PART III • Motor Neuron Disease

Amyotrophic Lateral Sclerosis 27 and its Variants

Electrodiagnostic (EDX) studies play a central role in the evaluation of patients with amyotrophic lateral sclerosis (ALS), the most common of all motor neuron disorders. Although described earlier by others, the French neurologist Jean-Martin Charcot is credited as naming the disorder amyotrophic lateral sclerosis in 1869. The name is derived from the Greek amyotrophic, which means "no nourishment to the muscle," lateral, which refers to the lateral area in the spinal cord where the corticospinal tract is located, and sclerosis, which describes the scarring in the spinal cord that occurs when motor neurons deteriorate. In the United States, ALS is commonly referred to as Lou Gehrig's disease, after the famous baseball player who died of the condition in 1941.

ALS is most often encountered as a sporadic, progressive, degenerative disorder of unknown etiology that characteristically affects both upper motor neurons (UMNs) and lower motor neurons (LMNs) and spares sensory and autonomic function. A small number of cases of ALS (approximately 10%) are familial and are discussed in Chapter 28. In addition, several variants of ALS are well recognized, including progressive bulbar palsy, progressive muscular atrophy (PMA), and primary lateral sclerosis (PLS). Other less common motor neuron disorders exist, including those with atypical motor neuron manifestations caused by genetic mutations, infections, and immunologic disorders (see Chapter 28). Because the prognosis in ALS is uniformly poor compared with other motor neuron disorders, it is essential that the correct diagnosis be reached.

Electromyography (EMG) and nerve conduction studies are most often used to support the diagnosis of ALS. More importantly, however, they are used to help exclude other conditions, some potentially treatable, which may mimic ALS.

Nowhere else is the clinical-electrophysiologic correlation more important than in ALS. EDX studies, by themselves, cannot make a diagnosis of ALS. Rather, ALS remains a clinical diagnosis supported by EDX findings. The electromyographer must appreciate that other disorders may display EDX findings similar to those found in ALS (e.g., coexistent cervical and lumbar radiculopathy) and that it is the combination of clinical and EDX findings that allows a final diagnosis to be reached.

CLINICAL

Classic Amyotrophic Lateral Sclerosis

ALS is a degenerative, progressive disorder that affects both UMNs and LMNs. Although younger patients may be affected, it occurs most frequently in those 55 to 60 years old, with a slight male predominance. Signs and symptoms of LMN dysfunction include muscle atrophy, weakness, fasciculations, and cramps. UMN dysfunction manifests as stiffness, slowness of movement, spasticity, weakness, pathologic hyperreflexia, and Babinski responses. The presence of both UMN and LMN signs in the same myotome is characteristic of ALS. The mean duration of illness from symptom onset to death is approximately 3 years. However, it is important to remember that about 10% of patients follow a more benign course, surviving for many more years.

ALS is remarkably specific for the motor system. Although detailed pathologic studies have shown some minor loss of sensory fibers, it is distinctly unusual to see sensory complaints or findings on examination. Likewise, there is no disturbance of vision, hearing or the autonomic system. Late in the course, spasticity can affect the bladder, creating symptoms of urinary urgency and frequency. Clinically, an association between abnormalities of cognition and ALS has been recognized in some patients, especially between ALS and Frontotemporal Dementia (FTD). This association is seen in both sporadic and familial forms of ALS and FTD. If patients with classic ALS undergo formal neuropsychological testing, some 40-50% will display some mild evidence of executive dysfunction. FTD develops in approximately 5 to 15% of patients with ALS, and conversely, 10–15% of FTD patients show an associated motor neuron syndrome. Most often, ALS is a regional disease that usually starts in one body segment and progresses to adjacent myotomes. Most cases begin with insidious weakness in either a distal upper or lower extremity. In the upper extremity, the initial presentation can mimic an ulnar neuropathy, especially one at the wrist. In the lower extremity, the presentation is often a progressive foot drop, sometimes misdiagnosed as a peroneal palsy or L5 radiculopathy. As time progresses, symptoms develop in

adjacent myotomes of the same limb and then spread to the contralateral limb. Progression continues to other extremities and ultimately to bulbar and respiratory muscles. Death usually results from respiratory insufficiency or from medical complications of prolonged inactivity (pulmonary embolus, sepsis, pneumonia, etc.).

The El Escorial criteria are most often quoted in reaching a diagnosis of ALS. These criteria were set by the World Federation of Neurology meeting in El Escorial, Spain, and published in 1994. They identify four separate body part regions: craniobulbar, cervical, thoracic and lumbosacral. Definite ALS requires that both UMN and LMN signs be seen together in at least three of these regions. Probable ALS requires UMN and LMN signs in two regions, with some UMN signs rostral to the LMN signs. Possible ALS requires UMN and LMN signs in one region or UMN signs in at least two regions. In addition to these criteria, there must be an absence of EDX, pathologic, or radiologic evidence that would support the diagnosis of another disease that may mimic ALS.

Patients with a typical ALS presentation including diffuse atrophy, weakness, fasciculations, and spasticity, in the appropriate age group and clinical setting, are relatively easy to identify. However, not all cases are straightforward, especially when patients present early in the illness with signs and symptoms that are anatomically restricted. In addition, several variants within the spectrum of classic ALS can present diagnostic problems (discussed in the following sections).

Progressive Bulbar Palsy

Patients with progressive bulbar palsy initially develop symptoms restricted to the bulbar muscles. They usually present with a several month history of progressive dysarthria with gagging, choking, and weight loss. The speech disturbance may lead to complete anarthria. These patients are commonly incorrectly diagnosed, and many undergo exhaustive ear, nose, and throat or gastrointestinal evaluations looking for the cause of dysarthria or dysphagia. Occasionally, patients may present with respiratory distress as the result of aspiration. Speech is most commonly slow and spastic with variable flaccid features, depending on the degree of LMN dysfunction. The tongue may be atrophied with fasciculations, accompanied by brisk jaw, gag, and facial reflexes (Figure 27–1). One of the characteristic signs is the "napkin or handkerchief sign." Because of excessive drooling from bulbofacial weakness, patients often carry a tissue in their hand to frequently clear their mouth and face of saliva. Occasionally the symptoms remain relatively restricted to the bulbar muscles. However, in the vast majority of patients the disorder eventually progresses to involve the limbs, as in typical ALS. Indeed, approximately 25% of patients with ALS will have the bulbar onset form.

Progressive Muscular Atrophy

Approximately 15% of patients with sporadic motor neuron disease present with a pure LMN syndrome referred to as

FIGURE 27-1 Tongue atrophy. One of the important findings in ALS is the presence of bulbar muscle weakness. The tongue is commonly affected in ALS. Typical lower motor neuron signs include atrophy, fasciculations and weakness; upper motor neuron dysfunction can also be discerned as difficulty moving the tongue

quickly from side to side. In the photo, note the prominent atrophy of

the tongue, especially on the left lateral side.

progressive muscular atrophy. These patients have distal limb wasting and weakness, fasciculations, and cramps, with no sensory symptoms or signs. Reflexes may be present but are generally reduced or absent in weak limbs. The clinical course is commonly long, with slow progression to proximal limb muscles. Bulbar involvement is unusual, occurring very late if at all. Unequivocal UMN dysfunction is not present, although some patients have retained or slightly brisk reflexes that appear inappropriate for the level of limb weakness and atrophy. Of all the ALS variants, progressive muscular atrophy is the one that especially warrants thorough evaluation to exclude other disorders, in particular multifocal motor neuropathy with conduction block (MMNCB, discussed in the section on Differential Diagnosis), which is potentially treatable.

