



## July 1997 EMG Case-of-the-Month

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### HISTORY

A 75-year-old right hand dominant man describes a two-year history of progressive left and right hand weakness. This weakness is manifest in an inability to tightly grip objects, which is worse on the left. Additionally, he notes increasing difficulty in arising from chairs and the commode as well as climbing stairs. Over the past several months the patient states he requires the use of a cane for climbing steps. He also needs moderate assistance in activities of daily living.

- **Prior to continuing, please develop a differential diagnosis and list each possible diagnosis in order of likelihood.**
- **Is there any additional information regarding the clinical history that might be helpful in clarifying your differential list or changing its order of priority?**
- **Other questions?**

### COMMENTARY I

Discuss answers to the questions above. Include inappropriate diagnoses that might have been considered and explain why they have been excluded. Relate your comments to the clinical history.

### HISTORY, continued: Past Medical History

The patient is being treated for hypertension and benign prostatic hypertrophy. He has a past history of laryngeal carcinoma with successful radiation treatment in 1960. At present there is a negative history for tobacco use for the past 30 years and he drinks about 12 beers per week.

- **If necessary, revise your differential diagnosis based on the additional clinical history.**
- **On what details of the physical examination do you think you should focus at this point?**
- **Other questions?**

### COMMENTARY II

Discuss answers to the questions above. Expand comments beyond the basic answers.



## PHYSICAL EXAMINATION

The patient is alert, oriented, and in no acute distress. Cranial nerves 2-12 are found to be intact. Pupils are symmetrically round and reactive to light. No eyelid ptosis is noted and extraocular movements are full. Muscles innervated by cranial nerves are not atrophic and no fasciculations are observed in the head, torso, or upper or lower limbs. Manual muscle testing of the upper limbs revealed grade 4/5 strength for the neck flexors/extensors, shoulder abductors/adductors/internal/external rotators, elbow extensors and flexors, and wrist flexors/extensors. The finger flexors and extensors are 3-/5 while the hand intrinsic muscles are 4/5. In the lower limbs the hip flexors/extensors/abductors are 3+/5 while the knee extensors/flexors and ankle dorsiflexors/plantar flexors are 4+/5. A mild degree of forearm muscle wasting is observed. There is noted to be a reduction in pinprick and light touch extending from the feet to the mid calf level bilaterally. Sensation in the hands is normal. The patient's gait is wide-based and Romberg is negative. Muscle stretch reflexes are 2/2 at the biceps and triceps and 1/2 for the brachioradialis, while they are unobtainable at the knees and ankles bilaterally. Plantar responses are flexor. There is noted to be normal tone in the upper and lower limbs with no spasticity or clonus noted.

- **At this point, review your differential diagnosis and revise as appropriate.**
- **Are there additional observations on physical examination that might be helpful in narrowing your differential list?**
- **Other questions?**

## COMMENTARY III

Discuss answers to the questions above. Tie the clinical history to the physical examination as appropriate.

## PHYSICAL EXAMINATION, continued

The patient was recently evaluated by another physician who found:

1. a peripheral neuropathy on electrodiagnostic medicine testing (report not available for review),
  2. small central bulging of the discs at levels C2-C7 with associated neural foraminal narrowing at the left and right C7 region, as well as mild stenosis at L3-L5 on MRI,
  3. normal serum CK, aldolase, CBC, SMA 20,
  4. normal serum protein electrophoresis and anti-ganglioside antibodies.
- **If necessary, revise your differential diagnosis based on the additional physical findings.**
  - **Design your approach to the electrophysiologic examination based on the existing data.**

## COMMENTARY IV

Discuss answers to the questions above.



