



## EMG Case No. 58, December 2002

**Presenting Symptom: 25 year-old woman with four years of exercise intolerance including muscle pain and fatigue.**

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**Appropriate Audience:** Residents and practicing physicians

**Learning Objectives:** After completing this educational activity, participant will be able to: 1) Identify the major categories of metabolic myopathy, 2) Obtain a focused history and review of systems for adult onset metabolic myopathy and perform a cost-effective workup of these symptoms, 3) Perform an ischemic forearm exercise test.

**This case is no longer available for CME credit.**

### History

Chief complaint: Exercise intolerance

KM is a 25 year-old woman with 4 years of muscle pain shortly after the onset of intense exercise. This began during her junior year of college when she was on a college varsity basketball team. Within one to two minutes of playing basketball or sprinting, she would develop achy pain in her legs. This would subside within a few minutes of ceasing activity. There was a clear threshold as she could jog or bike ride at an easy pace without difficulty. She denied cramps, contractures, or discolored urine (evidence of myoglobinuria).

- **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

Whenever exercise intolerance is reported, a primary metabolic myopathy should be considered. There are different types of metabolic myopathies depending on the pathway affected. One large subcategory includes disorders of glycogen or glucose breakdown. Examples of these include myophosphorylase deficiency, known as McArdle's disease, phosphofructokinase deficiency, and lactate dehydrogenase deficiency. These patients typically cannot perform high intensity activity such as sprinting. Another category is disorders of fatty acid transport such as primary carnitine deficiency or carnitine palmitoyltransferase deficiency. These patients can perform brief bursts of intense activity but have problems with sustaining activity such as jogging. Additionally, myoadenylate deaminase deficiency, a disorder of the purine nucleotide cycle, can cause such symptoms. Another category includes mitochondrial disorders, a subset of which includes pure myopathies. Although these can involve weakness, exercise intolerance may be the only manifestation.

Myasthenia gravis may cause muscular fatigue with exercise, but typically does not produce



pain. Lambert-Eaton myasthenic syndrome typically produces proximal weakness that may improve with exercise.

One should also keep in mind the common systemic disorders associated with muscle dysfunction such as thyroid disorders, Addison's disease, Cushing's disease, uremia, cirrhosis, and selected electrolyte imbalances (Na, K, Ca)

While pain is a common feature of dermatomyositis and polymyositis, the onset is insidious and is not associated with exercise.

Degenerative disk disease of the spine can give intermittent pain but this is usually lancinating burning pain that includes back pain and is often position dependent.

### **History, continued**

KM denied any back pain or positional dependence to her pain. Her symptoms were dependent on the intensity of her activity, i.e. she had no complaints at low intensity exercise. Furthermore, she denied any diplopia, dysphagia, or effect of cumulative activity on her symptoms. That is, she could cease intense activity and resume activity multiple times without developing fixed weakness or fatigue. She did not develop symptoms any sooner after a full day of activity. In addition, she denied any fixed weakness or progression of her symptoms over the past four years. She was however, unable to continue playing basketball to her satisfaction, and has since switched to more moderate exercise.

Otherwise, she denied any appetite changes. She had no problems with bowel or bladder habits. She did not have any substantial weight change, and she reported her mood as good.

- *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**

Based on the additional information, spinal disk disease is very unlikely, as is dermatomyositis or polymyositis. A metabolic myopathy such as McArdle's disease, myoadenylate deaminase deficiency, or mitochondrial disorder remains at the top of the differential. With the absence of fixed weakness, fatigue, or bulbar findings, myasthenia gravis is less likely.

### **Physical Examination**

Height: 6' 1", Weight: 165lbs; healthy, athletic appearing woman in no distress

Head and Neck: no abnormalities.

Heart: regular rate and rhythm no murmurs, gallops, or rubs

Lungs: clear to auscultation bilaterally

Abdomen: soft, nontender, nondistended with positive bowel sounds



Extremities: no clubbing, cyanosis, or edema

Neurological exam: mental status: intact to detailed history taking

Cranial nerves: II-XII in detail: intact

Motor: normal bulk and tone; 5/5 strength throughout

Coordination, Sensation, and Gait: all within normal limits

Reflexes: 2+ throughout with downgoing toes

- **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**

The physical examination is normal, however this is what we would expect in a mild form of metabolic myopathy. Laboratory testing should be performed to evaluate for thyroid and adrenal function as well as electrolytes and CPK level. This is elevated in 90% of patients with McArdle's disease and many patients with myoadenylate deaminase deficiency. Checking acetylcholine receptor antibodies would also be useful. An additional laboratory study that is helpful in identifying McArdle's disease and myoadenylate deaminase deficiency is the ischemic forearm exercise test. This is performed as follows:

1. Draw baseline lactate and ammonia blood levels.
2. Inflate blood pressure cuff to 20mmHg above systolic pressure on the dominant arm.
3. Exercise arm for 2 minutes then deflate cuff.
4. Draw ammonia/lactate at 1, 3, and 5 minutes following exercise cessation.
5. Rise of less than 3 times baseline for ammonia correlates with myoadenylate deaminase deficiency.
6. Rise of less than 3 times baseline for lactate correlates with McArdle's disease.
7. If neither the lactate nor ammonia rise appropriately, the level of exercise intensity was likely suboptimal.