Primary Lateral Sclerosis

Primary lateral sclerosis is a very rare disorder marked by progressive and selective UMN involvement with sparing of the LMNs. It accounts for less than 1% of patients with an acquired motor neuron disorder. The disorder is characterized by spasticity, weakness, pathologically increased reflexes, Babinski signs, and pseudobulbar speech and affect. Atrophy (except due to disuse), fasciculations, or other LMN signs are not seen. The disease commonly presents as a progressive paraplegia or quadriplegia. Occasionally, patients present with progressive bulbar weakness of the spastic type, or hemiplegia. The course tends to be prolonged, with a better prognosis than classic ALS. Some patients may live for decades after the onset of the illness.



Flail Arm and Flail Leg Syndromes

The flail arm (FA) and flail leg (FL) phenotypes have been recognized for over a century, but have recently been studied in more detail. The FA syndrome has gone by many names, including the scapulohumeral variant of progressive muscular atrophy, the hanging arm syndrome, and the manin-the-barrel syndrome. It presents with progressive weakness and wasting of both upper extremities, is often symmetric, and may affect proximal before distal muscles. However, there is little to no involvement of the lower extremities or bulbar muscles. Males are affected out of proportion to females (ratio 4:1). Many patients remain ambulatory for years. In a similar vein, FL syndrome (also known as the pseudopolyneuritic variant of ALS) presents with wasting and weakness of the lower extremities. UMN signs are either absent, subtle or occur late in the course. Unlike FA syndrome, FL syndrome shows no predilection for males over females. FA and FL syndrome often remain restricted to the upper or lower extremities, respectively, typically for 1 to 3 years.

Both the FA and FL presentations have important prognostic implications. Both progress very slowly and have significantly higher 5-year survival rates than classic limb onset ALS (FA: 52%; FL 64%; classic ALS: 20%). By 10 years out, however, the survival rates for FA and FL are similar to classic ALS.

ETIOLOGY

The etiology of sporadic motor neuron disorders is unknown. Immunologic, infectious, and excitotoxic etiologies have been speculated, but none have been proven. As new gene mutations associated with familial ALS are discovered, genetic screening of patients with sporadic ALS shows a very small percent of those patients have one of the genetic mutations associated with familial ALS.

DIFFERENTIAL DIAGNOSIS

The diagnosis of ALS usually is straightforward in patients who present with prominent UMN and LMN signs in both limb and bulbar muscles. However, most patients initially are seen early in the course of the disease, often when only one extremity is clinically affected. In addition, there are other disorders, some potentially treatable, which can mimic the clinical signs, electrophysiologic findings, or both in ALS and its variants (Box 27-1; also see Chapter 28). These disorders are discussed in detail later. In the case of classic ALS, the most important diagnosis to consider is coexistent cervical and lumbar stenosis. For PMA or predominantly LMN presentations of ALS, including the flail arm and flail leg syndromes, the most important diagnoses to consider are demyelinating motor neuropathy, especially MMNCB, and inclusion body myositis (IBM). In addition, benign fasciculation syndrome (BFS) and the myotonic disorders need to be kept in mind. In PLS, there is a large list

Box 27–1. Differential Diagnosis of Motor Neuron Disease

of neurologic conditions that can be confused with the disorder and need to be excluded by appropriate imaging and other laboratory testing (see the section on Primary Lateral Sclerosis below).

Cervical/Lumbar Stenosis

Degenerative disease of the neck and back is extremely common, especially in older individuals. The combination of cervical and lumbar spondylosis occasionally can mimic ALS, both clinically and in the EMG laboratory. Cervical spondylosis, by itself, is a common cause of gait disturbance in the elderly. Compression in the cervical area can result in a polyradiculopathy involving the cervical nerve roots as well as a myelopathy from direct cord compression. This can create a clinical picture of LMN dysfunction in the upper extremities and UMN dysfunction in the lower extremities (Figure 27-2). If additional compression occurs above the C5 level, UMN signs can be seen in the upper extremities as well. To complicate the situation further, patients with coexistent lumbar stenosis may have additional LMN signs in the lumbosacral myotomes. Taken together, the clinical picture can resemble ALS.

However, several points in the history and on the neurologic examination should raise the question of possible

FIGURE 27-2 Cervical spondylosis. In the differential diagnosis of amyotrophic lateral sclerosis, one of the most important diagnoses to exclude is cervical spondylosis. Compression of the cervical nerve roots (left, arrow) results in a polyradiculopathy while direct cord compression (right, arrow) results in a myelopathy. This can create a clinical picture of lower motor neuron dysfunction in the upper extremities and upper motor neuron dysfunction in the lower extremities. If additional compression occurs above the C5 level, upper motor neuron signs can be seen in the upper extremities as well.



cervical or lumbar (or combined) stenosis. Cervical stenosis often follows a stepwise progression, sometimes associated with periods of improvement. In addition, there is usually some neck or radicular pain, along with limitation of neck motion and sensory symptoms in the arms. Paresthesias and vibratory loss in the lower extremities may occur as a result of posterior column compression. A Romberg sign may be present. Back pain commonly accompanies coexistent lumbar stenosis. Moreover, increased pain or sensory disturbance may develop after walking a distance, which is relieved only by the sitting position.

The signs and symptoms noted above will usually suggest the diagnosis of cervical and lumbar stenosis. However, occasionally a patient with cervical and lumbar stenosis presents with a relatively pure motor syndrome consisting of muscle weakness, atrophy, and spasticity, making the clinical distinction from ALS difficult. It is in these patients that the clinical and EMG evaluation of the bulbar and thoracic paraspinal muscles assumes special significance, because they should never be abnormal in lesions restricted to the cervical or lumbar spine (see Chapter 26).

Multifocal Motor Neuropathy with Conduction Block

An important condition that can mimic the PMA presentation of ALS clinically is demyelinating motor neuropathy. Nearly all peripheral neuropathies have both sensory and motor symptoms and signs; therefore, they are not frequently confused with ALS. Very few neuropathies, however, are purely or predominantly motor. Of those, most are demyelinating and are believed to be immune mediated. Although the exact pathophysiology is not understood, presumably some component of motor nerve or myelin is selectively targeted by the immune system, leading to motor dysfunction. It is in these circumstances that a motor neuropathy may be mistaken for a motor neuronopathy (i.e., motor neuron disease). Although it is quite rare, the motor neuropathy that must be excluded. especially in patients with predominantly LMN dysfunction, is MMNCB (see Chapter 26).