**ELECTROPHYSIOLOGIC DATA:  
 Needle Electromyographic Studies**

ELECTROMYOGRAPHY								
N = normal incr = increased decr = decreased 0 = absent 1+ = minimal 4+ = maximal crd = complex repetitive discharge fasc = fasciculation potential myk = myokymic discharge myt = myotonic discharge nmt = neuromyotonic discharge p wave = positive sharp waves fib = fibrillation potentials recr = recruitment amp = amplitude dur = duration poly = polyphasic potentials								
R/L	MUSCLE	INSERT	SPONTAN		VOLUNTARY			
		activ	p wave	fib	recr	amp	dur	poly
L	deltoid	incr	1-2+	1-2+	incr	decr	decr	incr
L	biceps	incr	1-2+	1-2+	incr	decr	decr	incr
L	triceps	incr	1-2+	1-2+	incr	decr	decr	incr
L	pronator teres	incr	1-2+	1-2+	incr	decr	decr	incr
L	extensor carpi radialis	incr	1-2+	1-2+	incr	decr	decr	incr
L	flexor carpi radialis	incr	1-2+	1-2+	incr	decr	decr	incr
L	abductor pollicis brevis	incr	1-2+	1-2+	incr	decr	decr	incr
L	first dorsal interosseous	incr	1-2+	1-2+	incr	decr	decr	incr
L	extensor digitorum communis	incr	1-2+	1-2+	incr	decr	decr	incr
L	vastus medialis	incr	1-2+	1-2+	incr	decr	decr	incr
L	tibial anterior	incr	1-2+	1-2+	incr	decr	decr	incr
L	gastrocsoleus	incr	1-2+	1-2+	incr	decr	decr	incr
L	lumbosacral paraspinals	incr	1-2+	1-2+	incr	decr	decr	incr
L	cervical paraspinals	incr	1-2+	1-2+	incr	decr	decr	incr

\* Because of the qualitative impression of reduced MUAP amplitude and durations as well as increased phases, combined with increased or early recruitment, quantitative MUAP analysis was performed on the left biceps brachii and vastus medialis muscles. The mean durations of 20 MUAPs for the biceps brachii and vastus medialis muscles were found to be 8.0 ms and 7.5 ms respectively. MUAP phases were noted to be 5.5 for both muscles.



SENSORY NERVE CONDUCTION									
nr = no response									
NERVE	LATENCY (ms)			AMPLITUDE (µV)			CONDUC VEL(m/s)		
	R	L	Norm	R	L	Norm	R	L	Norm
sural	5.2	5.0	-	5.5	6.5	-	-	-	-
ulnar	-	3.0	-	-	15.0	-	-	-	-
median	-	3.6	-	-	14.0	-	-	-	-

MOTOR NERVE CONDUCTION									
nr = no response									
NERVE	LATENCY (ms)			AMPLITUDE (mV)			CONDUC VEL (m/s)		
	R	L	Norm	R	L	Norm	R	L	Norm
peroneal	5.0	5.0	-	0.7	-	1.0	38	35	-
tibial	5.0	6.0	-	2.0	-	3.0	33	34	-
median	-	3.7	-	-	-	7.0	-	51	-
ulnar	-	3.0	-	-	-	5.0	-	51	-

**Summary of Findings:**

1. Normal nerve conduction studies in the upper limbs.
  2. Mildly prolonged distal sensory latencies and reduced amplitudes for the sural SNAP bilaterally.
  3. Mildly prolonged distal motor latencies, slightly reduced conduction velocities and reduced CMAP amplitudes for the tibial and peroneal nerves bilaterally.
  4. Needle EMG reveals widespread membrane instability and MUAPs with primarily reduced durations.
- **On the basis of both the clinical and electrodiagnostic evaluations, formulate your final impression. List the most likely diagnosis followed by other possibilities that are not excluded by the data. Eliminate those diagnoses not supported by the data.**
  - **What other diagnostic procedures are needed?**
  - **What treatment would you recommend?**



## DIAGNOSTIC IMPRESSION

1. The electrodiagnostic exam reveals evidence of mild axonal neuropathy preferentially localized to the lower limbs.
2. The needle electromyographic examination confirms the presence of a generalized myopathy.

