



EMG Case No. 80, June 2006

Presenting Symptom(s):

49 year old male with a 1-year complaint of generalized weakness in an asymmetric pattern

This case is no longer available for CME Credit.

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Disclosures: J. Marks, None; S. Kishner, None.

Appropriate Audience: Residents and practicing physicians.

Learning Objectives: After completing this educational activity, participants will be able to: (1) Formulate an appropriate, cost effective workup in a patient who presents with asymmetric muscle weakness; (2) Evaluate the EMG/NCS presented in patients with asymmetric muscle weakness and summarize the pertinent findings; (3) Describe 3 types of inflammatory myopathies, how to diagnose them, and how to treat them.

Level of Difficulty: Intermediate.

History

A 49 year old male presented with a one year history of slowly progressive generalized weakness in an asymmetric pattern involving both upper and lower extremities. He was having increasing difficulty ascending stairs, and getting up from deep couches and chairs. The patient reported that the weakness had been gradual and progressive in onset. He also complained of frequent leg cramping, but denied any pain. He denied any muscle twitching or sensory symptoms. He presents today because of frequent falls secondary to his knees buckling. He is right hand dominant, but relates difficulty grasping objects with his right hand. He denies any recent trauma.

His past medical history includes hypertension, which is managed with a low salt diet and metoprolol. On review of systems, the patient denies any bowel or bladder control problems, headaches, double vision, dysarthria, chest pain, shortness of breath, dysphagia, abdominal pain, dysuria, constipation, diarrhea, recent weight loss, fever, chills, skin rashes, or symptoms of a psychiatric diagnosis.

Family history is unremarkable. No family history of neurological or connective tissue disorders. He had an appendectomy and tonsillectomy as a child. He reports an allergy to penicillin. He drinks wine very rarely, about twice a year. He does not currently smoke, but has a twenty pack-year history. He is married, and has two children in college. He works as an accountant, and enjoys his job. He has never traveled outside the United States.

- Prior to continuing, please develop a differential diagnosis.
- On which details of the physical examination should you focus at this point?



Commentary I

Possible etiologies can begin to be organized within a framework of potential abnormalities in the central nervous system, peripheral nervous system, neuromuscular junction, and in the muscle itself. The differential diagnosis of progressive asymmetrical weakness without sensory symptoms is extensive and includes multiple sclerosis, cervical myelopathy, motor neuron disease, myasthenia gravis, congenital myopathies, inflammatory myopathies, as well as hereditary and acquired peripheral neuropathies.

The progressive and generalized onset of his presentation makes most acute and focal processes of the central nervous system unlikely with the possible exception of multiple sclerosis. Furthermore, the patient does not have bowel or bladder issues, or cranial nerve symptoms.

In a patient with asymmetric distal weakness without sensory loss in this age group, motor neuron disease (i.e. amyotrophic lateral sclerosis) must be ruled out. In motor neuron disease, axonal motor loss and upper motor neuron abnormalities, such as upgoing plantar response and spasticity could be noted. Bulbar symptoms and hyper-reflexia can also be present. On electrodiagnosis fasciculations are common, and motor axonal changes in three limbs is required for diagnosis. The conduction velocities may be relatively normal until there has been major axonal loss.

Multifocal motor neuropathy also can present with asymmetric weakness, but is without sensory loss. It is autoimmune mediated. Bulbar involvement is rare and reflexes are normal or diminished. Distal upper extremities are affected first. Most patients are younger than fifty years of age. On electrodiagnosis, there is conduction block and prolonged F-waves. There is no axonal involvement. Laboratory testing for GM1 aids in diagnosis.

Mononeuritis multiplex is a type of peripheral neuropathy where two or more nerve areas sustain damage. A patient with mononeuritis multiplex commonly experiences numbness, tingling, dysesthesias, burning sensations, and difficulty controlling or moving part of their body. The femoral and sciatic nerves are commonly involved. The upper extremities can be affected also. An increased incidence of mononeuritis multiplex is seen in patients with diabetes mellitus, connective tissue disease, and vasculitis.

