



EMG CASE No. 61, April 2003

Presenting Symptom(s): Progressive left arm weakness, cramping, and muscle twitching.

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Appropriate Audience: Residents and practicing physicians

Learning Objectives: After completing this educational activity, participant will be able to:
1) evaluate patients presenting with limb weakness and muscular atrophy, 2) develop a differential diagnosis with regard to limb weakness and muscular atrophy, and 3) understand and differentiate between various lower motor neuron diseases.

This case is no longer available for CME credit.

History

Chief Complaint: Left arm weakness and muscle wasting

Presentation: A 20 year-old left-handed man has noticed insidious, painless, progressive weakness in his left arm over the last year associated with loss of muscle mass. He notices increasing muscle twitching in his forearm and hand, which in his hand results in coarse twitching movements of his fingers. He is finding it more difficult to use a computer keyboard and telephone at work secondary to compromised fine motor control. He has recently begun to have painful muscle cramps in his forearm, hand, and fingers.

Initial Differential Diagnosis

A lower motor neuron lesion is the most common cause of weakness and atrophy, although myopathies can also produce this combination. The presence of fasciculation in this case is strongly supportive of a lower motor neuron lesion. Considerations in this case include:

Neuropathic causes with (only) lower motor neuron signs:

- cervical radiculopathy
- brachial plexopathy
- multiple mononeuropathies
- nerve entrapments
- mononeuritis multiplex
- polyneuropathies with asymmetric involvement
- inflammatory demyelinating neuropathy (AIDP, CIDP)
- multifocal motor neuropathy
- hereditary neuropathies (hereditary liability to pressure palsy, for example)
- motor neuron diseases
- spinal muscular atrophy
- progressive muscular atrophy
- spinobulbar muscular atrophy (Kennedy's disease)
- progressive post-polio muscular atrophy
- monomelic amyotrophy



- motor neuron disease secondary to lymphoproliferative disorders

Neuropathic causes which can present with lower motor neuron signs in combination with upper motor neuron signs, such as spasticity and hyperreflexia.

- amyotrophic lateral sclerosis
- cervical radiculopathy with cervical myelopathy
- syringomyelia

Myopathic causes leading to weakness and atrophy:

- facioscapulohumeral muscular dystrophy
- inflammatory myopathies
- metabolic myopathies

Musculoskeletal causes leading to disuse atrophy and weakness:

- local arthropathy
- inflammatory arthritis
- trauma

Commentary I

The onset of symptoms has been insidious in this patient. The history of progressive weakness and muscle atrophy with fasciculation points to a lower motor neuron process. The initial painless progression of symptoms is extremely helpful in formulating the differential diagnosis. Mononeuropathies and motor neuron diseases and perhaps a few myopathic disorders are now favored because of lack of pain. The painless progression of symptoms makes plexopathy, particularly brachial neuritis, and radiculopathy less likely.

Among myopathic causes, facioscapulohumeral (FSH) dystrophy is still a viable thought. It often presents with asymmetric weakness and atrophy of the posterior shoulder muscles and biceps. However, the fasciculation described is not accounted for by myopathic disorders. Tremor, though, is often present in patients with FSH and perhaps the movements described could be due to tremor rather than fasciculation. His age would be consistent with onset of a dystrophy. Inflammatory and metabolic myopathies are less likely because of the profound asymmetry and the presence of the muscular twitching.

Musculoskeletal causes are unlikely in this case because of the lack of pain.

Additional history including further detail of symptoms, past medical history, and family history may help to pinpoint the cause of the progressive weakness in this patient. Ultimately, electrodiagnostic studies should allow definitive localization of the pathologic process.

History, continued

The patient denies any sensory changes or any deficits in the other three extremities. He occasionally has painful muscle cramping in his fingers, hand, and forearm. These symptoms began well after he first noticed weakness and atrophy. He reports no myalgia or



arthralgia. He denies cervical pain.

Past medical history is unremarkable except for an incident in childhood in which the patient had trauma to his left shoulder, resulting in joint dislocation. He recovered from that incident without apparent sequelae.

No other family members have had symptoms like those of the patient, and there is no family history of cancer. The patient does not smoke or drink alcohol. His health has otherwise been excellent.