## RECOMMENDATIONS

1. The patient is scheduled for a muscle biopsy.

## COMMENTARY

Explain the basis upon which the diagnostic impression was reached. Analyze the electrodiagnostic data electrophysiologically. Bring the clinical and electrical information together into a logical package that justifies the diagnosis.

Discuss the nature of the disease entity including pathology and pathophysiology.

If available, provide follow-up information on laboratory studies, and update the history, physical examination, electrodiagnostic data and results of treatment. Speculate about possible aspects of the case, if any, that have not been established.

## DIFFERENTIAL DIAGNOSIS

The formulation of a differential in the above described individual can be rather long and complicated. It helps to take a rather generic approach at first and subsequently whittle away at the various possibilities to a few more manageable disorders. We can use the information supplied by the history, physical examination, and laboratory data to help construct a list of likely diseases, and then apply the electrodiagnostic medicine evaluation to further refine a differential diagnosis.

There are a limited number of categories we can initially explore to home in on a likely diagnosis: central nervous system, peripheral nervous system, neuromuscular junction, and finally muscle. It is unlikely that a central nervous system disorder proximal to the foramen magnum would produce either the stocking distribution of sensory abnormalities or the complaint of proximal weakness combined with distal upper limb muscle wasting and weakness.

Our attention can next turn to the spinal cord region. A consideration in any person 75 years of age complaining of weakness should be some form of motor neuron disease such as amyotrophic lateral sclerosis or one of its variants. Persons first presenting with ALS can manifest with a unilateral foot drop, asymmetric hand intrinsic wasting, or other apparent focal peripheral nervous system involvement, in addition to the more diffuse or generalized clinical presentations. On careful physical examination, there are usually findings suggestive of a more widespread disease involving both the upper and lower motor neurons. In our patient, there are no signs suggestive of upper motor neuron disease in that there is normal muscle tone, a lack of spasticity or clonus, normal to absent (as opposed to increased) muscle stretch reflexes, and although not mandatory for the diagnosis, fasciculations could not be found. Similarly, cervical spinal stenosis, syringomyelia, or other mass lesion in the spinal cord do not quite fit with the patient's presentation.



Turning to the peripheral nervous system, a number of disorders may account for some of the patient's problems. The most proximal portion of the peripheral nervous system are the nerve roots. Certainly, in a person 75 years of age, spinal changes associated with aging, such as disc herniation and neural foraminal narrowing at multiple levels, can result in a number of his physical findings. Multilevel nerve root lesions in both the cervical and lumbosacral regions may produce weakness with or without muscle wasting. The patient does not complain of cervical or lumbosacral pain, has relatively easily obtainable stretch reflexes in the most commonly affected cervical root levels, and most importantly does not display a myotomal pattern of weakness. An MRI of the cervical and lumbosacral regions does reveal multilevel disease but not frank nerve root compression or displacement. Therefore, it appears unlikely that our patient is suffering from multilevel root disease. A cause for a bilateral brachial plexus lesions does not lend itself well to describing the patient's upper limb complaints. Also, a bilateral lumbar plexus to produce difficulty arising from low chairs is rather hard to imagine in this patient, as there are no associated complaints of a pelvic lesion so massive as to affect both the left and right lumbar nerves. A more generalized disease process, such as acute or chronic inflammatory demyelinating polyneuropathy, is rather remote given the lack of upper limb findings suggestive of peripheral nerve disease.

Clinical findings of a stocking distribution of sensation loss is suspicious for a peripheral neuropathy. A disease process resulting in a generalized peripheral neuropathy is a good candidate for some of the patient's symptoms and signs. In addition to the loss of sensation in the legs, some degree of lower limb muscle weakness and reflex changes is consistent with a peripheral nerve process. The lack of sensory abnormalities and preserved intrinsic hand strength in the upper limbs appears to go against this neuropathy accounting for the upper limb findings. The clinical findings do not suggest any of the more common focal entrapment neuropathies in the upper limb to result in finger flexor weakness with preservation of hand intrinsic muscle strength and bulk. At this point, a peripheral neuropathy affecting primarily the lower limbs is at least one disorder likely to be present in our patient.

