Electro Clinical Profiles of Motor Neuron Disease and Atypical Motor Neuron Disorders: A Case Series

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Abstract
Amyotrophic lateral sclerosis (ALS) is the commonest MND phenotype. Although many of the atypical motor neuron disorders share some features with ALS, they often can be distinguished by their clinical and electrophysiologic characteristics. Here we present five different cases with varied clinical findings. All the patients were referred from outpatient department to neurophysiology laboratory where electrodiagnostic (EDX) correlations helped to come to a conclusion. The nerve conduction study protocol for a suspected atypical motor neuron disorder is the same as that for ALS. Akin to the nerve conduction studies, the EMG evaluation of patients with suspected atypical motor neuron disorders is similar to that of ALS. An extensive study is indicated, often of all four limbs, the paraspinal muscles, and the bulbar muscles to reach a possible diagnosis. History, clinical findings and electrophysiologic correlation often help to differentiate these atypical motor neuron disorders. Correct diagnosis is needed for further evaluation and prognosis. In this case series five (5) cases have described who are referred from outpatient department to neurophysiology laboratory for electrodiagnostic (EDX) correlations. [Journal of National Institute of Neurosciences Bangladesh, 2017;3(1): 57-61]

Keywords: Motor Neuron Disease; MND; Atypical Motor Neuron Disorders; Electrodiagnostic test; EDX; Amyotrophic lateral sclerosis; ALS

Introduction
Motor neuron disease (MND) encompasses a group of rapidly progressive and universally fatal neurodegenerative disorders of the human motor system. Amyotrophic lateral sclerosis (ALS) is the commonest MND phenotype. In addition, the varied clinical presentations of MND also include (i) progressive muscle atrophy (PMA,
10% of MND cases), a clinically pure lower motor neuron (LMN) phenotype, (ii) primary lateral sclerosis (PLS, 1-3% of MND cases), a clinically pure upper motor neuron (UMN) phenotype and (iii) progressive bulbar palsy (PBP, 1-2% of MND cases), an isolated bulbar phenotype with relative preservation of spinal motor neurons. More recently, an association between ALS and fronto-temporal degeneration (FTD) has been established.

There are a heterogeneous group of motor neuron disorders that are rare but nonetheless important to recognize, because they often can mimic the presentation of amyotrophic lateral sclerosis (ALS). These often are referred to as atypical motor neuron disorders. Although many of the atypical motor neuron disorders share some features with ALS, they often can be distinguished by their clinical and electrophysiologic characteristics. Multifocal motor neuropathy with conduction block, Kennedy’s disease, spinal muscular atrophy (SMA), Monomelic amyotrophy often have predominantly lower motor neuron signs. Positive family history is found in Familial amyotrophic lateral sclerosis, spinal muscular atrophy and hereditary spastic paraplegia. Post-poliomyelitis syndrome occurs in at least one fourth of previously infected patients, usually 25 to 30 years after the attack of acute poliomyelitis. Despite the clinical heterogeneity, median survival of MND remains three years, although the atypical phenotypes exhibit a longer survival. In this case series five (5) cases have described who are referred from outpatient department to neurophysiology laboratory for electrodiagnostic (EDX) correlations.

Case Presentation 1
A 65 year old man was presented with progressive weakness and wasting of all four limbs with bilateral foot drop for 2 years. Neither the patient had any sensory complaints nor any complaints related to bladder and bowel. The patient also had fasciculation; prominent wasting of muscles of all limbs, exaggerated deep tendon reflexes, both limbs (B/L) foot drop with preserved sensory function. Motor NCS revealed reduced CMAP amplitude of all studied nerves with preserved SNAPs. Needle EMG showed features of denervation and reinnervation of sampled muscle of both upper and lower limbs including bulbar and paraspinal. The findings are consistent with Motor neuron disease their axons or both (ALS).

Case Presentation 2
A 46 year old man was referred with the complaints of weakness and wasting of left lower limb for 15 years. Recently he developed pain and weakness of right lower limb along with deterioration of left lower limb. The patient had history of Poliomyelitis in his childhood. He had distal wasting of lower limbs with reduced deep tendon reflexes. Motor and sensory NCS findings were normal. However EMG showed giant polyphasic, long duration, high amplitude MUAPs with reduced recruitment of sampled muscle of left lower limb.

Figure 1a: Muscle wasting in Post-polio syndrome

Figure 1b: Giant MUAPs in Postpolio syndrome
limb as well as some of the muscles of right lower limb. These findings were consistent with Post-Polio Syndrome (Figure I).