The patient's benign past medical and travel history and the lack of constitutional symptoms makes an infectious origin unlikely. Although at one time polio was common, it is now rare in the United States secondary to immunization. Weakness in polio can be asymmetric with the lower extremities more commonly involved. In an acute case the cerebrospinal fluid shows a lymphocytic pleocytosis.

Congenital disorders affecting the neuromuscular junction or muscles is unlikely given the lack of family history and the symptoms starting so late in life.

Facioscapulohumeral dystrophy is an autosomal dominant disorder, and therefore is seen in multiple generations. Therefore when obtaining the history, it is vital to inquire if other family members have the same symptoms. Genetic testing can aid in diagnosis. FSH dystrophy affects the facial and shoulder girdle muscles. On clinical exam, FSH can be distinguished by a progression of muscle weakness and atrophy involving the facial muscles and scapular stabilizers, including the latissimus dorsi, trapezius, rhomboids, and biceps. Pelvic girdle weakness can be noted. The disease course is variable. The creatine kinase may be normal or elevated. EMG can demonstrate myopathic EMG activity.



Limb girdle dystrophy is an autosomal recessive disorder of the 15Q gene. It is similar to Duchenne's or Becker's muscular dystrophy clinically, but with variable onset and severity. Prominent calves may be noted in some patients. Creatine kinase levels are variable. EMG can demonstrate myopathic motor units. Once again, genetic testing can be useful.

Inflammatory myopathies such as polymyositis, dermatomyositis, and inclusion body myositis can be considered. Polymyositis generally presents with a preferentially proximal symmetrical weakness. The lack of a rash makes dermatomyositis less likely.

With myasthenia gravis, the patient can complain of weakness and fatigue that improves with resting. The proximal muscles, external ocular muscles, and bulbar muscles are most often affected. Diplopia and ptosis are common. Dysphagia is another common symptom. On physical exam, sensation to light touch is generally intact, and deep tendon reflexes are normal. Ptosis may be noted, and can be enhanced by having the patient look upward for a prolonged period. A decrease gag reflex and decreased ability to open the mouth may be present. The lab test utilized in myasthenia gravis is the AChR antibody analysis. The NCS should include repetitive nerve stimulation in a muscle that is clinically weak and may be enhanced with the use of an exercise protocol.

Physical Examination

The patient is alert, oriented, pleasant, and in no acute distress. Patient is noted to have atrophy of his right flexor forearm compartment and of the quadriceps bilaterally. On manual muscle testing, patient is noted to have 3/5 strength in the left quadriceps, and 4/5 in the right quadriceps. There is 4/5 strength in the knee flexors and extensors on the right, and 3+/5 for both muscle groups on the left. Ankle dorsiflexion is 4/5 bilaterally. Plantar flexion is 3/5 on the left and 3+/5 on the right. In the upper extremity, the finger flexors are 3/5 on the right and 4/5 on the left. Intrinsic hand muscles are 3/5 on the left and 4+/5 on the right. Hip extension is 3/5 on the left and 4/5 on the right. All other muscle groups are within normal limits.

The patient's cranial nerve exam is within normal limits. No fasciculations are noted on exam of the head, trunk, or extremities. Sensation to light touch and proprioception is intact in the upper extremities. However, in the bilateral lower extremities from the level of the calf to the distal lower extremity, there is a patchy non-dermatomal loss of pinprick and light touch sensation. The patient has normal tone throughout. Range of motion of the joints is within normal limits. Patient ambulates slowly and uses a quad cane. Cerebellar testing and Romberg are within normal limits. Deep tendon reflexes are symmetric and 2+/4 throughout. Plantar responses are down going bilaterally. Pulses in the upper and lower extremities are normal.

- At this point, review your differential diagnosis and revise as appropriate.

Commentary II

At this juncture several more diagnoses can be eliminated from the differential. The presence of muscle atrophy, normal reflexes and tone, greatly reduces the chance of an upper motor neuron process. The absence of fasciculations upon inspection, and in the history, makes the diagnosis of amyotrophic lateral sclerosis less likely, but does not rule it out. Mononeuritis multiplex is unlikely as the patient does not report either pain or sensory disturbances. Myasthenia gravis would have cranial nerve and bulbar involvement. The



patient also does not report fatigue improving after rest; however, repetitive stimulation will yield more information. A polyneuropathy is not ruled out. Myopathic processes remain in the differential diagnosis, but lack of associated pain and other constitutional symptoms make diagnoses associated with an inflammatory component less likely.