The possibility of a neuromuscular junction disorder is rather unlikely given the patient's age and clinical findings. If a post-junctional disorder such as myasthenia gravis were considered, some degree of ocular muscle weakness would be anticipated. Also, neck flexor weakness, dysphagia, and symptoms of a more constitutional disease process would be anticipated. Similarly, a prejunctional disorder such as myasthenic syndrome does not seem likely. Patients with Lambert-Eaton syndrome typically have generally depressed stretch reflexes and more diffuse weakness, which can improve with repeated manual muscle testing. There are other reasons a neuromuscular junction disorder is unlikely in this patient, but for the sake of brevity will not be discussed.

Finally, an intrinsic muscle disease is a good possibility for a generalized disease process that can produce proximal muscle weakness resulting in patient's complaining of difficulty arising from low chairs and climbing stairs. A rather particular myogenic disorder would have produce proximal muscle weakness in the lower limbs and somewhat more distal than proximal muscle weakness in the upper limbs. Also, the laboratory data reveals relatively normal muscle enzymes, thus suggesting that a profound degree of myonecrosis is not present, i.e. the muscle membranes are generally intact. The more common and thus likely to be encountered myopathies are those categorized as inflammatory. There are three inflammatory myopathies to be considered: 1) polymyositis, 2) dermatomyositis, and 3) inclusion body myositis. The patient's lack of skin lesions suggests that dermatomyositis is



probably not present. Although polymyositis can be insidious, one would anticipate a patient with at least a two year history to be more weak and potentially demonstrate more signs of illness. Also, the normal muscle enzymes do not conform to the more typical course of polymyositis. Inclusion body myositis is a rather interesting disease with an atypical clinical presentation being rather typical for this disease. Of the rather large number of myogenic disorders, including the inflammatory myopathies, this patient may well have inclusion body myositis.

## **FORMULATION OF ELECTROPHYSIOLOGIC STUDIES**

In a patient with a possible diffuse disorder, it is a good idea to start with a few upper and lower limb nerve conduction studies of the motor and sensory nerves. In the upper limb, the median and ulnar nerves are a good place to begin. Routine studies of the median and ulnar motor fibers demonstrate normal distal motor latencies, amplitudes and conduction velocities. Similarly, the sensory components of these nerves are normal. There does not appear to be nerve conduction information suggestive of a focal neuropathy that could account for the forearm flexor muscle weakness. Nerve conduction studies assessing the deltoid and biceps brachii muscles were not performed, given the relatively preserved function of these muscles and lack of findings in either the motor or sensory fibers of the median and ulnar nerves.

In the lower limbs, the sural, tibial, and peroneal nerves were evaluated. The sural sensory data reveal low amplitude and prolonged sensory nerve action potentials. The peroneal nerve responses to the EDB are low in amplitude and slightly slowed in conduction. Similarly, the tibial nerve responses are borderline low in amplitude and slightly slowed. Femoral nerve studies were not performed since the patient demonstrated such good clinical strength of the knee extensors.

In any patient with a suspected myogenic disease, it is good practice to only evaluate one side of the body in the event that a muscle biopsy is to be performed. In this patient, the left upper and lower limbs were examined. Proximal, intermediate, and distal muscles were assessed with particular attention paid to motor unit action potential amplitude, duration, phases, and recruitment. Initially, only a qualitative assessment of the motor unit action potentials is performed, to determine if a more formal quantitative motor unit evaluation is indicated to firmly define a myogenic process.

All muscles examined with the needle electrode demonstrated membrane instability in the form of positive sharp waves and fibrillation potentials. Additionally, during qualitative motor unit assessment, the motor unit action potentials all appeared to be short in duration, reduced in amplitude, highly polyphasic, and recruitment was increased or early for the degree of force produced. This preliminary motor unit action potential evaluation suggested that a more formal quantitative motor unit action potential evaluation was necessary. Quantitative motor unit action potential analysis showed a definite reduction in duration and increase in phases.