MMNCB usually affects only motor fibers, sparing sensory fibers. It often is slowly progressive and begins distally, like ALS. In addition, fasciculations and cramps are common. Unlike ALS, however, it more commonly affects younger patients (<45 years) and has a strong male predominance (male-to-female ratio of approximately 2:1). Several important clues may suggest MMNCB on examination. Often, individual motor nerves are affected out of proportion to adjacent nerves that have the same myotomal innervation (hence, multifocal motor neuropathy). For instance, severe weakness in distal median-innervated muscles with relative sparing of ulnar-innervated muscles might occur in MMNCB, but would be very unusual in ALS, marking the disorder as a motor nerve rather than a motor neuron disorder. Second, muscle weakness may appear out of proportion to muscle atrophy in MMNCB. especially early in the course of the disease, reflecting that demyelination, not axonal loss, is the major underlying pathology. Finally, MMNCB does not result in any UMN dysfunction. Reflexes usually are depressed or normal. Pathologic hyperreflexia, spasticity, and Babinski signs are not seen.

The diagnosis of MMNCB may be suggested by the clinical presentation as well as by elevated titers of antiganglioside antibodies, which occur in more than half of patients. Most often, MMNCB is diagnosed through nerve conduction studies, which show evidence of conduction block along motor fibers, between distal and proximal segments. It is extremely important not to miss this diagnosis because the prognosis for these patients is far better than for patients with ALS. Most patients with MMNCB respond well to immune-modulating therapy, especially treatment with intravenous immunoglobulin.

Inclusion Body Myositis

IBM is an idiopathic inflammatory disorder of muscle that can be confused clinically and sometimes electrically with the PMA variant of ALS. IBM is now the most common inflammatory myopathy in individuals older than 50 years. Clinically, IBM presents as slowly progressive weakness. It is more common in men than in women. Along with proximal muscle weakness, distal muscles are commonly involved. In some patients, the distal muscles are weaker than the proximal ones. Although the distribution of weakness most commonly is symmetric, asymmetric presentations often occur. The disease has a predilection for certain muscles, including the iliopsoas, quadriceps, tibialis anterior, biceps, triceps, and long finger flexors. Prominent muscle atrophy, especially of the quadriceps, is common. Facial and ocular weakness does not occur. However, dysphagia is common. The deep tendon reflexes tend to be depressed or absent early in the course, especially the quadriceps reflex. Patients with IBM and severe distal and proximal weakness and wasting, with depressed reflexes, can easily be mistaken for an LMN disease such as PMA.

Unfortunately, the electrophysiology often complicates the diagnosis of IBM. Prominent fibrillation potentials and positive sharp waves are common. Motor unit action potentials (MUAPs) can be small and short, typical of a myopathy; large and long, suggestive of a neuropathic process; or a combination of both. Although large, long duration MUAPs are classically associated with neuropathic disorders, they are also seen in chronic myopathies, especially in those associated with denervation (i.e., usually myopathies with inflammatory or necrotic features).

One of the key differentiating features between LMN disease and IBM is the presence of fasciculations and cramps. Both fasciculations and cramps are neuropathic phenomena; they are not seen in any myopathy, including IBM. In the absence of fasciculations and cramps in a patient with a LMN syndrome, muscle biopsy sometimes is needed to make the differentiation between a motor neuron disorder and IBM.

Benign Fasciculation Syndrome

Fasciculations are noted in nearly all individuals and are a benign phenomenon. However, because of the wellrecognized association of fasciculations and ALS, some people, especially medical personnel or those with a family member with ALS, are more likely to be concerned about fasciculations and bring them to medical attention. The vast majority of persons who experience fasciculations have no neurologic disease. BFS is diagnosed in those individuals who have frequent fasciculations beyond what is normally experienced and have normal neurologic and EMG examinations (except for fasciculations). In some patients with BFS, there may be accompanying fatigue, cramps, and exercise intolerance. In extensive follow-up studies, no patient with BFS developed ALS or any other significant neurologic disorder. It is important to reassure patients with BFS that they have no greater risk of developing motor neuron disease than any other individual.

Myotonic Syndromes

Patients with one of the myotonic syndromes (see Chapter 36) typically are not confused clinically with ALS or other motor neuron disorders. However, occasional patients have

been given the diagnosis of motor neuron disease erroneously, based on an electromyographer misinterpreting myotonic discharges as denervating potentials (fibrillation potentials and positive sharp waves). A myotonic discharge is the spontaneous discharge of a muscle fiber (similar to fibrillation potentials and positive sharp waves) but is differentiated by its characteristic waxing and waning of both amplitude and frequency. On EMG, myotonic discharges have a characteristic "revving engine" sound due to the waxing and waning of amplitude and frequency. The error in interpretation occurs because both have the same basic morphology as both are generated in muscle fiber, and denervating potentials are common whereas myotonic discharges are uncommon in clinical practice. However, once the waxing and waning sound of myotonic discharges is recognized, the differentiation is easily made.

Primary Lateral Sclerosis Mimics

There are a large number of neurologic conditions that can present with UMN symptoms and signs similar to PLS. Most can be excluded by brain and cervical spine imaging. Occasionally, brain imaging will demonstrate abnormalities consistent with PLS. In these cases, abnormal T2 or fluidattenuated inversion recovery (FLAIR) signals restricted to the corticospinal tracts will be seen on magnetic resonance imaging (Figure 27–3). However, imaging is usually indicated primarily to help exclude certain disorders such as multiple sclerosis, multiple infarcts, cervical spondylosis, syringomyelia, Chiari malformation, compressive foramen magnum lesions, and spinal cord tumors, all of which may be confused with PLS.

In addition, some cases of familial spastic paraparesis (Strümpell disease) and adrenomyeloneuropathy may be difficult to differentiate from primary lateral sclerosis without an accurate family history and, in the case of adrenomyeloneuropathy, a blood assay for very long chain fatty acids. Many forms of familial spastic paraparesis can be definitively diagnosed through commercially available genetic testing. Tropical spastic paraparesis resulting from human T-lymphotropic virus type 1 (HTLV-1) may be difficult to differentiate from PLS, although these patients often have minor sensory loss in the lower extremities. A blood assay for HTLV-1 antibodies confirms the diagnosis. Lastly, there are rare reports of patients with PLS- or ALSlike syndromes who are positive for the human immunodeficiency virus. When treated with antiviral therapy, their motor neuron syndrome either improved or recovered.

ELECTROPHYSIOLOGIC EVALUATION

Nerve Conduction Studies

It is essential to perform both motor and sensory nerve conduction studies in patients suspected of having ALS (Box 27–2). At a minimum, routine motor and sensory nerve conduction studies along with late responses should

FIGURE 27–3 Magnetic resonance imaging (MRI) and motor neuron disease. Axial fluid-attenuated inversion recovery (FLAIR) MRI at the level of the upper midbrain (left) and basal ganglia/ internal capsule (right) in a patient with primary lateral sclerosis. Note the abnormal signal in the cerebral peduncle and internal capsule bilaterally, corresponding to the location of the corticospinal tracts. Similar findings occasionally are present in patients with amyotrophic lateral sclerosis.