Prior imaging has included MRI of brain, cervical spine, and brachial plexus (with contrast), as well as plain films of the left shoulder. All studies were normal. Laboratory evaluation has included a normal sedimentation rate, routine chemistry battery, CBC, and CPK level. No antibody to GM-1 was detected

Commentary II

Lack of sensory complaints is extremely helpful in narrowing the differential diagnosis. We can discard processes that affect both sensory and motor function, including most neuropathies, radiculopathies, and plexopathies. We now must consider the disorders on our differential that typically produce only motor abnormalities. FSH muscular dystrophy and perhaps other unusual myopathies remain, but are distinctly unlikely given the fasciculation. Disorders of the motor neuron or motor nerve are now most likely. Brachial neuritis (i.e., neuralgic amyotrophy) can affect only motor function, but it is typically an extremely painful, acute condition, whereas the process here is painless and more chronically progressive.

Revised Differential Diagnosis

- motor neuron diseases
- monomelic amyotrophy
- spinal muscular atrophy
- spino-bulbar muscular atrophy (Kennedy's disease)
- ALS
- progressive post-polio muscular atrophy
- motor neuron disease secondary to lymphoproliferative disorders
- motor neuropathies
- multifocal motor neuropathy
- hereditary motor neuropathy - not supported by family history and would be unlikely to have persistently asymmetric course

Physical Examination

Mental Status: Normal

Cranial Nerves: 2-12 intact

Muscular Examination: Left triceps, first dorsal interosseus, and thenar group have notable atrophy. Fasciculations are present. Strength is 5/5 throughout all muscle groups except in the left upper limb as noted in the following table:



Deltoid	Biceps	Triceps	Wrist Extensors	Median Hand Intrinsic	Ulnar Hand Intrinsic
5	5-	4+	5-	4	4

Reflexes: 2+ throughout the upper and lower extremities with the exception of the left triceps reflex, which is absent. Babinski was negative.

Sensation: intact to light touch, pinprick, vibration, and temperature in all four extremities, trunk, and neck.

Gait: normal, narrow-based; patient is able to walk on his toes, heels, and in tandem fashion with no difficulty.

Commentary III

Physical examination supports lack of sensory changes and lack of upper motor neuron signs. Weakness and atrophy are restricted to the left arm. The presence of fasciculations is confirmed. The definite presence of fasciculations allows us to discard the myopathies from our differential. We are left with motor neuron diseases and motor neuropathies. A diagnosis of definite ALS cannot be made in the absence of upper motor neuron signs, but often patients will present with a purely lower motor neuron syndrome and later go on to develop upper motor neuron signs, then allowing a diagnosis of ALS to be made. Thus we cannot discard ALS from our differential at this time, although the development of ALS in a 20-year-old man would be distinctly unusual. Other motor neuron disorders are rarely this asymmetric with the exception of monomelic amyotrophy. Multifocal motor neuropathy also remains highly possible.

Monomelic amyotrophy: Monomelic amyotrophy is a rare lower motor neuron disease that affects predominantly one upper limb with occasional minor involvement of the contralateral upper limb. It was described first in Japan (Hirayama et al., 1959) and perhaps is most common in Indian and Japanese populations, although cases are now being described worldwide. Average age of onset is between 15 and 25 years of age. Estimated male:female involvement ranges from 5:1 to 10:1. Onset is with insidious, painless wasting/weakness of muscles of one upper limb, often with sparing of the brachioradialis muscle. There is no sensory deficit; reflexes may be normal or may be reduced. With progression of the disease, tremor of fingers may be noted. Muscle stiffness/weakness may be exaggerated in cold environments. Hyperhidrosis is seen in some patients. The pathological process is related to focal loss of anterior horn cells often localized to one or two cervical levels with only minor involvement of anterior horn cells of neighboring cervical levels. Imaging of the cervical spine may be normal or may show asymmetric atrophy of one anterior horn region. Nerve conduction studies are often normal until later in the disease process when loss of axons may lead to low amplitude CMAP responses. Needle examination reveals denervative process in the distribution of the affected cervical segments. Often there is subclinical involvement in the contralateral arm detected on needle examination. There should be no abnormality in the legs or beyond the affected cervical segments. Disease progression generally halts after one to two years, though may continue longer in rare cases. There is no treatment currently. Absolutely positive differential from other motor neuron disorders may require prolonged observation. If there is no progression to other body segments over 1-2 years, then other motor neuron diseases have been excluded.



