CASE REPORT

Acute kidney injury due to rhabdomyolysis-associated gangrenous myositis

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Abstract. Rhabdomyolysis is associated with infectious diseases in approximately 5% of cases and acute kidney injury occurs in 33-50% of cases. Gangrenous myositis is a deep seated infection of the subcutaneous and muscular tissues. We report the case of an 18 year-old man who was admitted to the emergency room with leg pain, fever, nausea, vomiting and oliguria. Physical examination showed moderate dehydration, peripheral cyanosis and skin necrosis with severe myalgia and no subcutaneous gas. Laboratory findings at admission were: serum urea 111 mg/dL, creatinine 1.3 mg/dL, potassium 6.3 mEq/L, creatine kinase (CK) 112,452 IU/L, aspartate amino transaminase (AST) 1116 IU/L, alanine amino transaminase (ALT) 1841 IU/L, pH 7.31, bicarbonate (HCO_3) 11 mEq/L and lactate 4.3 mmol/L. Emergency hemodyalisis was started, and antibiotics were given due to high suspicion for bacterial infection. The patient developed respiratory insufficiency and septic shock needing mechanical ventilation and vasoactive drugs. He presented spontaneous gangrenous myositis in both legs and in his left arm. After 26 sessions of hemodialysis, partial recovery of renal function was observed. He was discharged from the ICU after 38 days, still with leg pain. Acute kidney injury due to rhabdomyolysis should be considered as a possible complication of gangrenous myositis. (www.actabiomedica.it)

Key words: Rhabdomyolysis, gangrenous myositis, acute kidney injury, oliguria, dialysis

Introduction

Rhabdomyolysis is a clinical and laboratory syndrome resulting from skeletal muscle injury and release of muscle cell contents into the plasma. The most common causes are severe physical exercise, infection, inflammatory processes and trauma (1). Non-traumatic rhabdomyolysis has been recognized in association with myopathy, electrolyte abnormalities, hyperthermia, drug overdose, tissue hypoxia, and viral infections (2).

Acute kidney injury occurs in 33-50% of patients with rhabdomyolysis and it is the main cause of death in this syndrome (2, 3). The main mechanisms involved are renal vasoconstriction, intraluminal cast formation and direct heme protein-induced tubular toxicity (4). There are few studies on muscular injury associated with bacterial infection (5).

The aim of this paper is to report a severe case of acute kidney injury due to rhabdomyolysis-associated gangrenous myositis.

Case report

An 18 year-old man was admitted to the emergency room with fever, nausea, vomiting, oliguria, and dark brown urine. He had been practicing vigorous

exercise for two consecutive days five days before admission. The exercise consisted in intense running (about 10 Km per day). The day after the physical activity, his legs were extremely painful. There was no history of drug intake, alcohol or cocaine abuse. Physical examination showed moderate dehydration, peripheral cyanosis and skin necrosis with severe myalgia and no subcutaneous gas. His blood pressure was 130/79 mmHg and the cardiac and respiratory rates were 130 bpm and 24 rpm, respectively. Laboratory findings at admission were: serum urea 111 mg/dL, creatinine 1.3 mg/dL, potassium 6.3 mEq/L, creatine kinase (CK) 112,452 IU/L, aspartate amino transaminase (AST) 1116 IU/L, alanine amino transaminase (ALT) 1841 IU/L, pH 7.31, bicarbonate (HCO_3) 11 mEq/L and lactate 4.3 mmol/L. The laboratory findings during his hospital stay are shown in Table 1. Emergency hemodyalisis was started due to anuria, refractory hyperkalemia and hypercatabolism. Antibiotic therapy with teicoplanin and meropenem was started before collecting hemocultures because of a high suspicion of bacterial infection. The patient was transferred to the intensive care unit. Blood cultures were negative. In the second day of hospitalization, the patient presented respiratory insufficiency and septic shock needing mechanical ventilation and vasoactive drugs. He presented gangrenous myositis in both legs and in his left arm (Figures 1 and 2). In the third week of hospital stay, the patient needed surgical debridement of wounds and amputation of the left leg. After 26 sessions of hemodialysis, urine volume began to increase, and the levels of urea and creatinine decreased to normal levels, as illustrated in Figure 3. He was discharged from the ICU after 44 days with an important improvement of his general condition, still with leg pain and total recovery of the renal function.