- Design your approach to the electrophysiologic examination based on the existing data.

Commentary III

At this juncture, an EMG and NCS were performed. The patients' limbs were an appropriate temperature and did not require warming prior to the study.

SENSORY NERVE CONDUCTION STUDIES							
NERVE	SIDE	STIM SITE	RECORD	cm	AMPL	LAT	CV
Sural	Right	Calf	Lateral malleolus	14	11	5.06	33.6
Sural	Left	Calf	Lateral malleolus	14	7	4.70	36.1
Ulnar	Right	Wrist	Little finger	14	17	4.04	37.3
Ulnar	Left	Wrist	Little finger	14	16	3.94	40.7

MOTOR NERVE CONDUCTION STUDIES							
NERVE	SIDE	STIM SITE	RECORD	cm	AMPL	LAT	CV
Ulnar	Right	Wrist	Abductor Digiti Minimi	8	5.0	3.28	
Ulnar	Right	Elbow	Abductor Digiti Minimi	23.5	5.0	7.94	50.4
Peroneal	Left	Ankle	Extensor Digitorum Brevis	8	2.8	5.41	
Peroneal	Left	Head of Fibula	Extensor Digitorum Brevis	32	2.6	13.4	41.2
Peroneal	Right	Ankle	Extensor Digitorum Brevis	8	4.2	5.30	
Peroneal	Right	Head of fibula	Extensor Digitorum Brevis	32	3.6	13.05	41.3



NEEDLE ELECTROMYOGRAPHY									
Insertional activity: N, sust, unsust FIB: 0, 1+, 2+, 3+, 4+ PSW: 0, 1+, 2+, 3+, 4+ Effort: N, decr Recruitment: N, inc or dec 1+, 2+, 3+, 4+ Amplitude: N, inc or dec 1+, 2+, 3+, 4+ Duration: N, inc or dec 1+, 2+, 3+, 4+ Polyphasia: N, inc or dec 1+, 2+, 3+, 4+									
R/L	MUSCLE	INSER	FIB	PSW	EFF	REC	AMP	DUR	POL
L	Deltoid	N	0	0	N	N	0	normal	N
L	Triceps	N	0	0	N	N	0	normal	N
L	1 st Dorsal Interosseous	N	0	0	N	N	0	normal	N
R	1 st Dorsal Interosseous	unsust	2+	2+	N	Inc 2+	Dec 4+	Dec 4+	N
R	Vastus Medialis	N	3+	2+	N	Inc 1+	0	Dec 1+	N
L	Vastus Medialis	N	3+	2+	N	Inc 2+	0	Dec 2=	N
L	Gastrocs Med. Head	unsust	0	1+	N	Inc 3+	Dec 3+	Dec 3+	N
L	Tibialis Anterior	unsust	3+	2+	N	Inc 3+	Dec 4+	Dec 2+	Inc 3+
L	Peroneus Longus	unsust	2+	2+	N	Inc 1+	0	normal	Inc 2+
L	Gluteus Medius	unsust	0	0	N	Inc 2+	Dec 3+	Dec 1+	N
L	Gluteus Maximus	N	0	0	N	N	0	normal	N
L	Paraspinals, Lumbar	unsust	1+	2+	N	Inc 1+	0	normal	Inc 2+

Evaluation of the sensory nerve conduction studies reveal prolonged distal latencies in the sural and ulnar nerves bilaterally. The motor nerve conduction studies were within normal limits for the nerves and muscles tested.

Abnormal spontaneous activity is noted during needle exam of the right first dorsal interosseous, bilateral vastus medialis, left tibialis anterior, left peroneus longus, and left lumbar paraspinals.

- On the basis of both the clinical and electrophysiologic evaluations, formulate your diagnostic impression. List the most likely diagnosis first and follow in order with the

other possibilities that are not excluded by the data. Eliminate those diagnoses not supported by the data.

