

A Rare Case of Rhabdomyolysis Probably Due to Donepezil

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Abstract

Rhabdomyolysis ranges from an asymptomatic illness with the elevations in the Creatine Kinase (CK) levels to a lifethreatening condition associated with electrolyte imbalances, Acute Renal Failure (ARF). The causes of non-traumatic rhabdomyolysis may include defects in skeletal muscle metabolism, electrolyte disturbances, alcohol intoxication, illicit drug use, infections and various medications. Donepezil is a cognitive-enhancing medication for treating dementia of Alzheimer's disease. We present a rare case of acute kidney injury secondary to rhabdomyolysis probably induced by donepezil.

The possibility of a drug induced rhabdomyolysis should also be considered in the differential diagnosis after excluding other causes when a patient having ARF associated with elevations in CK levels and the presence of a dipstick indicating large amount of myoglobin in the peripheral blood and urine without red cells on the microscopic examination.

Keywords: Creatine kinase; Donepezil; Rhabdomyolysis

Introduction

Rhabdomyolysis means destruction or disintegration of striated muscle [1]. Rhabdomyolysis ranges from an asymptomatic illness with elevation in the Creatine Kinase (CK) level to a lifethreatening condition associated with extreme elevations in CK, electrolyte imbalances, Acute Renal Failure (ARF) and disseminated intravascular coagulation [2].

ARF develops in 33% of the patients with rhabdomyolysis [3]. Acute rhabdomyolysis occasionally develops in patients with structural myopathies when they are performing strenuous exercise, are under anesthesia, have taken drugs that are toxic to muscles, or have viral infections [4].

We present a rare case of acute kidney injury secondary to rhabdomyolysis probably induced by donepezil.

Case Report

84-year-old male patient with a medical history of hypertension, cerebrovascular disease and Alzheimer's disease presents with nausea, vomiting, generalized muscle pain and impaired general condition. These symptoms began approximately 3 days earlier. On further questioning the patient states that he has been taking his medications (including lisinopril hydrochlorothiazide 20/25 mg 1×1, verapamil 120 mg 1×1, donepezil 10 mg 1×1, acetylsalicylic acid 100 mg 1×1) as prescribed. He has been taking these drugs for a long time.

There is no history of trauma, headache, visual changes, convulsion, previous fall, illicit intravenous drug use, or statin intake. He denied drinking alcohol. There was no loss of consciousness or head trauma. His past medical history is otherwise unremarkable. Review of the systems is unremarkable.

On physical examination he was an ill-appearing, apathic male. The vital signs were; the blood pressure was 120/65 mm/Hg, the pulse 84 beats per minute, the temperature 36.8°C. the respiratory rate 14 breaths per minute, and the oxygen saturation 100% while the patient was breathing ambient air. Decreased muscle strength was noted. He had bilateral moderate pretibial edema.

Laboratory studies revealed the following: urea: 179 mg/ dL; creatinine: 5 mg/dL; aspartate aminotransferase: 42 U/ L; CK: 2422 U/L; calcium: 9.5 mg/dL; phosphorous: 5.5 mg/dL; sodium: 138 mmol/L; potassium: 5 mmol/L; albumin: 3.7 g/ dL; lactate dehydrogenase:

332 U/L; hemoglobin: 12 g/dL. Arterial blood gas and erythrocyte sedimentation rate, serum albumin level, thyroid function tests, serum vitamin D level, antinuclear antibody, anti-neutrophil cytoplasmic antibody values were within normal limits. Viral or bacterial infectious causes was ruled out. The patient's urine dipstick analysis revealed that indicating large amount of myoglobin in the peripheral blood and urine without red cells on the microscopic examination. Significant proteinuria was observed. An abdominal ultrasound demonstrated small-sized kidneys with the evidence of a thin parenchyma. Echocardiography was performed and left ventricular ejection fraction was reported as 40%.

The administration of dextrose, bicarbonate, and intravenous crystalloid was begun. He was admitted to the medical service. During the next 3 days, heparin added, and intravenous furosemide and fluids were administered to maintain urine output. Cultures of the blood and urine were sterile. Nerve-conduction studies were essentially normal; there was no evidence of axonal or demyelinating sensorimotor polyneuropathy.

Our patient is an old man presenting with ARF which in this case probably caused by nontraumatic rhabdomyolysis. The diagnosis of ARF secondary to rhabdomyolysis is suggested by the marked rise in muscle enzymes in the presence of a dipstick indicating large amount of myoglobin in the peripheral blood and urine without red cells on the microscopic examination. The patient developed acute kidney injury secondary to rhabdomyolysis probably induced by donepezil and may have a component of ATN. He will likely recover, but not until after an unpredictable period has elapsed that may require long term dialytic support in terms of being low EF and ATN on the kidneys having already chronic renal parenchymal disease. Using of donepezil in this patient with chronic renal insufficiency might be complicated by

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Causes of Rhabdomyolysis						
Drugs	Electrolyte imbalances	Infections	Trauma and compression	Endocrine disorders	Autoimmune diseases	Others
Sedative hypnotics Antilipemic agents Antipsychotics and antidepressants Emetics Others (Cocaine, Alcohol, Salicylates, Paracetamol, Theophylline, Thiazides)	Hyperosmotic conditions Hypernatremia Hypocalcemia Hyponatremia Hypokalemia Hypophosphatemia	HIV, Coxsackie and Herpes viruses Falciparum malaria Legionella Salmonella Streptococcus Tularemia	Crush injuries Motor vehicle accidents Physical torture and abuse Prolonged hours of surgery without changing position	Hyperaldosteronism Hypothyroidism Ketoacidosis Hyperaldosteronism	Polymyositis and Dermatomyositis	Toxins Excessive muscular activity Temperature extremes Muscle ischaemia Genetic disorders

Table 1: The most common causes of rhabdomyolysis [3,8].

rhabdomyolysis. For that reason; donepezil was discontinued. Showed significant decreases in serum CK levels. His CK levels had regressed completely to normal levels in the outpatient follow up.

Discussion

Donepezil is a cognitive-enhancing medication for treating mild-to-moderate dementia of Alzheimer's disease and inhibits the cholinesterase enzyme that breaks down acetylcholine, a neurotransmitter. Rhabdomyolysis is a potentially life-threatening condition that must be suspected in all patients with a history of any circumstance that can result in damage of skeletal muscle. The most common causes of rhabdomyolysis in adults are illicit drugs, alcohol abuse, medical drugs, muscle diseases, trauma, Neuroleptic Malignant Syndrome (NMS), seizures and immobility [5]. (The most common causes of rhabdomyolysis can be seen in the Table 1). It ranges in severity from an asymptomatic elevation of CK levels in blood, to severe life-threatening cases associated with very high CK levels, myoglobinuria and ARF. In our case ARF was a result of rhabdomyolysis probably induced by donepezil and not a direct nephrotoxic effect of the drug. Rhabdomyolysis, is one of the rare side effects of donepezil. But we don't know that how donepezil can cause rhabdomyolysis. In the literature donepezil caused by acute

renal failure secondary to rhabdomyolysis, there were only two cases [6-8]. We offer a third case of acute renal failure secondary to rhabdomyolysis probably induced by donepezil.

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