Box 27-2. Recommended Nerve Conduction Study Protocol for Motor Neuron Disease

Routine motor studies (ipsilateral to the most symptomatic side):

- 1. Median study, recording abductor pollicis brevis and stimulating the wrist and antecubital fossa
- 2. Ulnar study, recording abductor digiti minimi and stimulating the wrist and below and above the elbow
- 3. Ulnar study, recording first dorsal interosseous and stimulating the wrist and below and above the elbow
- 4. Peroneal study, recording extensor digitorum brevis and stimulating the ankle, below the fibular neck, and lateral popliteal fossa
- 5. Tibial study, recording abductor hallucis brevis and stimulating the ankle and popliteal fossa
- *Routine sensory studies (ipsilateral to the most symptomatic side):*
- 1. Median SNAP, stimulating the wrist and recording digit 2
- 2. Ulnar SNAP, stimulating the wrist and recording digit 5
- 3. Radial SNAP, stimulating the forearm and recording the snuffbox
- 4. Sural SNAP, stimulating the calf and recording posterior ankle
- Late responses (ipsilateral to the most symptomatic side):
- 1. F responses: median, ulnar, peroneal, and tibial
- 2. H reflexes

SNAP, sensory nerve action potential.

Special considerations:

- The yield of searching for conduction block increases as additional motor nerves or segments are studied. In selected patients, either the contralateral routine motor nerves can be studied or proximal stimulation studies can be performed (or both). The ulnar and median nerves can be stimulated with surface electrodes in the axilla and at Erb's point. Needle stimulation can be performed at the C8 root. Proximal tibial studies can be performed by needle stimulation at the gluteal fold and at the S1 root. Proximal stimulation studies have significant technical limitations.
- Contralateral motor studies should be considered, especially in patients with predominantly lower motor neuron syndromes without definite upper motor neuron signs. Proximal stimulation studies should also be considered in patients with predominantly lower motor neuron syndromes and in patients in whom the routine motor studies are normal but the late responses are abnormal, a pattern suggestive of a proximal lesion.
- Compute the amplitude ratios of the APB/ADM and FDI/ ADM. In some cases of ALS, the lateral hand is affected more than the medial hand. This results in an APB/ADM ratio <0.6 and an FDI/ADM ratio of <0.9. If both of these are abnormal, in the appropriate clinical setting, they are supportive of the diagnosis of ALS.

be performed in an upper and a lower extremity, preferably on the most symptomatic side, before proceeding to the needle EMG study.

Results of motor nerve conduction studies may be normal in ALS, especially in clinically unaffected limbs, but more often show evidence of axonal loss. Axonal loss results in similar changes on motor nerve conduction studies regardless of whether the lesion is at the level of the motor neuron, root, plexus, or peripheral nerve. Compound muscle action potential (CMAP) amplitudes decrease, whereas distal latencies and conduction velocities remain relatively intact. If the larger and faster motor axons are lost, some slowing of conduction velocity and distal latency may occur (Figure 27–4), although the slowing usually never reaches the unequivocal demyelinating range (i.e., conduction velocity <75% of the lower limit of normal; distal latency >130% of the upper limit of normal). It is not unusual to find some mild to moderate slowing of conduction velocity and distal latency, especially when CMAP amplitudes are very low.

Although not completely specific to ALS, one pattern that may be seen is the "split-hand syndrome," a term first coined by Wilbourn. In patients with ALS, muscle wasting may affect the lateral hand (thenar muscles and first dorsal FIGURE 27–4 Conduction velocity and distal latency in amyotrophic lateral sclerosis. Ulnar compound muscle action potential (CMAP) amplitude, recorded over hypothenar muscles and plotted against conduction velocity (top) and distal latency (bottom). Each dot represents a patient; the dark solid line shows the mean value. Note that both the mean conduction velocity and distal latency remain within the normal range but slow as CMAP amplitude decreases.

(Reprinted from Lambert EH. Electromyography in ALS. In: Norris HF Jr, Kurland LT, eds. Motor neuron diseases. New York: Grune & Stratton, 1969. With permission.)



interosseous) out of proportion to the medial hand (hypothenar) muscles. Similarly on nerve conduction studies, the motor amplitudes from the abductor pollicis brevis (APB) and first dorsal interosseous (FDI) may be decreased more than the amplitude from the abductor digiti minimi (ADM), though all three muscles are C8-T1 innervated. In one study, both the APB/ADM ratio and FDI/ADM ratios were lower in patients with ALS than controls. These ratios are calculated simply by measuring the amplitudes of the CMAPs of the APB, FDI, and ADM, during routine median and ulnar motor conduction studies. An APB/ADM ratio of <0.6 (considered abnormal) was present in 40% of patients with ALS, compared to only 5% of normals. An FDI/ADM ratio of <0.9 (considered abnormal) was seen in 34% of patients with ALS, compared to only 1% of normals. Twenty percent of patients with ALS had both an abnormal APB/ADM and FDI/ADM ratio with no normal controls showing both. These results suggest that the split-hand syndrome is supportive of a diagnosis of ALS. The reason behind this pattern in some patients with ALS is not completely understood. However, in the cortex, the number of cortical motor neurons that supply the APB and FDI outnumber those to the ADM. Another possible explanation is the relative contribution of C8 and T1 fibers in the FDI. APB, and ADM. The FDI and APB have a relatively greater amount of T1 innervation compared to the ADM, which has a large contribution from C8. Thus, motor neuron degeneration at T1 would disproportionally affect the FDI and APB compared to the ADM.

The most important reason to perform motor nerve conduction studies is to look for unequivocal evidence of demyelination, especially conduction block along motor nerves. *The presence of conduction block along motor nerves* signifies that (1) the underlying disorder is a motor neuropathy and not a motor neuron disease, (2) the major cause of weakness is conduction block and not loss of motor neurons or axons, and (3) the disorder is potentially treatable with immune-modulating therapy. Conduction block of motor fibers is the major electrophysiologic finding in patients with MMNCB (Figure 27–5). Other electrophysiologic evidence of demyelination (slowed conduction velocities, prolonged distal latencies, and prolonged late responses) may be seen.

Because temporal dispersion without conduction block may cause some decrease in both CMAP amplitude and area between proximal and distal stimulation sites, the electrophysiologic criteria for conduction block are complicated. Computer simulation models have shown that marked temporal dispersion can cause the CMAP amplitude to drop by more than 50% between proximal and distal sites, even in the absence of conduction block. In contrast, these models have shown that any drop of CMAP area greater than 50% between proximal and distal stimulation sites always signifies conduction block, and cannot be explained on the basis of temporal dispersion alone. The effects of temporal dispersion are always more pronounced when a nerve is studied over a long distance. In practice, when routine nerve segments (wrist-to-elbow, ankle-toknee) are studied in normal individuals and in patients with axonal loss, CMAP area and amplitude rarely drop by more than 20%. Therefore, any drop in CMAP area or amplitude of more than 20% over a short segment, especially if associated with focal slowing, usually indicates conduction block.

