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CASE SET #20

A Chemistry Case:

Rhabdomyolysis and the Kidney in a Fall-Risk Patient

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Clinical Laboratory Investigations

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LEARNING OBJECTIVES

Upon completion of reading the case, the learner will be able to:

1. Identify the biochemical marker(s) that contribute to the diagnosis of an acute rhabdomyolytic event and describe how laboratory tests may be used to differentiate rhabdomyolysis from other processes.
2. Demonstrate a general knowledge of the etiology and risk-factors associated with rhabdomyolysis.
3. With a diagnosis of rhabdomyolysis and appropriate laboratory results, determine clinical dangers associated with the disease process and possible treatment modalities.

Rhabdomyolysis and the Kidney in a Fall-Risk Patient

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CASE PRESENTATION

Patient history

A 69-year old female was brought to the hospital emergency department from a retirement/assisted care facility because of a ground level fall. The patient had apparently been down for several hours before being found. She reported some back pain but no chest pain or palpitations. Her medical history included type II diabetes with related neuropathy, hypertension, non-alcoholic steatohepatitis (NASH), morbid obesity, hypothyroidism, dementia, a history of falls, and recurrent urinary tract infections (UTI). The patient had undergone a right nephrectomy 30 years prior and had a cholecystectomy performed at an undetermined point in the past.

Initial examination and laboratory tests

A physical examination showed no signs of processes other than those mentioned in the patient's medical history. Computerized tomography (CT) scans of the patient's lumbar, thoracic, and cervical spine showed some degenerative narrowing and signs of arthritis but no signs of fractures. Similarly, 16-slice CT scans of the head revealed cortical and cerebellar atrophy but no acute abnormalities or signs of trauma, and a chest scan gave no indication of serious cardiopulmonary disease.

Initial chemistry laboratory results (Table I) revealed elevated blood urea nitrogen (BUN) of 39 mg/dL as well as an elevated creatinine level of 1.8 mg/dL, signifying

reduced kidney function.[1] A complete blood count (CBC) and white blood cell differential showed only slightly elevated hemoglobin and hematocrit (Table II).

Table I: Initial Chemistry Laboratory Tests

Chemistry Test	Result	Reference Range*	Units
Creatinine	1.8	0.6-1.2	mg/dL
Blood Urea Nitrogen (BUN)	39	8-23	mg/dL
Glucose	102	82-115	mg/dL
Chloride	104	98-107	mmol/L
Sodium	141	136-145	mmol/L
Potassium	4.7	3.5-5.1	mmol/L
Ionized Calcium	5.2	4.64-5.28	mg/dL
CO_2	25	23-31	mmol/L
Anion gap	17	10-20	mmol/L

*Reference ranges as defined for a 69 year-old female[1]

Table II: Initial Complete Blood Count (CBC) Results with Differential

Complete blood count	Result	Reference Range*	Units
White blood cells	9.6	4.0-11.0	10^3/µL
Red blood cells	5.04	3.50-5.50	10^6/µL
Hemoglobin	16.7	11.7-16.1	g/dL
Hematocrit	49.6	35.0-47.0	%
Mean corpuscular volume	98.4	81.0-102.0	fL
Mean corpuscular hemoglobin	33.2	27.0-35.0	pg
Mean corpuscular hemoglobin concentration	33.7	32.0-36.0	%
Red cell distribution width	14.3	11.5-14.5	%
Platelets	127	150-450	10^3/µL
Differential			
Neutrophils	66.5	40.0-80.0	%
Lymphocytes	23.0	10.0-48.0	%
Monocytes	9.1	3.0-11.0	%
Eosinophils	0.3	0.0-4.7	%
Basophils	1.1	0.0-2.0	%

*Reference ranges as defined for a 69 year-old female[1]

Urinalysis (UA) with urine microscopic evaluation was performed (Table III). The urine microscopic showed hyaline, granular, and cellular casts, and the UA dipstick demonstrated the presence of blood, indicating reduced kidney function. It should be

noted that a positive blood result in the UA dipstick may be falsely positive resulting from the presence of myoglobin in the urine.[2] Positive leukocyte esterase, and a high number of white blood cells in the urine indicated the presence of an infection, and the urine was referred to the microbiology department to perform a culture.