Discussion

Rhabdomyolysis is a clinical and biochemical syndrome which occurs when skeletal muscle cells erupt, resulting in the release of creatine kinase (CK),

Table 1. Laboratory findings during hospitalization of an 18 year-old male patient with rhabdomyolysis-associated gangrenous myositis

Day	1	2	3	5	7	10	12	15	18	19	26	28	38	41
Urea (mg/dL)	111	103	-	125	182	-	198	140	-	156	107	119	-	34
Creatinine (mg/dL)	1.3	3.0	2.8	2.3	2.2	-	2.7	2.8	-	3.8	2.7	2.9	-	0.5
Potassium (mEq/L)	6.3	6.3	4.1	3.9	3.9	4.5	4.8	5.0	5.6	5.0	4.1	4.3	4.2	4.9
Sodium (mEq/L)	134	131	140	137	133	137	134	133	134	133	134	133	138	139
Total Calcium (mg/dL)	6.2	-	7.2	8	-	-	7.0	7.4	-	7.6	8.2	7.8	-	7.3
Hematocrit (%)	44.2	37	32.1	30.5	31.2	24.3	20.4	16.8	-	16.5	27.2	23.8	23.2	22.7
Hemoglobin (g/dl)	15.9	13.2	10.9	10.4	10.2	8.76	7.51	5.76	5.08	5.76	9.23	8.2	7.81	7.66
WBC ($x10^3/mm^3$)	19,5	24,1	21,9	27,3	30,5	16,1	9,3	13,8	17,3	11,3	11,3	10,9	3,3	7,5
Platelets ($x10^3/mm^3$)	186	127	83,9	65,9	74,9	240	511	761	504	278	204	301	415	588
Prothrombin time (%)*	43.5	56.7	-	74.6	-	-	-	-	-	-	111	-	-	-
PTT (")**	1.25	1.02	-	1.19	-	-	-	-	-	-	-	-	-	-
AST (IU/L)	1841	1363	-	-	-	-	89	-	-	-	149	-	-	-
ALT (IU/L)	402	387	-	-	-	-	68	-	-	-	50	-	-	-
LDH (IU/L)	6558	6403	-	-	-	-	1353	-	-	-	-	-	-	-
CK (IU/L)	112,452	-	42,910	-	-	1,609	3,053	-	-	-	-	-	-	-
Urinalysis														
pH	6,0	-	-	-	-	6,5	-	-	-	-	-	-	-	-
Gravity	1010	-	-	-	-	1010	-	-	-	-	-	-	-	-
Red blood cells (hpf)	>100	-	-	-	-	4	-	-	-	-	-	-	--	
Hemoglobin	++++	-	-	-	-	++	-	-	-	-	-	-	-	-
Protein	++	-	-	-	-	trace	-	-	-	-	-	-	-	-

WBC – white blood cells, PTT-Partial thromboplastin time, AST-aspartate amino transaminase, ALT-alanine amino transaminase, LDH-lactate dehydrogenase, CK-creatine kinase, hpf- high-power field. * Control for prothrombin time = 13"; *** control for partial thromboplastin time = 28"

Figure 1. Necrotic lesions and ecchymosis in lower limbs

Figure 2. Edema and necrosis in upper limb

lactate dehydrogenase (LDH) and myoglobin into the interstitial space and plasma. We described a case of very severe rhabdomyolysis caused by gangrenous myositis, complicated with acute kidney injury.

After the occurrence of muscular injury, myoglobin is released into the circulation and is freely filtered by glomeruli, with a depuration rate that corresponds to 75% of creatinine clearance. The serum levels of myoglobin may remain in the normal range while urinary levels are high, due to its rapid filtration. The serum level of myoglobin returns to normal values in 1-6 hours after injury, due to hepatic metabolism and renal excretion (4). The main mechanisms involved in acute kidney injury in rhabdomyolysis are renal vasoconstriction, intraluminal cast formation and direct heme protein-induced tubular toxicity. Myoglobin toxicicity is higher in hypovolemia and shock (4). In the present case, the patient was admitted with oliguria and decreased renal function, needing dyalisis. In this case, the main factor leading to the development of acute kidney injury was likely exercise-induced rhabdomyolysis, precipitated by gangrenous myositis.

Although only 5% of rhabdomyolysis cases are associated with infectious diseases (6), many agents are related to this condition, especially viruses. Rhabdomyolysis due to influenza virus, para-influenza type 1, coxsackie virus, dengue virus, human immunodeficiency virus and herpes virus (HSV-2) has been reported (7).

The most frequent bacteria associated with rhabdomyolysis are Legionella, Streptococus, Salmonella and Francisella tularensis (8, 9). Prognosis is generally poor for rhabdomyolysis during the course of pneumococcal pneumonia, with increased morbidity and mortality (6). Rhabdomyolysis is presumed to be caused by the direct toxic effect of bacteria on muscle or by hemodynamic abnormalities caused by the septic condition, with a shift of the blood supply away from the muscle causing muscle hypoxia and necrosis.