To increase the yield of nerve conduction studies for detecting conduction block, more proximal stimulation (axilla, Erb's point, cervical nerve roots) often is attempted



FIGURE 27–5 Conduction block in multifocal motor neuropathy. Median motor and sensory studies, with the abductor pollicis brevis and digit 2 co-recorded and the wrist and elbow stimulated. The hallmark finding in patients with multifocal motor neuropathy with conduction block is the presence of conduction block between proximal and distal stimulation sites in motor but not sensory fibers. Note complete block of motor fibers (**top**). The drop of sensory amplitude is within the normal range, expected for normal phase cancellation (**bottom**). Motor conduction block is not seen in patients with amyotrophic lateral sclerosis or other motor neuron diseases.

in patients with suspected ALS. Although this technique may be of value in selected individuals, several important technical considerations must be kept in mind. First, supramaximal stimulation can be difficult to achieve, even with maximum current output, especially at Erb's point and at the root level. If submaximal stimulation is mistaken for supramaximal, a conduction block may be erroneously identified. Second, proximal stimulation often results in co-stimulation of adjacent nerves. For instance, at Erb's point and the C8 root, it is not possible to stimulate ulnar motor fibers without also stimulating median motor fibers. Unless collision techniques are used to eliminate the contribution from the co-stimulated nerve, the findings may be difficult if not impossible to interpret (see Chapter 30). Finally, with increased distance the effects of temporal dispersion are greater. For example, when studying the ulnar nerve between the elbow and wrist, one allows a drop in CMAP area or amplitude of up to 20% to account for the normal effects of temporal dispersion. However, stimulating the ulnar nerve at Erb's point (hence, doubling the distance), one must allow a drop in CMAP amplitude and area of up to 40% between distal and proximal sites to account for normal temporal dispersion. In proximal stimulation studies performed on patients with well-documented ALS, the drop in CMAP area and amplitude does not exceed 50%.

The presence of conduction block along motor fibers usually signifies a demyelinating neuropathy; in a patient

with suspected motor neuron disease, especially PMA, it often signifies MMNCB. Of course, the diagnosis of MMNCB cannot be based on finding conduction blocks only at the usual entrapment sites, such as ulnar neuropathy at the elbow or peroneal neuropathy at the fibular head. Thus, a patient with ALS who develops an ulnar neuropathy at the elbow due to weight loss and immobility still has ALS, not MMNCB.

Like motor studies, sensory nerve conduction studies must be performed in an upper and a lower extremity. Sensory nerve conduction studies are always normal in ALS and its variants. Unless there is a clear reason that a patient should have an underlying polyneuropathy or entrapment neuropathies, the presence of abnormal sensory conduction studies should always cause the clinician to seriously question the diagnosis of ALS. The only notable exception to normal sensory conduction studies in a motor neuron disorder is X-linked bulbospinal muscular atrophy, in which patients may have absent or abnormal sensory nerve action potentials (SNAPs), probably due to involvement of the dorsal root ganglia (see Chapter 28).

It is critical to note that motor and sensory nerve conduction studies can be identical in patients with ALS and in patients with cervical/lumbar stenosis. In patients with either diagnosis, the SNAPs will be normal, but for different reasons. Patients with ALS have no sensory findings, whereas patients with cervical/lumbar stenosis may have sensory loss, but since the lesion is proximal to the dorsal root ganglia, the SNAPs are spared. In both cases, motor studies may be normal or may show evidence of axonal loss. The late responses may help to differentiate the two, but should never be used as the sole differentiating factor. F-wave abnormalities (prolongation, impersistence, dispersion, or absence) are more likely to occur in a polyradiculopathy. Likewise, the H reflexes may be absent or delayed in lumbar stenosis affecting the S1 nerve roots.

In some patients with ALS, especially late in the course, late responses may also show subtle abnormalities. As motor neurons are lost, fewer motor units are available to participate in the F response. Indeed, some muscles may be left with only a few motor units. In this situation, F responses may be impersistent, simply reflecting the reduced number of motor units available to backfire. If the largest and fastest firing motor units have been lost, minimal F-wave latency may be slightly prolonged, reflecting the normal though more slowly conducting motor neurons still present. In addition, "repeater F responses" may occur with some frequency. In general, it is unusual to see the same F-wave morphology twice because there usually are many motor units available to participate in the F response. In ALS, however, if only a few motor units remain, only those few motor units are available to create the F response. Accordingly, the chance of seeing the same F response twice is increased. In summary, although lateresponse abnormalities are more suggestive of polyradiculopathy than ALS, they cannot definitively differentiate between the two, since similar abnormalities can also be seen in ALS.

Electromyographic Approach

The EMG evaluation of patients with suspected ALS usually is extensive (Box 27–3). It is not unusual to sample all four limbs, the paraspinal muscles, and the bulbar muscles. Even though symptoms are often restricted to one or two limbs when a patient first presents for neurologic evaluation, EMG often reveals widespread denervation and reinnervation, even in the early stages of the disease. Because the diagnosis of ALS portends a grave prognosis, a thorough evaluation must always be conducted before a conclusion is reached. In order for the EMG study to support a diagnosis of ALS, active denervation with reinnervation must be found in three of four body segments (craniobulbar, cervical, thoracic, lumbosacral) and be unexplained by multiple mononeuropathies or radiculopathies.

In each muscle sampled, one looks for evidence of prior axonal loss (reinnervation) as well as evidence of ongoing axonal loss (denervation). Spontaneous activity usually is prominent, in the form of fibrillation potentials, positive sharp waves, and fasciculations. Fasciculations, the spontaneous depolarizations of motor units, often are irregular and quite slow (<1 Hz). The best way to look for fasciculations is to place the needle in the muscle, have the patient relax, and then, most importantly, remove one's hand from the needle. Fasciculations by themselves are insufficient

Box 27–3. Recommended Electromyographic Protocol for Motor Neuron Disease

Limb muscles:

Sample at least three limbs, making sure to sample the following in each limb: distal and proximal muscles, muscles with different nerve innervation, and muscles with different root innervation

Thoracic paraspinal muscles:

Sample at least three segments

Avoid sampling T11–T12 (may rarely be affected by spondylosis)

Bulbar muscles:

Sample at least one muscle (patients with bulbar weakness should have more muscles sampled)

Tongue, masseter, sternocleidomastoid, and facial muscles can be sampled

Special considerations:

- Electrophysiologic evidence consistent with amyotrophic lateral sclerosis usually is defined as active denervation and reinnervation in three of four body segments (craniobulbar, cervical, thoracic, lumbosacral) that cannot be explained by multiple individual mononeuropathies or radiculopathies. Thus, examination of the thoracic paraspinal and craniobulbar musculature assumes special importance in the electrophysiologic differentiation of amyotrophic lateral sclerosis from cervical/lumbar polyradiculopathy.
- Patients with old poliomyelitis often display diffuse chronic reinnervation with reduced recruitment of motor unit action potentials. Prominent active denervation, however, is unusual.

evidence of active denervation. The conclusion that active denervation is present must be based on finding fibrillation potentials or positive sharp waves, because fasciculations occur in many other disorders and are also seen as a benign phenomenon in many normal individuals.

Despite the presence of prominent denervation, it is unusual to find complex repetitive discharges in ALS. Complex repetitive discharges are a chronic phenomenon; when observed in patients with motor neuron disease, they more often imply a very chronic motor neuron disorder, such as old poliomyelitis, or the LMN presentation of adult-onset hexosaminidase A deficiency (see Chapter 28).

Along with abnormal spontaneous activity, there is always evidence of compensatory reinnervation in ALS. With the exception of poliomyelitis, all motor neuron disorders usually are slowly progressive. The pattern of acute or subacute neuropathic loss (active denervation, with normal MUAP morphology and decreased recruitment of MUAPs) is not seen in ALS.

