS

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Abstract

Motor neuron disease comprises progressive neurodegenerative disorders affecting upper and lower motor neurons. Mills' syndrome, the hemiplegic variant of amyotrophic lateral sclerosis, is a rare phenotype characterized by unilateral spastic hemiparesis without sensory deficits. We report a 50-year-old woman with a two-year history of progressive left-sided motor impairment, initially presenting with lower back pain followed by stiffness and weakness, leading to severe gait impairment. Neurological examination revealed spastic hemiparesis, hyperreflexia, and preserved sensory function. Magnetic resonance imaging and cerebrospinal fluid analysis were normal. Electromyography demonstrated widespread chronic neurogenic changes, while other investigations excluded alternative diagnoses. These findings support the diagnosis of the hemiplegic variant of ALS (Mills' syndrome).

Keywords: Amyotrophic lateral sclerosis, Mills Syndrome, magnetic resonance imaging.

Introduction

Motor neuron disease encompasses a spectrum of progressive neurodegenerative disorders involving upper motor neurons (UMNs) in the motor cortex and lower motor neurons (LMNs) in the brainstem and spinal cord [1,2]. Amyotrophic lateral sclerosis (ALS) is the most common form, typically characterized by a combination of UMN and LMN signs in multiple body regions [1,3]. Mills' syndrome, also referred to as the hemiplegic variant of ALS, represents a rare and atypical phenotype marked by slowly progressive unilateral spastic hemiparesis, often ascending or descending in distribution, without sensory deficits [4,5]. Because of its asymmetric presentation and relatively slow progression, it frequently poses a diagnostic challenge and requires extensive exclusion of structural, inflammatory, infectious, metabolic, and neoplastic causes [2,6].

We present a case illustrating the clinical and electrophysiological features of this rare ALS variant.

Case Presentation

A 50-year-old woman presented with a two-year history of progressive motor impairment. The onset was marked by lower back pain associated with sweating and fever. Shortly thereafter, she developed pain in the left leg, followed within days by stiffness and progressive weakness. Walking became increasingly difficult, eventually progressing to near inability to ambulate independently. Initial treatment with analgesics and corticosteroids did not result in clinical improvement. Over the subsequent six months, her condition deteriorated significantly. She developed severe difficulty climbing and descending stairs, impaired balance, frequent falls, clumsiness, and involuntary movements of the left arm. Fine motor control of the left hand became impaired. The patient denied paresthesias or sensory disturbances and maintained full urinary continence throughout the disease course. She reported intermittent muscle twitching around the left knee and left shoulder, as well as a sensation of tightness in the left scapular region.

Neurological assessment revealed:
Spastic weakness in the left upper and lower limbs
Spastic hypertonia in the left leg
Exaggerated patellar and Achilles reflexes
Positive Babinski sign on the left
Foot clonus on the left
Pseudoathetosis of the left hand
Spastic-paretic gait with circumduction of the left leg
All sensory modalities were intact. Cognitive function was preserved. The clinical course of the disease is summarized in Table 1.

Table 1. Timeline of Disease Progression

Time	Clinical events
Onset	Lower back pain associated with sweating and fever
Few days later	Pain in the left leg followed by stiffness and progressive weakness
Following months	Progressive difficulty walking
6 months	Impaired balance, frequent falls, difficulty climbing and descending stairs
Later course	Involuntary movements of the left arm and impaired fine motor control
At presentation	Severe gait impairment and spastic hemiparesis

Investigations

Laboratory Studies:
Routine biochemical analyses, tumor markers, thyroid hormone levels, virusologic serology, antinuclear antibodies and paraneoplastic antibodies testing were within reference ranges.
Lumbar puncture with cytochemical, virological, and immunological cerebro-spinal fluid (CSF) analysis yielded normal results.
Neuroimaging:
Magnetic resonance imaging (MRI) of the cervical and thoracolumbar spine demonstrated disc herniations at the C6/C7 and T7/T8 levels without evidence of myelopathy.
MRI of the brain with intravenous contrast was normal.
To exclude lumbosacral plexopathy of compressive or infiltrative origin, computed tomography (CT) of the abdomen and pelvis was performed and revealed no abnormalities.
A blood analysis revealed paraproteinemia.