Table III: Urinalysis

UA (catheter specimen)	Results	Reference Range*
Color	Yellow	Straw-Yellow
Clarity	Cloudy	Clear-Hazy
Specific gravity	1.010	1.005-1.030
pH	5.0	5.0-8.0
Leukocyte esterase	1+	Neg
Nitrites	Neg	Neg
Protein	1+	Neg
Ketones	NEG	Neg
Urobilinogen	2.0 mg/dL	Neg
Bilirubin	Neg	Neg
Blood	3+	Neg
Ascorbate	Neg	Neg
Culture reflex?	Yes	--
Squamous epithelial cells	+2	Neg
Transitional epithelial cells	+1/hpf	Neg
White blood cells	55/hpf	Neg
Red blood cells	2/hpf	Neg
Hyaline casts	45/lpf	Neg
Granular casts	2/lpf	Neg
Cellular casts	6/lpf	Neg

*Reference ranges as defined by the clinical laboratory

Cardiac biomarker levels were performed (Table IV), showing a highly elevated creatine kinase (CK) but a negative cardiac troponin I (11,535 U/L and 0.00 ng/mL, respectively). Because it is specific to the myocardium, the negative troponin I level

signified that no acute myocardial infarction or other myocardial or cardiopulmonary process had occurred, but rather that the tissue damage was most likely of the skeletal muscle.[3]

Table IV: Cardiac Biomarkers

Cardiac Biomarker	Result	Reference Range*	Units
Creatine Kinase (CK)	11,535	20 - 180	U/L
Troponin I	0.00	0.00 – 0.06	ng/mL

*Reference ranges as defined for a 69 year-old female[1]

Diagnosis

The highly elevated CK is strongly suggestive of rhabdomyolysis and considered by some to be alone diagnostic, as will be discussed below.[4] Because the patient did not appear to be taking any medication that would cause rhabdomyolysis, as determined by pharmacy staff, and because there was no neural injury apparent upon examination, the causation was assumed to be physical muscular damage due to the ground level fall.

Treatment

Treatment for both rhabdomyolysis and UTI were initiated immediately upon emergency department admission. Aggressive hydration was employed to support kidney function and prevent renal tubular damage.[5] Ceftriaxone, a third-generation cephalosporin with broad spectrum activity, was given as an antibiotic in response to the apparent concomitant UTI in lieu of culture results that would take days to finalize.

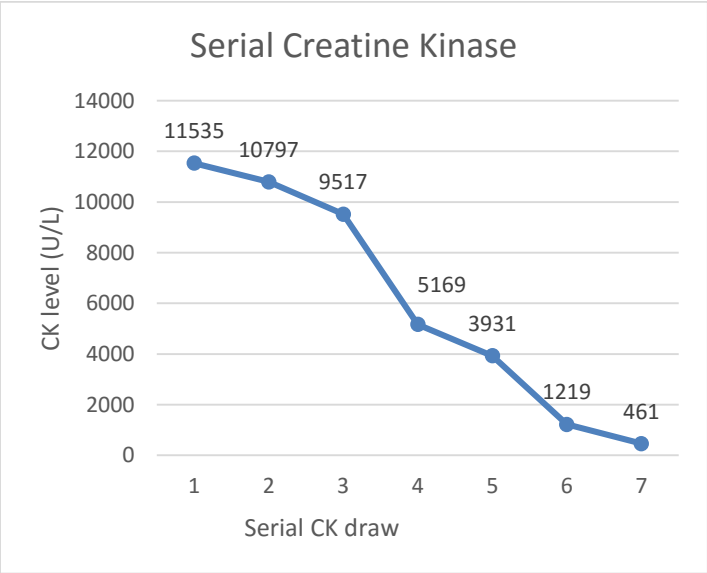
Ceftriaxone is a common choice in cases such as this because it is generally effective against UTIs and, importantly, it does not need to be adjusted to accommodate renal dysfunction because it can be eliminated from the body by both renal and biliary modes.[6]

Resolution

Over the course of hospitalization, the patient's CK trended downward, arriving at an acceptable level of 461 U/L five days after admission (Figure I). The patient was released five days after entering the hospital in markedly improved condition with respect to rhabdomyolysis, kidney function, and UTI. Culture of the urine had revealed Lactobacillus (80,000 CFU/mL) which was sensitive to the Ceftriaxone. The patient returned to the retirement/assisted care facility with a plan of care including physical therapy and a follow-up appointment with the primary care physician one week later. Because the rhabdomyolysis was attributed to recurrent falls, the patient's discharge plan of care included the recommendation that more extensive supportive care be considered to prevent future falls.