Multifocal Motor Neuropathy: Multifocal motor neuropathy is characterized by slowly progressive, asymmetric weakness with atrophy, although the weakness may often be more severe than expected for the degree of atrophy. Peak age of onset is from the 20s to the 40s; men are more affected than women. Upper limbs are often affected first and more severely. Progression may continue for years. Patients may or may not have muscle cramps and fasciculations. Nerve conduction studies are significant for complete or partial conduction blocks in motor nerves. Focal slowing of conduction may also be seen. Sensory nerve conduction studies are normal. The needle examination documents denervation in the territories of individual nerves, with multiple nerves often being affected. Laboratory studies reveal the presence of GM-1 antibodies in 40-80% of cases. There is effective treatment for multifocal motor neuropathy and therefore it is important to differentiate from motor neuron diseases and other diseases for which there is no treatment. Treatment for multifocal motor neuropathy is with IVIG or cyclophosphamide; steroids may worsen the disease.

Commentary IV

Median nerves and ulnar nerves across the elbows should be examined to evaluate the clinical abnormalities. Electrodiagnostic evaluation should include motor and sensory nerve studies in three limbs to evaluate for peripheral polyneuropathy. F-waves should be performed to evaluate for a condition affecting proximal nerve function such as chronic idiopathic demyelinating polyradiculopathy. Electromyographic examination should include the hand muscles, which are the most involved clinically. A lower limb, including a foot muscle, should be studied to evaluate for a loss of motor innervation in a distal to proximal gradient.

Electrophysiologic Data

SENSORY NERVE CONDUCTION STUDIES

NERVE	SIDE	STIM SITE	RECORD	cm	AMPL (uV)	LAT (mS)	CV (m/sec)
Median	L	Wrist	Index	14	51.5	3.2	58.3
Median	R	Wrist	Index	14	47.5	2.8	66.7
Radial	L	Forearm	Wrist	10	46.0	1.9	66.7
Radial	R	Forearm	Wrist	10	35.4	2.0	71.4
ulnar	L	Wrist	5th	14	39.0	2.8	66.7
ulnar	R	Wrist	5th	14	34.5	2.9	63.6
Sural	L	Calf	Ankle	14	42.3	3.1	56.0

MOTOR NERVE CONDUCTION STUDIES

NERVE	SIDE	STIM SITE	RECORD	cm	AMPL (mV)	LAT (mS)	CV(m/sec)
Median	L	Wrist	Thenar	7	11.5	3.0	
Median	R	Wrist	Thenar	7	11.7	3.1	



Median	L	Elbow	Thenar				61.1
Median	R	Elbow	Thenar				56.0
Ulnar	L	Wrist	Hypothenar	7	2.0	3.2	
Ulnar	R	Wrist	Hypothenar	7	14.1	3.0	
Ulnar	L	Below Elbow	Hypothenar		2.0		65.9
Ulnar	R	Below Elbow	Hypothenar		13.3		62.1
Ulnar	L	Above Elbow	Hypothenar		1.7		58.8
Peroneal	L	Ankle	EDB	9	7.8	4.5	
Peroneal	L	Below Knee	EDB		7.5		58.0
Tibial	L	Ankle	Abd. Hal.	8	13.6	3.8	
Tibial f-response	L						45.3

NEEDLE ELECTROMYOGRAPHY

INSERtional activity: N, sust, unsust

FIB: 0, 1+, 2+, 3+, 4+

OTHer: 0 or fascic, myotonia, myokymia

EFFort: N, decr

RECRuitment: N, inc or dec 1+, 2+, 3+, 4+

AMPliitude: 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	OTH	EFF	REC	AMP	DUR	POL
L	Biceps Brachii	N	0	0	N	↓ +/-	↑ +/-	↑ +/-	N
L	Triceps	N	1+	fascic	N	↓ 3+	↑ 2+	↑ 1+	↑ +/-
L	deltoid	N	0	0	N	N	N	N	N
L	EI	N	0	0	N	↓ 2+	↑ 1+	↑ 2+	↑ 2+
L	FDIH	N	0	fascic	N	↓ 2+	↑ 1+	↑ 1+	↑ 1+
L	APB	N	0	0	N	↓ +/-	↑ +/-	↑ 1+	↑ 1+
L	Pronator Teres	N	1+	0	N	↓ 4+	↑ +/-	↑ 3+/-	↑ 3+/-
R	Pronator Teres	N	0	0	N	↓ +/-	↑ 1+	↑ +/-	↑ +/-
R	FDIH	N	0	0	N	↓ 1+	↑ +/-	↑ +/-	↑ +/-
R	Triceps	N	0	0	N	↓ 1+	↑ 1+	↑ 1+	↑ 1+