- Are there additional electrophysiologic data that you feel would further delineate the diagnosis? (Remember, collecting data that are not needed for the diagnosis is costly and uncomfortable for the patient.)
- Make the final revisions of your diagnostic impression(s).

Diagnostic Impression

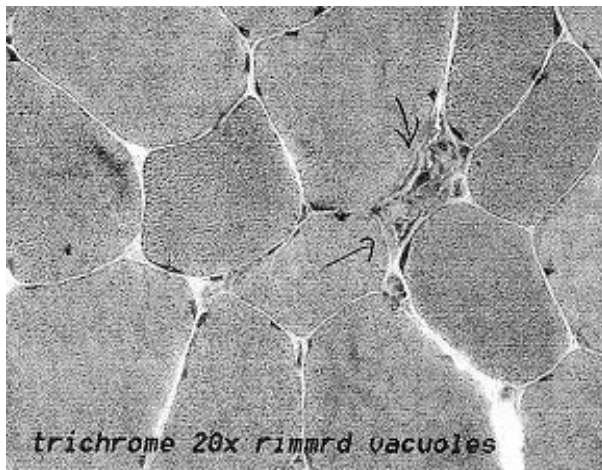
The motor units on needle exam are fast firing with early recruitment and appear polyphasic with low amplitudes and decreased durations. Coupled with the spontaneous activity of positive sharp waves and fibrillations, the EMG results are consistent with an active myopathic process revealed in the distal and proximal musculature; with the distal muscles more affected. In addition, the presence of a peripheral sensory polyneuropathy is supported by prolonged distal latencies in the sural and ulnar nerves. This is consistent with a myopathic process with a sensory peripheral neuropathy.

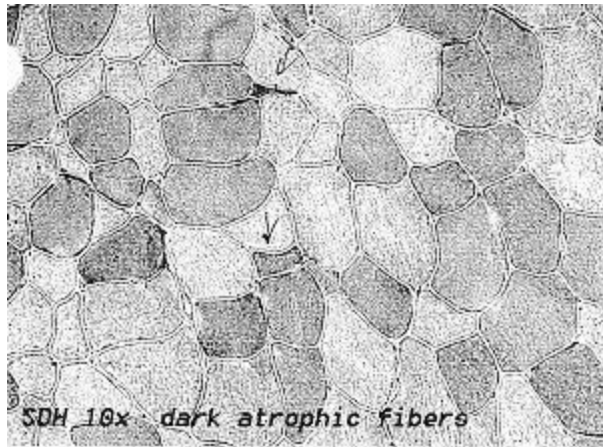
- What other diagnostic procedures (laboratory tests, etc.), if any, are needed?
- What treatment would you recommend?

The patient had the following lab tests done prior to this evaluation: basic metabolic profile (within normal limits), CBC with differential (within normal limits), thyroid profile (within normal limits), creatine phosphokinase (362 - elevated).

Commentary IV

The patient was scheduled for a muscle biopsy of the quadriceps. The report stated that on light microscopy, there were atrophic muscle fiber groups, eosinophilic cytoplasmic inclusions, and endomysial inflammation surrounding and invading nonnecrotic muscle fibers. Eosinophilic cytoplasmic inclusions and fibers with rimmed vacuoles lined with granular material were present.





The patient's muscle biopsy was found to be diagnostic for inclusion body myositis. A steroid trial was initiated. He also was enrolled in a physical therapy program to maximize his functional status.

Discussion

IBM requires differentiation from the other idiopathic inflammatory myopathies- dermatomyositis (DM), and polymyositis (PM). Of the three, DM is generally the most responsive to treatment. Steroids and intravenous immunoglobulin are considered first line treatments. Immunosuppressants utilized as second line treatment in refractory DM cases include azathioprine and methotrexate.

Inclusion body myositis is the most common of the inflammatory myopathies but the one that is most difficult to treat. Steroids and immunosuppressants generally do not help. Polymyositis responds to treatment with steroids, and immunosuppressants give a variable response.