In patients with suspected ALS, many muscles should be sampled to demonstrate the underlying widespread nature of the disease. *Neuropathic changes must be demonstrated in muscles innervated both by different nerves that share the same myotome, and by different myotomes.* This point cannot be overemphasized. For example, if a C7 medianinnervated muscle is severely abnormal and a C7 radialinnervated muscle is normal, one must seriously question the diagnosis of any type of motor neuron disorder. By its nature, motor neuron disease is a myotomal disease; it does not spare individual nerves in the same myotome, as MMNCB often does.

In addition to documenting denervation and reinnervation, one must pay particular attention to MUAP recruitment. Decreased recruitment signifies loss of motor units, which is the primary problem in motor neuron disease. Judging recruitment of MUAPs allows the electromyographer to assess the number of functioning motor units. Although there are electrophysiologic techniques available to count the number of motor units in a particular muscle, most are time consuming, and each has its own set of potential technical problems.

The evaluation of MUAP recruitment also plays a crucial role in differentiating motor neuron disorders from some cases of chronic myopathy with denervating features. As noted earlier, some patients with IBM and other chronic myopathies may have profuse fibrillation potentials and positive sharp waves associated with long-duration, highamplitude, polyphasic MUAPs (i.e., the pattern typically associated with acute and chronic axonal loss). Although some patients with chronic myopathy may also have briefduration, low-amplitude, polyphasic MUAPs (so-called myopathic motor unit potentials), others may not. It is in such cases, wherein myopathic motor unit potentials are not seen, that the assessment of MUAP recruitment usually allows the differentiation of neuropathic from myopathic conditions. In contrast to motor neuron disease, in which recruitment is reduced, in chronic myopathy, recruitment usually remains normal or early. If, in rare situations, it is reduced, the degree to which it is reduced often is less than would be expected for the degree of denervation and reinnervation.

Along with decreased recruitment, decreased activation may be seen in patients with ALS. Activation, the ability to fire available motor units faster, is a central nervous system process. The UMN dysfunction in patients with ALS results in decreased activation. On the whole, the EMG picture of classic ALS is one of denervation, reinnervation, decreased recruitment, and decreased activation of MUAPs in multiple muscles innervated by different nerves and myotomes.

In patients with suspected ALS, the limb muscles often are sampled first. Of course, widespread EMG abnormalities found in the limb muscles cannot differentiate severe cervical/lumbar polyradiculopathy from ALS. It is in these cases that the evaluation of the thoracic paraspinal and craniobulbar muscles assumes diagnostic importance.

Denervation is often found in the thoracic paraspinal muscles in patients with ALS. This finding is important in eliminating the possibility of coexistent cervical and lumbar spinal stenosis mimicking ALS. One prospective study of patients referred with the suspected diagnosis of ALS found that 78% of all patients who eventually were diagnosed with ALS by conventional means had evidence of denervation in the thoracic paraspinal muscles when three or four segments were assessed. In a control group of patients with spondylosis, denervation in the thoracic region was extremely uncommon, occurring in only 1 (5%) of 21 patients. This single patient had severe stenosis of the lumbar and adjacent thoracic spine. The thoracic paraspinal muscles generally constitute a safe and accessible site for needle EMG and are one of the most useful areas to examine to help differentiate patients with spondylosis from those with ALS. The only difficulty often encountered is inadequate muscle relaxation. This is a problem especially in very weak patients, in whom thoracic paraspinals may activate with each breath, making it difficult to determine the presence of spontaneous activity.

The other area in which EMG abnormalities assume great diagnostic significance is in the craniobulbar musculature. Clear-cut evidence of denervation and reinnervation in the bulbar muscles removes the possibility of cervical or lumbar spondylosis as the sole cause of the motor dysfunction. Muscles often chosen for study include the tongue, masseter, and facial muscles. However, several points must be taken into account when evaluating the bulbar muscles. First, it is difficult for patients to relax the tongue, so the assessment of spontaneous activity often is demanding. In addition, the size and firing pattern of MUAPs in the bulbar muscles are different from those in the limb muscles. Bulbar MUAPs are shorter in duration than those found in the limb muscles and may be misinterpreted as fibrillation potentials or myopathic MUAPs. In addition, the onset firing frequency is higher for bulbar than for limb muscles and may suggest a neuropathic

recruitment pattern even in normal muscles. Every electromyographer should gain familiarity with normal bulbar MUAPs before examining the bulbar muscles in patients with suspected ALS.



Case 27–1 History and Physical Examination

A 54-year-old woman was referred for progressive weakness over the past 8 months. Weakness began as a footdrop in the left lower extremity, and similar symptoms developed in the contralateral leg 2 months later. There was no history of trauma, pain, paresthesias, or sensory loss. The patient had no complaints in the upper extremities.

On neurologic examination, mental status and cranial nerve function were normal. In the upper extremities, there was slight atrophy of the intrinsic hand muscles bilaterally, noted in the thenar eminence. However, strength was normal. In the lower extremities, there was spasticity with prominent wasting and fasciculations in all muscles below the knees. Strength testing showed marked bilateral footdrops. In addition, there was weakness of plantar flexion, ankle inversion, and ankle eversion distally. Proximally in the lower extremities, there was mild weakness of hip flexion, extension, abduction, and adduction. Deep tendon reflexes were present and normal in the upper extremities. In the lower extremities, reflexes were pathologically brisk with clonus at the ankles. Plantar responses were extensor bilaterally. Sensory examination showed normal sensitivity to light touch, temperature, and vibration.

Summary

The history in this case is essentially one of bilateral footdrops. The history alone might suggest the possibility of bilateral peroneal neuropathies, due to either compression or entrapment at the fibular neck. Likewise, there may be bilateral peroneal neuropathies from another cause, such as mononeuritis multiplex. It is not unusual for mononeuritis multiplex to affect the peroneal nerves and to progress in an asymmetric, stepwise manner. However, several points argue against either of these diagnoses. First, the patient describes her problem as slowly progressive. Second and more important is the notable absence of sensory symptoms (i.e., numbness or paresthesias). Accordingly, the clinical sensory examination and the sensory nerve conductions will be of particular importance.

On examination, the cranial nerves and upper extremities are relatively normal, with only the suggestion of slight atrophy in the thenar eminence bilaterally. In the lower extremities, there are marked bilateral footdrops with wasting of the lower legs, as expected from the history. However, the weakness of plantar flexion and ankle inversion (both tibial-innervated functions) clearly places the abnormalities beyond the territory of the

CASE 27–1. Nerve Conduction Studies														
Nerve	Stimulation	Recording	Amplitude Motor = mV; Sensory = μV		Latency (ms)			Conduction Velocity (m/s)		F-Wave Latency (ms)				
Stimulated	Site	Site	RT	LT	NL	RT	LT	NL	RT	LT	NL	RT	LT	NL
Median (m)	Wrist Antecubital fossa	APB APB	4.2 4.0		≥4	4.6 8.4		≤4.4	53		≥49	24		≤31
Ulnar (m)	Wrist Below elbow Above elbow	ADM ADM ADM	8.8 8.4 8.4		≥6	3.9 7.3 8.4		≤3.3	59 65		≥49	25		≤32
Ulnar (m)	Wrist Below elbow Above elbow	FDI FDI FDI	5.2 5.1 5.0		≥6	4.2 8.5 9.7		≤4.5	57 59		≥49 ≥49	27		≤32
Median (s)	Wrist	Index finger	46		≥20	3.3		≤3.5	55		≥50			
Ulnar (s)	Wrist	Little finger	35		≥17	2.9		≤3.1	57		≥50			
Radial (s)	Forearm	Snuffbox	42		≥17	2.5		≤2.9	62		≥50			
Tibial (m)	Ankle Popliteal fossa	AHB AHB	11.8 8.9		≥4	6.4 14.1		≤5.8	43		≥41	46		≤56
Peroneal (m)	Ankle	EDB	2.4		≥2	4.9		≤6.5				45		≤56
	Below	EDB	2.3			12.8			46		≥44			
	Lateral popliteal fossa	EDB	2.0			13.1			51		≥44			
Sural (s)	Calf	Posterior ankle	9		≥6	4.3		≤4.4	47		≥40			

m = motor study; s = sensory study; RT = right; LT = left; NL = normal; APB = abductor pollicis brevis; ADM = abductor digiti minimi; AHB = abductor hallucis brevis; EDB = extensor digitorum brevis.