Case Presentation 3
Two (2) years old developmentally delayed girl of consanguineous parents was referred to neurophysiology laboratory with the complaints of weakness and gradual wasting of all 4 limbs, feeding difficulties and history of repeated respiratory tract infection for 9 months. On examination, the child was well alert but had hypotonia, hypoflexia, symmetrical muscle wasting with intact sensory function. NCS revealed reduced CMAP amplitude in all studied nerves. Needle EMG showed features of denervation and reinnervation with reduced recruitment of the sampled muscle in both upper and lower limbs. These findings were consistent with Disease of motor neuron, their axon or both (Anterior horn cell disease? SMA).

Case Presentation 4
A 60 year old male presented with gradual onset and progressive difficulty in swallowing and nasal intonation of speech for 1 year. The patient also had generalized muscle wasting along with twitching from same duration. On examination, the patient was grossly emaciated having bilateral gynaecomastia, nasal speech, wasted tongue with fasciculation and absent gag reflex. The case also had postural tremor, generalized muscle wasting predominantly involving proximal muscle with flaccid quadriplegia. CK level was moderately elevated. NCS revealed reduced CMAP amplitude in motor nerves and absent SNAPs with neuropathic MUAPs on needle EMG. Kennedy’s disease was diagnosed based on typical history, findings and EDX (Figure II).

Case Presentation 5
A 20 year old male was presented with weakness and wasting of right upper limb for 8 months which was gradually progressing. There was wasted small muscles of hand with preserved deep tendon reflexes and sensory function. On EDX testing, CMAP amplitude was reduced in right median and ulnar nerves with preserved SNAPs. Needle EMG found increased spontaneous activities with neuropathic MUAPs of sampled muscles innervated by C 8-T1. The findings were consistent with segmental anterior horn cell disease affecting the C8-T1 segment on right side (Monomelic Amyotrophy).

Discussion
When evaluating the patient with ALS/MND, the neurologist must consider a number of other motor neuron disorders and related motor syndromes that may have clinical features resembling ALS/MND. In addition, certain motor syndromes, such as monomelic amyotrophy, postpolio muscular atrophy, Kennedy’s disease, Spino muscular atrophy and multifocal motor neuropathy, can clinically mimic ALS/MND. Therefore, not only may the diagnosis of ALS/MND be clinically missed in the early stages, but worse, the patient may be wrongly labeled as having ALS/MND. In this case series, all patients were referred from outpatient department to neurophysiology laboratory where electrodiagnostic (EDX) correlations helped to come to a conclusion. The diagnosis of ALS depends upon the recognition of a characteristic constellation of symptoms and signs 7,11 and supportive
Table 1: Age distribution of the study patients (n=31)

<table>
<thead>
<tr>
<th>Number</th>
<th>Diagnosis</th>
<th>Predominant clinical feature</th>
<th>EDX findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>Amyotrophic lateral sclerosis</td>
<td>Wasting of muscles of all limbs, exaggerated deep tendon reflexes, fasciculation, B/L foot drop</td>
<td>Reduced CMAP amplitude, Preserved SNAPs, EMG - features of denervation and reinnervation</td>
</tr>
<tr>
<td>Case 2</td>
<td>Post-Polio Syndrome</td>
<td>History of Poliomyelitis Recently developed pain and weakness of right lower limb along with deterioration of left lower limb</td>
<td>EMG - giant polyphasic, long duration, high amplitude MUAPs with reduced recruitment of muscle of left lower limb as well as right lower limb.</td>
</tr>
<tr>
<td>Case 3</td>
<td>Anterior horn cell disease ? SMA</td>
<td>Developmental delay Parental consanguinity, feeding difficulties, hypotonia, hypoflexia, symmetrical muscle wasting.</td>
<td>Reduced CMAP amplitude, Preserved SNAPs, EMG-features of denervation and reinnervation</td>
</tr>
<tr>
<td>Case 4</td>
<td>Kennedy’s disease</td>
<td>Difficulty in swallowing and nasal intonation of speech, generalized muscle wasting, flaccid quadriplegia, bilateral gynaecomastia, wasted tongue with fasciculation and absent gag reflex</td>
<td>NCS - reduced CMAP amplitude in motor nerves, Absent SNAPs, Neuropathic MUAPs on needle EMG</td>
</tr>
<tr>
<td>Case 5</td>
<td>Monomelic Amyotrophy</td>
<td>Weakness and wasting of right upper limb, wasted small muscles of hand with preserved deep tendon reflexes</td>
<td>Reduced CMAP amplitude, Preserved SNAPs, Neuropathic MUAPs of muscles innervated by C 8-T1 on needle EMG</td>
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Mentioned electrophysiological findings. The combination of lower motor neuron (LMN) weakness and muscle atrophy that crosses both peripheral nerve and myotomal distributions and that is accompanied by upper motor neuron (UMN) spasticity and hyperreflexia in a middle-aged or elderly person is most often due to ALS. There are other potentially treatable disorders, which can mimic the clinical signs, electrophysiologic findings, or both in ALS and its variants like coexistent cervical and lumbar radiculopathy. The motor nerve conduction studies are identical in both, either are normal or show evidence of axonal loss. SNAPs are spared in both case. The only difference is involvement of the thoracic paraspinous muscles in Polyradiculopathy on EMG is rare. Atypical motor neuron disorders often make confusion with MND, radiculopathy, peripheral neuropathy, distal myopathy and many more. The nerve conduction study and EMG protocol for a suspected atypical motor neuron disorder are the same as that for ALS. The most important reason to perform motor nerve conduction studies is to look for CMAP amplitude and conduction block. Sensory nerve conduction studies are always normal in ALS unless the patient has a superimposed disorder like diabetes mellitus. Abnormal sensory conduction studies are often seen in Kennedy’s disease. Akin to the nerve conduction studies, the EMG evaluation of patients with suspected atypical motor neuron disorders is similar to that of ALS. An extensive study is indicated, often of all four limbs, the paraspinous muscles, and the bulbar muscles to reach a possible diagnosis.