## **FORMULATION OF AN IMPRESSION**

The documentation of reduced amplitude and slightly prolonged sural sensory potentials suggests that there is loss of axons in this nerve distribution. Finding only a mild delay in latency is more consistent with axon loss instead of demyelination. A similar reduction in the



peroneal and tibial compound muscle action potentials is consistent with the findings in the sural nerves. There may also be a contributing component to amplitude reduction from the concomitant intrinsic muscle disease process. These findings only in the lower limbs at this point suggest the early manifestation of an axonal peripheral neuropathy. A number of patients with inclusion body myositis have been reported to have coincident peripheral or focal entrapment neuropathies.

Needle electromyographic documentation of both membrane instability and motor unit action potential changes indicative of a lesion intrinsic to muscle tissue suggests that the patient has a generalized myopathic disorder. Although the electrodiagnostic medicine evaluation cannot identify specific myogenic disorders, the combination of the patient's clinical presentation and electrophysiologic findings strongly suggests that inclusion body myositis should be considered. A muscle biopsy is essential in this patient to confirm the electrodiagnostic and clinical impression.

**Muscle Biopsy.** A muscle biopsy confirmed the presence of inclusion body myositis.

Inclusion body myositis was first described in 1971. It accounts for about 16-30% of all adult idiopathic inflammatory myopathies. Males are affected three times more than females, with 50% of patients having an onset between 50-70 years and 20% between 10-30 years. Patients usually described a steady progression of weakness affecting a wide range of muscles. Both proximal as well as distal muscles may be affected, usually in a symmetric pattern. The forearm flexors are typically affected irrespective of whether the patient presents with proximal upper or lower limb weakness. Facial muscles may occasionally be affected, but extraocular muscles are spared. Respiratory muscles may be affected during the course of the disease. Muscle atrophy can be observed particularly in clinically weak muscles. Many patients demonstrate clinical evidence of generalized or focal peripheral neuropathies.

Light microscopy reveals variable inflammatory infiltrates of mononuclear cells, i.e. lymphocytes and macrophages. Variation in muscle fiber diameter can be present in association with occasional clusters of angular fibers. A few hypertrophied fibers can be observed. Perifascicular atrophy is distinctly lacking. Muscle fiber necrosis can be highly variable and is case specific, associated with muscle fiber regeneration. Intracytoplasmic vacuoles containing cytoplasmic degradation products are usually observed on cryostat sections.

The above histochemical changes clearly explain the electrophysiologic findings. Muscle fiber necrosis results in the positive sharp waves and fibrillation potentials observed as well as the reduction in compound muscle amplitudes. Fiber size variation produces an increase in the temporal dispersion of action potential arrival times at the recording electrode, resulting in highly polyphasic motor unit action potentials. Fiber hypertrophy and splitting can lead to large amplitude motor unit action potentials. The combination of membrane instability and large amplitude motor units (especially on a cursory examination) can lead one to conclude that a neurogenic as opposed to myogenic process is present. Similarly, fiber splitting along with local reinnervation of regenerating muscle fibers can lead to an increase in fiber density on single fiber EMG, again suggesting a neurogenic and not myogenic process. It is possible to see some long duration motor unit potentials as well secondary to the fiber size variation. The above noted findings suggesting a possible neurogenic process require a careful quantitative analysis of motor units. Only when a sufficiently large number of motor units are sampled does it become clear that a myogenic and not neurogenic process is present to account for the muscle changes. It is the compensatory attempt at muscle repair that can



lead one to conclude that a neurogenic process is present and hence lead to an erroneous diagnosis.

Treatment is less than optimal presently. Response to immunotherapy is variable. Prednisone alone or in combination with other agents appears to be ineffective. IVIG may hold some promise but requires further evaluation. Additional investigations trying new therapies or old ones in new combinations may hold some hope for better control of this disorder.

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