Note: All sensory latencies are peak latencies. All sensory conduction velocities are calculated using onset latencies. The reported F-wave latency represents the minimum F-wave latency.

peroneal nerves. In addition, there is mild weakness of hip flexion, extension, abduction, and adduction. Fasciculations are also noted in the lower extremities. At this point, the clinical abnormalities do not correspond to any one nerve or root distribution. The lesion must involve multiple nerves, the lumbosacral plexus, or multiple nerve roots in both lower extremities. However, the sensory examination is completely normal. The finding of weakness with sparing of sensation indicates that we are dealing with a predominantly motor problem. The normal sensory examination makes multiple mononeuropathies, a lumbosacral plexopathy, or polyradiculopathy seem unlikely. Finally and probably most importantly, the deep tendon reflexes are pathologically brisk with clonus at the ankles. The plantar responses are extensor bilaterally. The hyperreflexia, increased tone (spasticity), and extensor plantar responses denote an additional UMN lesion in this patient. Thus, the neurologic examination reveals evidence of both lower and upper motor neuron dysfunction in the lower extremities and sparing of the sensory system. Furthermore, the lower and upper motor neuron signs are in the same spinal segments. For example, the plantar flexors (L5–S1 segments) are weak, wasted, and fasciculating, but there is also spasticity and clonus at the ankles (S1 segment). This is a very unusual situation that is strongly suggestive of ALS.

The nerve conduction studies are performed first, with the electromyographer keeping in mind the strong

CASE 27–2. Electromyography											
		Spontan	eous Activity	Voluntary Motor Unit Action Potentials							
					_	Configuration					
Muscle	Insertional Activity	Fibrillation Potentials	Fasciculations	Activation	Recruitment	Duration	Amplitude	Polyphasia			
Right tibialis anterior	Ŷ	+2	+1	Fair	$\downarrow\downarrow$	+3	+2	+2			
Right medial gastrocnemius	Ŷ	+2	+2	Poor	$\downarrow\downarrow$	+2	+2	+2			
Right vastus lateralis	Ŷ	+1	+1	NL	\downarrow	+1	+2	+2			
Right iliacus	\uparrow	+1	0	NL	\downarrow	+1	+1	+1			
Right gluteus medius	Ŷ	+2	+1	Fair	$\downarrow\downarrow$	+2	+2	+2			
Right gluteus maximus	\uparrow	+2	0	NL	\downarrow	+1	+1	+1			
Left tibialis anterior	\uparrow	+3	0	Poor	$\downarrow \downarrow \downarrow \downarrow$	+3	+3	+2			
Left medial gastrocnemius	\uparrow	+2	+2	Fair	\downarrow	+2	+2	+2			
Left vastus lateralis	\uparrow	+2	+1	Fair	\downarrow	+2	+1	+1			
Left iliacus	\uparrow	+2	0	NL	\downarrow	+1	+1	+1			
Left gluteus medius	\uparrow	+2	+1	NL	$\downarrow\downarrow$	+2	+1	+1			
Right first dorsal interosseous	\uparrow	+1	0	NL	\downarrow	+1	NL	+1			
Right abductor pollicis brevis	\uparrow	+1	0	NL	\downarrow	+1	+1	+1			
Right pronator teres	\uparrow	+1	+1	NL	\downarrow	+1	NL	+1			
Right biceps brachii	Ŷ	+1	+1	NL	NL	NL/+1	+1	NL			
Right pronator teres	Ŷ	+1	0	NL	\downarrow	+1	+1	+2			
Right triceps brachii	Ŷ	+2	+1	NL	\downarrow	NL/+1	+1	+1			
Right T6 paraspinal	Ŷ	+2	0								
Right T8 paraspinal	Ŷ	+2	0								
R. tongue	NL	0	0	NL	NL	NL	NL	NL			
\uparrow = increased;↓= slightly reduced; ↓↓ = moderately reduced; ↓↓↓ = markedly reduced; NL = normal.											

possibility of ALS. As mentioned earlier, the primary role of nerve conduction studies in a patient with suspected ALS is to exclude the possibility of a demyelinating polyneuropathy, especially one associated with conduction block. To this end, nerve conduction studies are performed in one upper and one lower extremity. The median, ulnar, tibial, and peroneal motor nerve conduction studies all show normal motor amplitudes, conduction velocities, and minimal F-wave latencies. The only exception is slightly reduced motor amplitude recording the FDI during ulnar motor studies. The only other abnormalities found on the motor nerve conduction studies are slightly prolonged median, ulnar, and tibial distal motor latencies. None of the nerves studied shows an abnormal drop in CMAP amplitude with proximal stimulation, except for the tibial nerve, where the amplitude drops from 11.8 to 8.9 mV. However, this amount of drop would be considered normal for the tibial nerve.

Moving next to the sensory nerve conduction studies, the median, ulnar, radial, and sural sensory conduction studies show robust amplitudes throughout, with normal latencies and conduction velocities. Thus, the sensory nerve conduction studies correlate well with the history and examination; the sensory system appears intact.

During the EMG examination, attention is focused first on the weak lower extremities. There is evidence of diffuse spontaneous activity, manifest as fibrillation and fasciculation potentials in most muscles tested in both lower extremities. The amount of fibrillation potentials is marked. In addition, all muscles studied in the lower extremities show very large amplitude, long-duration, polyphasic MUAPs with decreased recruitment. Several distal muscles also show reduced activation.

Although the upper extremities are clinically unaffected, with the exception of mild distal atrophy, there is evidence of diffuse denervation with occasional fasciculations in the right upper extremity. There also is evidence of mild reinnervation in all muscles tested, along with decreased recruitment of MUAPs. A very important finding is that the thoracic paraspinal muscles at the T6 and T8 levels show profuse fibrillation potentials. Finally, one bulbar muscle, the tongue, is sampled and is normal.

At this time we are ready to formulate our electrophysiologic impression.

IMPRESSION: The electrophysiologic findings are consistent with an active, generalized disorder of the motor neurons, their axons, or both.