Conclusions

Motor neuron disorders appear to be a clinically heterogeneous disorder with varied clinical presentation encompassing a range of upper or lower motor neuron dysfunction or both. History, clinical findings and electrophysiological correlation often help to differentiate these disorders. Correct diagnosis is needed for further evaluation and prognosis.

References

neurodegenerative disorders of the human motor

Introduction

MND remains three years, although the atypical
Despite the clinical heterogeneity, median survival of
sclerosis, spinal muscular atrophy and hereditary spastic
atrophy (SMA), Monomelic amyotrophy often have
motor neurons. More recently, an association between
bulbar phenotype with relative preservation of spinal
bulbar palsy (PBP, 1-2% of MND cases), an isolated
motor neuron (UMN) phenotype and (iii) progressive
neuron (LMN) phenotype, (ii) primary lateral sclerosis
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characteristics4. Multifocal motor neuropathy with
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These often are referred to as atypical motor neuron

The patient had history of Poliomyelitis in his
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weakness and wasting of left lower limb for 15 years.
NCS revealed reduced CMAP amplitude in motor
wasting predominantly involving proximal muscle with
findings were consistent with Disease of motor neuron,
and reinnervation with reduced recruitment of the
muscles to reach a possible diagnosis4.

There are other potentially treatable disorders, which
make confusion with MND, radiculopathy, peripheral
amyotrophy, postpolio muscular atrophy, Kennedy`s
addition, certain motor syndromes, such as monomelic
syndrome (Figure I).

A 20 year old male was presented with weakness and
preserved SNAPs. Needle EMG showed features of
denervation lability with reduced recruitment of sampled muscle of left lower
findings were normal. However EMG showed giant
nerve fibers.运动神经营养 are consistent with segmental anterior horn cell
disease, Spino mascular atrophy and multifocal motor
amyotrophy, postpolio muscular atrophy, Kennedy`s
syndrome (Figure I).

Reference

3. El Escorial “Clinical Limits of Amyotrophic Lateral Sclerosis”
4. Preston D C, Shapiro B E. Electromyography and Neuromuscular
Disorders Clinical- Electrophysiological Correlations. Third edition
2013;417,432
5. Hardiman O, van den Berg LH, Kiernan MC. Clinical diagnosis and
management of amyotrophic lateral sclerosis. Nat Rev Neurol
2011;7:639-49
6. Ashok V, Walter G B. Atypical Motor Neuron Disease and Related
7. Brooks BR. El Escorial World Federation of Neurology criteria for
the diagnosis of amyotrophic lateral sclerosis. Subcommittee on Motor
Neuron Diseases/Amyotrophic Lateral Sclerosis of the World Federa-
tion of Neurology Research Group on Neuromuscular Diseases and the

11. Eisen A. Amyotrophic Lateral Sclerosis. Cambridge: Cambridge
University Press; 1998