R	Deltoid	N	O	O	N	N	N	N	N
L	Vastus Medialis	N	O	O	N	N	N	N	N
L	Medial Gastroc	N	O	O	N	N	N	N	N
L	Anterior Tibialis	N	O	O	N	N	N	N	N

Summary: The sensory nerve conduction studies are normal, even in the ulnar nerve where the CMAP amplitude is markedly reduced. No motor conduction block is detected, given the preservation of amplitudes with proximal stimulation. Needle examination reveals prominent denervation and reinnervation changes in the left arm with the C7 spinal level being most severely affected, but clearly involving muscles of the C6 - C8 myotomes. In addition, milder, chronic denervation changes are noted in similar spinal levels in the clinically asymptomatic right arm. Needle examination of select leg muscles is normal.

Diagnostic Impression

This study provides electrodiagnostic evidence of a denervating disorder affecting the left greater than right arms. Multilevel cervical radiculopathy or a disorder of the anterior horn cells best explain the electrodiagnostic findings. No conduction block was identified, making the diagnosis of multifocal motor neuropathy unlikely. This study, in combination with the clinical situation, is most suggestive of left monomelic amyotrophy.

Commentary IV

This case of slowly progressive weakness without pain or sensory abnormality in a young man represents a nearly classic presentation of monomelic amyotrophy. One question that has been raised in the past is whether monomelic amyotrophy might be an early presentation of ALS and whether or not the disease will eventually involve all limbs. Gourie-Devi et al. (2003) have recently addressed these issues in their long term follow up of 44 patients with monomelic amyotrophy. They included 44 patients in their study who had met criteria for monomelic amyotrophy for a minimum of five years, to a maximum of 23 years (mean 9.7 years, 68% for longer than 10 years). The mean age of onset of symptoms was 19.8 years with a range of 13-32 years, however, 82% of patients had symptom onset between the ages of 16 and 25. Male:female ratio was 10:1. An equal distribution between sides (right:left) was noted. In 18.2% of patients, the contralateral upper limb was affected, but to a much milder degree. Regarding course of the disease, 70.3% of patients had no further progression of their symptoms after the first two years. 94.6% had no progression after 5 years. Of perhaps more importance to the patient is that the level of final disability was regarded to be mild in 68.2%, moderate in 22.7%, and severe in only 4.5%. No one in the study progressed to ALS or any other diagnosis. (It is not clear if that would be the case in persons who had not held the diagnosis for at least 5 years.) One case report (Rowin et al., 2001) suggests progression of monomelic amyotrophy after a period of 31 years of stability. One might hypothesize that progression in this case is due to aging and death of surviving anterior horn cells, much as has been proposed in post polio syndrome.



Monomelic amyotrophy, when first noted in the literature in 1959 (Hirayama et al., 1959), was called "juvenile muscular atrophy of the unilateral upper extremity," and the term, in its general use, refers to upper extremity involvement. There have been descriptions of a few cases of monomelic amyotrophy of the lower limb (Uncini et al., 1992); however, it is a less well-defined entity than monomelic amyotrophy affecting the upper limb(s). Only a few cases have been described overall. From the cases described, onset is more variable, having been noted to be from 26-42. Anatomical abnormalities such as pes cavus may be associated. There is evidence of a diffuse, subclinical anterior horn cell involvement in all four limbs. Disease course has not been well-described.

The majority of cases reported in the literature are sporadic. Gucuyener et al. (1991) report a case of affected siblings.

No further diagnostic procedures are indicated at this time. Observation of this patient over the next 1-2 years will solidify the diagnosis.

Additional studies that might have been done as a point of interest include needle examination of the brachioradialis and ECR, which are reported to be spared in a significant number of cases of monomelic amyotrophy (Orvema et al., 1990).

Autonomic testing would also be of interest in this patient as there have been studies documenting involvement of the autonomic nervous system in monomelic amyotrophy. In a study of sympathetic skin responses of 9 patients and 25 controls (Gourie-Devi et al., 2001), sympathetic skin response (activation of sweat glands) was prolonged in the 9 patients relative to the controls, and the response was seen in both upper limbs.

Treatment

There is no treatment for monomelic amyotrophy. Observation over time is warranted. Progression generally stops in 1-2 years though may go on for up to 5 years in rare cases. Patients who have carried a diagnosis of monomelic amyotrophy for 5 years may be reassured that they will not progress to more serious diseases with poor prognosis such as ALS. Patients generally will stabilize with mild to moderate physical impairment in one upper limb with occasional minor impairment in the contralateral upper limb. Progression to lower limbs should not occur.

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