This case displays many of the prominent clinical and electromyographic features of ALS, the prototypic motor neuron disorder. Commonly, ALS begins in a distal limb, resulting in hand weakness or a footdrop. Thus, it is often initially mistaken for an ulnar neuropathy or a peroneal palsy. The course is relentlessly progressive; progression to the contralateral side usually occurs within several months. ALS usually starts as a regional disease and then progresses to adjacent myotomes. One of the major clues to the diagnosis is the complete absence of sensory symptoms, confirmed by both the clinical examination and the sensory nerve conduction studies. The only motor neuron disorder that regularly results in sensory disturbances is the rare X-linked bulbospinal muscular atrophy (Kennedy disease), in which SNAPs may be decreased or absent.

Several important questions can be addressed at this point.

How are the Nerve Conduction Studies Helpful in the Evaluation of Motor Neuron Disease?

Nerve conduction studies are essential in the evaluation of patients with motor neuron disease. Beyond confirming that sensory fibers are normal, their primary role is to exclude a demyelinating motor neuropathy with conduction block mimicking motor neuron disease. This differentiation is especially important in patients with predominantly LMN syndromes (i.e., with no clinical evidence of UMN dysfunction such as spasticity or hyperreflexia), in whom it is essential to perform extensive motor studies. Studies can be performed bilaterally as well as proximally to look for conduction blocks in motor nerves. In rare patients with a demyelinating motor neuropathy, proximal studies (e.g., stimulating axilla, Erb's point, cervical nerve roots) occasionally may be abnormal when the distal sites are normal. Proximal studies may be especially helpful in patients with normal distal conduction studies but abnormal late responses, a pattern suggestive of proximal demyelination. However, it is important to remember that proximal stimulation is technically difficult and, if not performed correctly, may lead to confusing and misleading results.

How are the Upper Extremity Nerve Conduction Motor Amplitudes Helpful in the Evaluation of Motor Neuron Disease?

When performing the routine median and ulnar motor studies, all the amplitudes are normal with the exception of the amplitude of the FDI which is borderline low. Looking at the median amplitude, however, it is just slightly above the lower limit of normal. This is in contradistinction to the ADM amplitude which is well above its lower limit of normal. If we compute the APB/ADM and FDI/ADM ratios, both are low are 0.5 and 0.6, respectively. In the appropriate clinical setting of possible ALS, an APB/ADM ratio <0.6 and FDI/ADM ratio < 0.9 together are supportive of the electrical diagnosis of ALS. This "split-hand" pattern, wherein the lateral hand (ADM), is a pattern seen in classic ALS.

Is this Study Consistent with a Diffuse Severe Polyradiculopathy?

EMG cannot differentiate between a severe polyradiculopathy and LMN disease. Indeed, there is no good electromyographic way to distinguish between a disorder of nerve roots and one of motor neurons. In both cases, nerve conduction studies will be essentially normal. In LMN disease, the SNAPs are spared. In polyradiculopathy, the SNAPs also are spared because the lesion is proximal to the dorsal root ganglion. The motor nerve conduction studies are identical in both; they either are normal or show evidence of axonal loss. The EMG findings in both may show evidence of diffuse denervation and reinnervation. Although polyradiculopathy from structural causes rarely involves the thoracic paraspinal muscles, they certainly may be involved with infectious, inflammatory, and infiltrative lesions. Only the late responses (especially the F responses) are more likely to be abnormal in a polyradiculopathy than in motor neuron disease. However, one would hesitate to make a distinction between the two on the basis of F responses alone.

Thus, although there is no difference between polyradiculopathy and LMN disease based on EMG and nerve conduction studies, the clinical difference is clear and unequivocal. Patients with polyradiculopathy have prominent sensory symptoms including pain and paresthesias. whereas in motor neuron disease, sensory symptoms and signs are completely lacking. Accordingly, the same EMG can be interpreted quite differently depending on the history and physical examination. If the EMG results in this case were found in a patient with progressive spinal pain associated with radiating paresthesias into the legs, thorax, and upper extremities and whose clinical examination showed hyporeflexia and sensory loss, the same nerve conduction study and EMG would more properly be interpreted as consistent with a severe ongoing diffuse polyradiculopathy.

Why Sample so Many Muscles on Needle Electromyogram?

The EMG examination in a patient with suspected ALS must be extensive, with the electromyographer looking for both active denervation and reinnervation. Sampling multiple muscles innervated by different nerves and different roots is important to avoid mistakenly interpreting multiple radiculopathies or mononeuropathies as ALS. One must document a diffuse process. Although most patients present with symptoms restricted to one or two limbs, it is not unusual to find evidence of diffuse reinnervation and denervation in clinically unaffected limbs.

There are two areas that assume special significance on EMG studies: the thoracic paraspinal muscles and the craniobulbar musculature. The thoracic paraspinal muscles usually are unaffected by spondylosis, and abnormalities there cannot be explained by coexistent cervical and lumbar spine disease, which can mimic ALS. Profuse denervation in the thoracic paraspinals usually suggests the diagnosis of ALS rather than spondylosis with polyradiculopathy, although, as noted earlier, in the rare case of infectious, inflammatory, and infiltrative lesions, the thoracic paraspinal muscles may be involved. In addition, it is always important to check the craniobulbar muscles because abnormalities there certainly exclude an isolated cervical lesion as the source of a patient's weakness. In the case described here, the symptoms began in the lower extremities, and the bulbar musculature was not yet affected. However, if the patient is tested several months later, abnormalities likely will be found there as well.

Does this Patient also have Superimposed Carpal Tunnel Syndrome?

The distal median motor latency to the abductor pollicis brevis muscle is prolonged. Does this suggest that the patient also has carpal tunnel syndrome (CTS)? One must remember that CTS is a clinical diagnosis; this patient had no clinical symptoms or signs suggesting a diagnosis of CTS. One might then ask whether the patient simply has an asymptomatic median neuropathy at the wrist, given the prolonged distal median motor latency to the abductor pollicis brevis. That possibility might be considered, but note that the ulnar and tibial motor nerves also show slightly prolonged distal motor latencies. It is unlikely that the patient also has an ulnar neuropathy at Guyon's canal and a tibial neuropathy at the tarsal tunnel. In addition, the median sensory latency is normal. Slowing of median motor, but not sensory, fibers is not the typical pattern seen in CTS (sensory fibers are more often abnormal than motor fibers in CTS). The slowing of the distal latencies in this case simply represents axonal loss with dropout of some of the largest and fastest motor neurons/axons. EMG examination of the median, ulnar, and tibial muscles is very helpful in clarifying this situation because it shows clear evidence of ongoing axonal loss in the form of fibrillation potentials and large, reinnervated MUAPs. Thus, the prolonged distal motor latencies, albeit mild, are simply a manifestation of axonal loss from the underlying motor neuron disease.

What is the Electromyographic Correlate of the Patient's Spasticity and Upper Motor Neuron Pathology?

Although EMG and nerve conduction studies are usually thought of as primarily assessing the peripheral nervous system, they often provide some insight into the central nervous system. The central nervous system can be assessed by the MUAP firing pattern on EMG. Activation (the ability to fire available motor units faster) is entirely a central process. Patients with a UMN lesion resulting in weakness will have decreased activation of MUAPs on EMG. Accordingly, in ALS, which is a disorder of both UMNs and LMNs, one often sees the unusual combination of both decreased activation and decreased recruitment of MUAPs. The decreased activation pattern represents the UMN pathology, and the decreased recruitment pattern represents the loss of LMNs.

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