Electrophysiological Studies:
Initial EMG suggested chronic radicular lesions of moderate severity involving C4–C7 and L4–L5–S1 roots bilaterally. A repeat EMG demonstrated widespread chronic neurogenic changes:
Left m. extensor digitorum brevis**:** rare fibrillations and severe chronic neurogenic lesion with rare remaining motor units
Right side**:** pronounced denervation activity at rest with severe chronic neurogenic changes
Bilateral m. tibialis anterior**:** frequent fibrillations and positive sharp waves; repetitive high-frequency discharges on the left
Bilateral m. vastus medialis**:** denervation activity and high-frequency discharges; occasional fasciculations on the right

Left arm muscles**:** increased insertional activity with rare fibrillations; moderate-to-severe chronic lesion in m. abductor pollicis brevis
Trunk muscles**:** increased insertional activity, otherwise unremarkable
These findings indicated widespread chronic neurogenic changes of varying severity.
Motor evoked potentials showed reduced amplitudes in the left median, ulnar, peroneal, and tibial nerves, and in the right tibial nerve. F-wave latency was prolonged in the left peroneal nerve. Sensory nerve conduction parameters were within physiological limits.
Genetic testing for spinocerebellar ataxias was negative.

Table 2. Summary of Clinical and Diagnostic Findings

Category	Findings
Motor	Progressive unilateral spastic hemiparesis
Reflexes	Hyperreflexia, Babinski sign, clonus
Sensory	Intact
MRI	No myelopathy
CSF	Normal
EMG	Widespread chronic denervation
Other findings	Paraproteinemia

Differential Diagnosis

Given the unilateral presentation and spastic features, the patient was initially evaluated for:
Cervical or thoracic myelopathy
Radiculopathy
Lumbosacral plexopathy
Inflammatory or infectious myelitis
Paraneoplastic syndromes
Spinocerebellar ataxias
Neuroimaging excluded compressive or structural myelopathy. CSF analysis showed no inflammatory or infectious process. Genetic testing ruled out spinocerebellar ataxias. Sensory nerve conduction studies were normal, arguing against peripheral neuropathy or plexopathy.
The progressive course, absence of sensory deficits, and combination of UMN signs with EMG-confirmed chronic denervation ultimately supported a motor neuron disease.
The differential diagnosis and reasons for exclusion are summarized in Table 3.

Table 3. Differential Diagnosis and Exclusion Criteria

Condition	Reason for Consideration	Reason for Exclusion
Cervical/thoracic myelopathy	Spastic weakness and gait impairment	No spinal cord compression on MRI
Radiculopathy	Initial pain and disc herniation	Symptoms extend beyond single root distribution
Lumbosacral plexopathy	Lower limb weakness	Normal sensory conduction studies
Inflammatory/infectious myelitis	Subacute onset with systemic symptoms	Normal CSF findings
Paraneoplastic syndrome	Presence of paraproteinemia	Negative paraneoplastic antibodies and imaging
Spinocerebellar ataxia	Gait disturbance	Negative genetic testing

Discussion

This case demonstrates a rare hemiplegic presentation of ALS consistent with Mills' syndrome [4,5]. The defining features include progressive unilateral spastic hemiparesis, preservation of sensory function, and electrophysiological evidence of widespread lower motor neuron involvement [5,7]. The early presentation with back and limb pain may have contributed to initial consideration of radiculopathy or disc disease, particularly given the MRI findings of disc protrusions. However, the absence of myelopathic changes and the progressive involvement beyond a single root distribution argued against a purely compressive etiology [2,6].

The widespread chronic neurogenic changes on EMG, combined with reduced motor evoked potentials and preserved sensory conduction, are characteristic of ALS and are emphasized in current electrophysiological diagnostic frameworks [3,8]. The slow progression and hemibody predominance align with previously described cases of Mills' variant [4,5].

The presence of paraproteinemia is noteworthy but, in the absence of clinical or laboratory evidence of a plasma cell disorder causing neuropathy or myelopathy, was considered incidental [9]. This case further emphasizes the importance of considering atypical ALS variants in patients with asymmetric motor presentations.

Conclusion

This case highlights the diagnostic challenges posed by unilateral, slowly progressive motor symptoms. Comprehensive clinical, radiological, laboratory, and electrophysiological evaluations excluded alternative etiologies. The combination of progressive unilateral spastic hemiparesis, preserved sensory function, and widespread chronic denervation supported the diagnosis of the hemiplegic variant of ALS (Mills' syndrome) [4,5].

Early recognition of this rare phenotype is crucial for appropriate counseling, monitoring, and management [1,3].

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