Figure I: Serial Creatine Kinase (CK)

A total of seven levels performed over the course of five days of hospitalization. (Reference range: 20-180 U/L[1]).



It is possible that unmanaged diabetes and the accompanying neuropathy were partially responsible for the patient's falls. Therefore, a glycosylated hemoglobin A_{1c} level was performed and shown to be 6.0% (Reference range: 4.0-5.2%[1]), indicating that blood glucose levels were slightly high but moderately well-controlled and that the falls were unlikely to be a result of diabetic-induced neuropathy. The patient's diabetic diet was continued. Also, because many medications can cause rhabdomyolysis, the patient's medication list was to be thoroughly checked by a pharmacist for any drugs that should be discontinued to prevent future rhabdomyolytic risk. A list of the patient's medications prior to emergency department admission appear in Table V. None of these were deemed to be etiologic agents of myolytic injury by pharmacy staff.[7]

Table V: Medications Prior to Emergency Department Admission

	Medication	Purpose
1	Byetta	Blood glucose control
2	Colace	Constipation relief
3	Cyclobenzaprine	Muscle relaxer
4	Invega	Antipsychotic
5	Invokana	Blood glucose control
6	Levemir	Insulin analog
7	Lunesta	Sleep aid
8	Lyrica	Diabetes-related neuropathy relief
9	Miralax	Constipation relief
10	Mirapex	For tremors and muscular restlessness
11	Multivitamin	General health
12	Myrbetriq	Overactive bladder control
13	Namenda	Dementia relief
14	Oxybutynin	Bladder relaxer
15	Ramipril	Antihypertensive
16	Synthroid	Thyroid hormone replacement

DISCUSSION

Rhabdomyolysis is caused by physical or biochemical injury to muscle cells (myocytes). This damage compromises the myocytic membrane (sarcolemma), and subsequently releases cellular contents into the bloodstream. It has a wide range of etiologies, causative mechanisms, and presentations as well as a broad spectrum of severity. Causes include physical trauma, burns, many medications (notably statins, stimulants, antidepressants, antipsychotics, and recreational drugs) and can in rare cases be due to hereditary predispositions.[5,8,9] It is somewhat difficult to determine the incidence in the general population because many cases undoubtedly go unreported or are subclinical.[10] When the myocytes lyse or the sarcolemma is compromised, the resulting physiological impact, especially on the kidneys, can be devastating. Myoglobin, a protein present in large quantities in the muscle tissue, if released into the

bloodstream, may pass through the glomerulus and cause renal tubular damage, giving rise to renal dysfunction, and in some cases acute renal failure (ARF).[11]

There are a number of ways to detect a rhabdomyolytic event. The most common and easily measureable biochemical marker is creatine kinase (CK, also known as CPK or creatine phosphokinase), a phosphorylating enzyme specific to muscle and neural tissues. A fractionated CK separated to the multiple isoenzymes can be used to differentiate between the possible sources of the CK, however in practice this is not necessary to make a diagnosis of rhabdomyolysis if one can rule out a cardiac event as was done in the above case by measuring the cardiac troponin I level. Neural and brain trauma must also be eliminated from the differential diagnosis because these tissues also contain a significant amount of its specific CK enzyme fraction (CK-BB).[1] Also of possible importance in the detection of rhabdomyolysis is myoglobin, both in blood and urine. However, myoglobin is not often tested because the CK is more readily measured and can provide more specific diagnostic and prognostic information.[11] A diagnostic threshold for CK is considered by some sources to be approximately five times a normal CK level.[4] Myalgia and darkly colored urine can also suggest rhabdomyolysis, and rhabdomyolysis should always be considered in any differential diagnosis of crush-type injuries.[8,11]

When a diagnosis of rhabdomyolysis is made, it is of critical importance to begin treatment as soon as possible to prevent permanent renal tubular damage by free myoglobin and support kidney function.[8] Depending on severity, hydration may be the only treatment necessary, however in more acute, life-threatening cases, acidosis may occur due to the release of intracellular organic acids and thus must be treated with a

pH-raising agent such as bicarbonate.[7] Acute hyperkalemia (excess blood potassium) may also occur in some cases and must be treated with serum potassium-lowering agents.[8,10] Once hydration is begun, CK levels in the blood should steadily decrease toward normal levels as seen in the above case and the patient can be expected to recover full renal function.[4]

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