Dermatomyositis affects the proximal musculature and the skin. The rash may present prior to the complaint of weakness. The upper eyelids may have a blue-purple rash, called a heliotrope rash. A Gottron's rash may also be present, with erythema of the knuckles. A rash may also be noted on the anterior chest, back, or shoulders.

In a dark skinned person, noting the rash may be more difficult. The patient in this case did not have a rash. However, a patient with dermatomyositis may not have a rash at the time of evaluation. Creatine kinase in DM can range widely, from a normal value up to fifty times normal. DM responds well to corticosteroids. In addition, a double blind placebo controlled study with IVIG was of benefit in DM that was refractory to standard treatment. 1

Polymyositis is relatively rare and should be a diagnosis of exclusion. It has a sub-acute onset, like DM. Also, like DM, it affects the proximal musculature. Multiple articles emphasize that the majority of treatment resistant PM in the past was most likely IBM misdiagnosed. Most patients with PM have a good response to prednisone. There is no standard prednisone dosing regimen. Often a high dose prednisone is maintained until the patient's strength returns normal, or if a plateau is noted. This usually occurs after four to six months of treatment.



Inclusion body myositis is the most common acquired muscle disease in patients over age fifty. CK is elevated in approximately 80% of patients, but is rarely greater than ten times normal. It is more common in males than females by a ratio of 3:1. The pathogenesis is unknown, but is most likely immunologically mediated. Swallowing dysfunction is present in 40%-60%. Facial weakness is seen in approximately one third of cases. The respiratory muscles can be affected. It affects both distal and proximal muscles.

The diagnosis of IBM (and PM) should never be made without a muscle biopsy. Open biopsy is preferred to needle biopsy as it will yield a better sample for evaluation. Both in IBM and PM, the most common treatment mistakes are made secondary to a muscle biopsy not being done, or secondary to misinterpretation of the biopsy findings. It is also recommended to obtain a biopsy sample from a muscle that did not undergo EMG testing so the muscle sample will be undamaged. The muscle biopsy in IBM will show the following: rimmed vacuoles, intracellular amyloid deposits or tubofilamentous inclusions on electron microscopy, endomysial inflammation and non-necrotic fiber invasion.

Contrary to popular belief, proximal weakness is a common feature in PM AND IBM. However, IBM also affects distal muscles, such as the finger flexors. The distribution of muscle weakness can be symmetric or asymmetric in IBM. Muscles commonly affected include forearm flexors, biceps, triceps, quadriceps, and iliopsoas. The most frequent clinical symptom is frequent falling, secondary to weak quadriceps. Atrophy in the medial forearm can give a scooped out appearance. Deep tendon reflexes can be normal or depressed.

With regards to nerve conduction studies, the sensory conduction studies are usually within normal limits. However, some patients, such as the one described in our case study, can have a mild distal, primarily sensory peripheral neuropathy. Distal sensory nerve action potentials may be absent, prolonged, or decreased in amplitude.

On needle EMG, it is common to see prominent positive sharp waves and fibrillations in the majority of muscles sampled. The motor unit action potentials (MUAPs) are usually short in duration.

On single fiber EMG, increased jitter and fiber density can be noted, however, these same findings can be seen in polymyositis.

IBM is considered to be a treatment resistant disorder. The routine use of immunosuppression is not recommended. Most patients will continue to deteriorate in spite of corticosteroids and immunosuppressive treatment. Intravenous immunoglobulin is not recommended as controlled trials have only shown mild improvement in muscle strength, and without significant functional benefits. It is recommended to give a trial of steroids, although most IBM patients will not respond to it.

It appears that in IBM, an abnormal accumulation of amyloid B precursor protein appears to be a key component of its pathogenesis. More research needs to be done with immunomodulating drugs. There currently are studies underway investigating beta-interferon.

The disease is steadily progressive. When a patient with IBM is followed over a decade or more, a marked functional decline is noted. Physical therapy is paramount to maintain as much function as possible. Most IBM patients will require an assistive device for ambulation, and a percentage will progress to wheelchair dependency. Poor prognosticators include malignancy, vasculitis, advanced age, or if there is a long time lapse prior to diagnosis.



Therefore, it is important to have the patient participate in physical therapy as soon as possible.

Bibliography

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