



EMG Case No. 55, June 2002

Presenting Symptom: Slowly Progressive Weakness

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Appropriate Audience: Residents and practicing physicians

Learning Objectives: After completing this educational activity, participants will be able to: 1) Differentiate among different forms of motor neuron disease, 2) Identify key diagnostic features of Kennedy disease (spinal and bulbar muscular atrophy), 3)

Formulate an electrodiagnostic study appropriate to evaluate for possible motor neuron disease.

History

The patient is a 34-year-old man with an 8-year history of slowly progressive weakness. He first noticed the weakness in his legs while downhill skiing, with difficulty standing up from the chairlift. Since then, it has progressed to involve his arms as well. At the present time, he complains of weakness primarily in his hands and thigh muscles, with particular difficulty rising from a chair, difficulty grasping objects and performing fine motor skills with his hands.

The patient denies numbness or tingling although he frequently drops objects. He has no difficulty with bowel or bladder function. Other symptoms include shortness of breath with exertion, difficulty swallowing, and frequent snoring during sleep noticed primarily by his wife.

- *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?*

Commentary I

The patient complains of diffuse weakness that is very slowly progressive and does not have a clear proximal or distal distribution based on the history. A hereditary or acquired myopathic or peripheral neuropathic disorder is possible. In addition, complaints consistent with bulbar dysfunction makes a disorder of the anterior horn cells a consideration. An upper motor neuron disease such as multiple sclerosis is also possible, as is a neuromuscular junction disorder.

In order to differentiate between a hereditary and acquired disorder, family history would be helpful. Other medical problems predisposing to myopathy or neuropathy would be relevant, as well as symptoms suggesting central nervous system pathology.

History, continued

The patient's maternal grandfather had similar symptoms, although he was never diagnosed with any specific disorder. His one son, aged 8, appears normal. He denies any other medical problems although a recent infertility workup revealed a low sperm count. He



denies muscle spasms or stiffness. He is a nonsmoker and nondrinker, and takes no medications. There are no HIV risk factors.

Although the patient works as a manager of a large fruit orchard, he does not knowingly receive ongoing exposure to any toxins.

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

Commentary II

The family history of a grandfather with similar symptoms is suspicious but not conclusive for a hereditary neuromuscular disorder. There are no symptoms to suggest an upper motor neuron process, although the physical examination often reveals abnormal findings not evident from the history. Other common etiologies for peripheral neuropathy such as diabetes, thyroid disease, drug toxicity, or alcoholism are unlikely.

Important physical examination details include discerning the presence of upper motor neuron signs, which could signify either a primary central nervous system disease or, if combined with lower motor neuron findings, be suggestive of amyotrophic lateral sclerosis. The proximal versus distal predilection of weakness, along with any signs of sensory involvement, would help differentiate a motor neuron or myopathic process from a peripheral neuropathic disorder.

Physical Examination

Physical examination reveals a moderately obese male who is notably dysarthric and becomes short of breath with exertion. There is no ptosis and he is able to bury his lashes and purse his lips. Neck strength is normal. There is obvious gynecomastia, and breath sounds are diminished bilaterally. Range of motion is full in all limbs.

There is no obvious muscle atrophy. Motor examination reveals mild (4/5) weakness in the shoulder abductors, elbow flexors and extensors bilaterally. The wrist extensors are 4+/5 with wrist flexors, long finger flexors, hand intrinsics and thumb abductors 4-/5. The lower limbs reveal 4/5 bilateral hip flexors and extensors, 4+/5 knee flexors and extensors, 4/5 ankle dorsiflexors, and 5/5 plantar-flexors. Sensation is preserved with the exception of diminished pinprick in the thumb, index, and long fingers bilaterally. Muscle tone is normal and muscle stretch reflexes are 1+ and symmetric throughout. Hoffman's sign is negative and the plantar response is flexor, with no sustained clonus at the ankles.

- *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?*

Commentary III

There is no evidence to suggest upper motor neuron pathology. Symmetry of motor involvement suggests a systemic rather than multifocal process. There is no clear proximal versus distal predilection to help delineate a peripheral neuropathic from myopathic process, although the relative preservation of the ankle musculature would be unusual in polyneuropathy. Sensation appears normal with the exception of pinprick loss in the median distribution. Further evidence of concomitant carpal tunnel syndrome would be helpful.



The presence of dysarthria, along with reported dysphagia, is consistent with bulbar muscle dysfunction. This finding makes one suspicious for anterior horn cell disease without upper motor neuron involvement.

Pulmonary signs and symptoms, in conjunction with an obvious neuromuscular disorder, may be indicative of significant restrictive lung disease.

Physical Examination, continued

No tongue fasciculations are present. Carpal compression test and Phalen's sign are present bilaterally.

- *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

Although the presence of tongue fasciculations would increase the likelihood of bulbar anterior horn cell disease, its absence certainly does not rule out this disorder. There is further evidence for carpal tunnel syndrome.

The electrodiagnostic examination should include nerve conduction studies sufficient to establish the absence or presence of a peripheral neuropathic process. During needle EMG, the examiner should carefully observe motor unit morphology to discern between a myopathic and neuropathic process, and determine the distribution of the abnormalities. The presence of median neuropathy at the wrist should be confirmed.