### **Physical Examination, continued**

Results of lab testing for KM: TSH:0.97mcl/ml (wnl); CPK: 48U/L; sodium, potassium, urea nitrogen, creatinine, calcium, ALT, AST: all within normal limits, AM cortisol: 26, acetylcholine receptor antibodies: <0.5nmol/L, Carnitine (free and total): within normal limits.



The results of the ischemic forearm exercise test were as follows:

time	ammonia(umol/L)	lactate(meq/L)
0	<1.0	1.0
1	26	5.7
3	44	5.5
5	40	4.4

- *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**

The results of the blood work eliminate systemic causes of muscle dysfunction. The ischemic forearm exercise test showed an appropriate rise in lactate, making McArdle's disease highly unlikely. Likewise, the ammonia level also rose greater than 3 times baseline making myoadenylate deaminase deficiency unlikely as well.

EMG testing should include basic nerve conduction studies (focusing on motor responses) of the upper and lower extremities. These are typically normal in metabolic myopathies. The needle examination should focus on the lower extremity, as this is where the symptoms are occurring. The needle examination may show "myopathic" changes if there is significant weakness, but often is normal as well.

**Electrophysiologic Data**

**SENSORY NERVE CONDUCTION STUDIES**

NERVE	SIDE	STIM SITE	RECORD	cm	AMPL	LAT	CV
sural	r	calf	ankle	14	32	3.7	
median	r	wrist	2nd digit	14	22	3.1	
ulnar	r	wrist	5th digit	14	13	3.0	



**MOTOR NERVE CONDUCTION STUDIES**

NERVE	SIDE	STIM SITE	RECORD	cm	AMPL	LAT	CV
median	r	wrist	apb	7	14.3	3.4	
median	r	elbow	apb	26.7	13.7	8.0	58.1
ulnar	r	wrist	adq	7	8.7	2.8	
ulnar	r	elbow	adq	285	8.5	8.0	54.9
peroneal	r	ankle	edb	9	4.7	5.9	
peroneal	r	fibular head	edb	40.2	4.3	15.0	44.2
tibial	r	ankle	ah	8	9.2	4.6	
tibial	r	knee	ah	476	7.2	15.5	43.7

**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+

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	OTH	EFF	REC	AMP	DUR	POL
R	tibialis anterior	N	0	0	N	N	N	N	N
R	edb	N	0	0	N	N	N	N	N
R	medial gastroc.	N	0	0	N	N	N	N	N
R	vastus lateralis	N	0	0	N	N	N	N	N
R	iliopsoas	N	0	0	N	N	N	N	N
R	gluteus medius	N	0	0	N	N	N	N	N
R	gluteus maximus	N	0	0	N	N	N	N	N
R	paraspinals L3/L4	N	0	0	N	N	N	N	N



R	paraspinals L4/L5	N	0	0	N	N	N	N	N
R	paraspinals L5/S1	N	0	0	N	N	N	N	N

- *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 normal EMG results markedly reduce the likelihood of an inflammatory myopathy but are consistent with a metabolic myopathy. The ischemic forearm exercise test eliminated two of the metabolic myopathies but did not eliminate the possibility of other metabolic derangements, including mitochondrial myopathy.

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

**Commentary V**

The gold standard for mitochondrial myopathy diagnosis is a muscle biopsy. KM had a biopsy of the right vastus lateralis. This demonstrated the presence of some moth-eaten muscle fibers as well as some mitochondrial dysmorphic changes. While these findings are subtle and do not meet diagnostic criteria, they are consistent with a mitochondrial myopathy. At present there are 7 identified mitochondrial DNA mutations associated with isolated skeletal myopathies. They involve a transfer RNA gene in 5 cases, the cytochrome b gene, and the COX III gene, also. Genetic testing is an emerging diagnostic tool for these patients.

The prognosis is good and KM's course is likely to be slowly progressive but relatively benign. With aging, mitochondrial function can also deteriorate; therefore she may have some progression over decades. Creatine, Coenzyme Q10, riboflavin, vitamin E, and carnitine are the dietary supplements which sometimes provide improvement of symptoms. Physical therapy and strategies for brief rest at onset of symptoms can also prolong exercise tolerance.

**Bibliography**

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