Gangrenous myositis is a rare soft-tissue infection generally caused by Streptococcus pyogenes. It has an extremely high mortality (in excess of 80%). A literature review from 1985 by Adams et al (10) reported only 21 cases from 1900 to 1984. It is likely

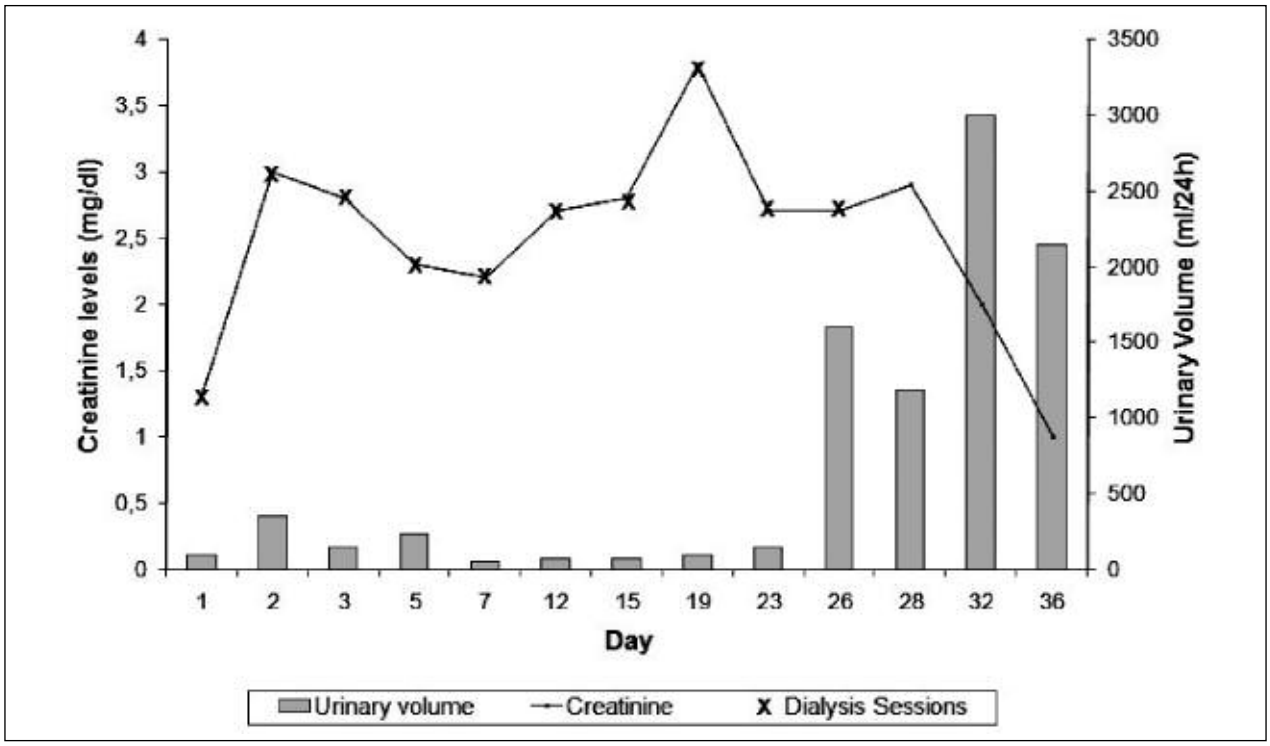

Figure 3. Urinary volume, serum creatinine levels and dialysis sessions during hospitalization, for an 18 year-old male patient with rhabdomyolysis-associated gangrenous myositis

that recent or preexisting muscle injury is needed for the bacteria to infect the muscle. Overuse of muscles, blunt trauma, and skin abrasions all appear to predispose patients to this infection.

Muscle cell destruction leads to a high peak of serum creatine kinase such as in the case described here (133,510 IU/L). Although no correlation between renal function and creatine kinase levels was described, the main factor leading to renal failure in this patient was undoubtedly rhabdomyolysis.

Treatment of rhabdomyolysis should be instituted immediately to avoid the development of acute kidney injury. Intravascular volume expansion by using saline solution and mannitol should be performed. Alkalization of urine can be attempted to reduce the formation of myoglobin casts in renal tubules (11). In the case presented here the mainstay of treatment consisted in hemodialysis and use of antibiotics, with total recovery of renal function.

In summary, rhabdomyolysis may be associated with bacterial infection and is an important cause of acute kidney injury. It may also occur after strenuous exercise associated with dehydration. In the case presented here, rhabdomyolysis developed after vigorous physical activity and spontaneous gangrenous myositis. There was improvement of renal function after a period of renal replacement therapy. Rhabdomyolysis should be considered as a possible complication in various infectious diseases.

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