Electrophysiologic Data

MOTOR NERVE CONDUCTION STUDIES							
NERVE	SIDE	STIM SITE	RECORD	Cm	AMPL	LAT	CV
Median	R	Wrist	APB	8	3.7	6.1	-
		Elbow	APB	20	3.8	10.1	50
Median	L	Wrist	APB	8	3.8	6.0	-
		Elbow	APB	20.5	3.5	10.2	49
Ulnar	R	Wrist	ADM	8	7.6	3.3	-
		Elbow	ADM	20	7.7	6.8	57
Ulnar	L	Wrist	ADM	8	6.0	3.0	-
		Elbow	ADM	20.5	6.2	6.2	64
Peroneal	L	Ankle	EDB	8	7.6	4.8	-
		Fib Head	EDB	30	7.4	11.0	48



SENSORY NERVE CONDUCTION STUDIES							
NERVE	SIDE	STIM SITE	RECORD	Cm	AMPL	LAT	CV
Sural	L	Calf	Ankle	14	5	4.2	-
Median	R	Wrist	Index	14	2	5.1	-
Median	L	Wrist	Index	14	8	4.5	-
Ulnar	L	Wrist	Small dig	14	7	3.5	-
Ulnar	R	Wrist	Small dig.	14	5	3.3	-
Radial	L	Wrist	Dors. Hand	12	12	2.4	-

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+ AMPlititude: 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	Vastus Lateralis	N	0	0	N	Dec 2+	Inc 4+	Inc 4+	N
L	Tibialis Anterior	N	0	0	N	N	Inc 2+	Inc 2+	N
L	Gluteus Medius	N	0	0	N	Dec 2+	Inc 2+	Inc 2+	N
L	Thoracic Paraspinal T8 level	N	0	0	N	N	Inc 2+	Inc 1+	N
L	Deltoid	N	0	0	N	N	Inc 2+	Inc 2+	Inc 1+
L	Pronator Teres	N	0	1+ fascic	N	Dec 2+	Inc 4+	Inc 4+	Inc 1+
L	1 st Dorsal Interosseus	N	0	0	N	N	Inc 2+	Inc 2+	N
	Tongue	N	0	0	N	Dec	Inc	Inc	Inc



						1+	2+	2+	1+
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- *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.)*

Sensory nerve conduction studies reveal, in addition to focal slowing in the median fibers across the wrist, generalized low amplitude responses for a person of this age. This is consistent with a sensory neuronopathy. The motor nerve conduction studies are normal with the exception of focal median nerve slowing across the wrists and low median CMAP amplitudes.

Needle EMG was only performed on the left side in case a muscle biopsy was needed in the near future. The needle EMG does not demonstrate active membrane instability but findings are consistent with chronic denervation in all muscles tested, including thoracic paraspinals and a bulbar muscle.

- *Make the final revisions of your diagnostic impression(s).*

Diagnostic Impression

The electrodiagnostic impression includes:

1. Widespread, chronic neuropathic findings on needle EMG in the presence of normal motor nerve conduction studies, compatible with a motor neuron disorder.
2. There appears to be a sensory neuronopathy on the basis of low SNAP amplitudes.
3. Bilateral median neuropathies at the wrist, consistent with carpal tunnel syndrome.

In addition, important findings from the clinical history and examination include:

1. Gynecomastia and a history of low sperm count suggest androgen insensitivity.
2. Symptoms and signs consistent with restrictive lung disease.

This constellation of findings, along with a family history of an affected male, strongly suggests Kennedy Disease (spinal and bulbar muscular atrophy).

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

Commentary V

The findings of diffuse, chronic denervation in limb and bulbar muscles raises the possibility of amyotrophic lateral sclerosis. However, several findings are not consistent with this disorder. First, there is no clinical evidence of upper motor neuron involvement. Second, a sensory neuronopathy should not be present with ALS. Finally, due to the rapid progression of the disease, most ALS patients will show signs of acute as well as chronic denervation with needle EMG. Another possible motor neuron disorder might be an adult form of hereditary spinal muscular atrophy, but the other electrodiagnostic and clinical findings are more compatible with Kennedy disease.



Spinal and bulbar muscular atrophy, or Kennedy disease, is a disorder involving slowly progressive limb and bulbar muscle weakness associated with mild androgen insensitivity. As it is inherited as an X-linked recessive disorder, only males are affected. Neurologic symptoms typically present after age 20, and about one-third require a wheelchair for mobility 20 years after the onset of symptoms. Due to bulbar muscle involvement, difficulty with speech articulation and swallowing is common, and aspiration pneumonia is a concern. Virtually all affected males have gynecomastia as a sign of androgen insensitivity. Testicular atrophy and oligospermia are other signs of this condition.

Electrodiagnostic findings demonstrate diffuse chronic denervation. The common presence of an associated sensory neuronopathy, often in the absence of sensory symptoms, helps differentiate Kennedy disease from other motor neuron disorders.

All patients with Kennedy disease have increased CAG trinucleotide repeats (>35 CAGs) in the androgen receptor gene at chromosome locus Xq11-q12. There is an association between the number of repeats and severity of the disease. This testing is clinically available.

This patient's symptoms and signs are fairly classic for Kennedy disease. His bulbar and pulmonary symptoms are concerning and out of proportion to the severity of limb weakness. He underwent chromosomal testing which revealed 47 CAG repeats at locus Xq11-q12.

Our recommendations for the patient at this time include:

1. Pulmonary function testing including nighttime oximetry.
2. Speech Pathology consultation to assess swallowing function and instruction on safe swallowing techniques.
3. Treatment of carpal tunnel syndrome.

Bibliography

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