Life-threatening Rhabdomyolysis Complicating Surgical Reperfusion of Peripheral Arterial Occlusive Disease — A Case Report and Literature Review

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Rhabdomyolysis is a rare complication following successful reperfusion of occluded peripheral arteries. Acute renal failure frequently develops in these patients, and it carries a high mortality rate. We report a 78-year-old female with near-total occlusion of bilateral femoral arteries. After successful femoral-popliteal artery bypass, she developed rhabdomyolysis with acute renal failure. Despite intensive support and treatment, she died of multiple-organ failure.

Key Words: Rhabdomyolysis • Acute renal • Failure peripheral • Arterial occlusive disease

INTRODUCTION

Rhabdomyolysis, compartment syndrome, and crush syndrome represent a spectrum of the same disease,1,2 which may be induced by numerous factors, including alcoholism, crush injury to a limb, overuse of skeletal muscle, heat, viral infections, metabolic disorder, myopathies, drugs, toxins, and hyperkalemia.1,3 Rhabdomyolysis is a rare complication after successful bypass surgery for peripheral vascular disease. Acute myoglobinuric renal failure may further complicate the situation, with catastrophic results. In a recent study of crush injuries, acute renal failure developed in 16.5% of patients with rhabdomyolysis, and 42.3% of them died.3 We report a case of severe rhabdomyolysis with acute renal failure after successful peripheral vascular surgery.

CASE REPORT

A 78-year-old female suffered from right leg swelling, pallor, and pain and was not able to move her leg for 2 weeks prior to admission. The patient had a history of hypertension treated with amlodipine for 2 years and type 2 diabetes mellitus for 3 years. She did not smoke. Toes of both legs were cyanotic and cold, and dorsalis pedis pulses were weak bilaterally.

Selective angiographic examination (Figure 1) revealed near-total occlusion of several segments of bilateral femoral arteries. She underwent a femoral-popliteal bypass with 10 mm ringed vascular grafts and bilateral femoral artery endarterectomy. After surgery, her legs became warm and strong dorsalis pedis pulses were palpable bilaterally. She was treated with intravenous heparin and prostaglandin E1 postoperatively. Neither hemodynamic compromise nor hypoglycemia were found during and on the first day after the surgery.

Three days after surgery, the patient suddenly became dyspneic and oliguric. Her urine was dark red in
color and her plasma creatinine increased from 0.8 to 2.0 mg/dL, creatine kinase (CK) level was 3526 U/L on the next day, and 1 day later it reached peak (21659 U/L, 200 times higher than normal)(Table 1). Serum myoglobin measured several days after the acute episode was within normal limits. The patient was treated with saline infusion to keep adequate hydration and intravenous sodium bicarbonate to maintain the urine pH above 6.5. Her right toes subsequently developed gangrene and swelling, and compartment syndrome was suspected. She therefore underwent fasciotomy. Unfortunately, the right toe was persistent in gangrene and subsequent right above-the-knee amputation was performed a few days later. The CK decreased to 938 U/L and creatinine level to 0.9 mg/dL 10 days after the amputation.

However, the patient later developed pneumonia with septic shock and became comatose. She subsequently developed multiple-organ failure syndrome and died 1 month later.

**DISCUSSION**

Rhabdomyolysis has been defined as reversible or irreversible injury of skeletal muscle in which cell membrane loses its integrity and cell contents leak out to the extracellular compartment. It can be triggered by any process which diminishes the production of adenosine triphosphate, such as inadequate oxygen supply secondary to ischemia, hypotension or vasospasm, or increased consumption of ATP beyond the production rate of the skeletal muscle. In crush syndrome, a rapidly progressive pressure-stretch myopathy is thought to be the earliest predominant event. Besides compartment pressure-induced ischemia, another important cause of skeletal muscle damage is reperfusion injury mediated by oxygen free radicals. In our patient, neither hemodynamic compromise nor metabolic disorders such as hyperkalemia, acidosis, and hypoglycemia were found during and in the first 2 days after surgery. In addition, rhabdomyolysis secondary to anastomosis leakage and thrombosis usually occurs within 24 hours after the surgery, but in our patient after bypass, strong bilateral dorsal pedis pulses persisted for 2 days, and rhabdomyolysis with subsequent acute renal failure did not happen until 3 days later. We therefore suspected that the cause of rhabdomyolysis in our patient was at least in part from reperfusion injury following bypass.

The mechanism of reperfusion injury involves calcium, leukocytes, and oxygen free radicals, the last of which is thought to have major impact on the progression.
of injury. The primary source of superoxide in reperfused tissue appears to be the product of xanthine oxidase, which is converted from xanthine dehydrogenase by a calcium-triggered proteolytic attack.\(^7,8\)

The diagnosis of rhabdomyolysis is based on a 5-fold increase in the serum CK or the presence of myoglobinemia, with or without myoglobinuria.\(^1,4\) Myoglobinemia correlates poorly with myoglobinuria, since the level of myoglobin in the urine depends on a variety of factors, including the amount of myoglobin released into plasma, the glomerular filtration rate, and the urine concentration.\(^1\) Thus, not all patients with myoglobinemia have visibly red urine. Myoglobin is rapidly cleared from the blood, usually within 1 to 6 hours. Therefore the plasma level may be within normal limits a few hours to days after the onset of rhabdomyolysis. This may explain the normal myoglobin level in our patient.

The pathogenesis of acute renal failure in rhabdomyolysis is still not clearly understood. One possibility is that decomposed myoglobin products, such as ferrihemate that is usually present when urine pH < 6.5, have direct toxic effects. In this regard, there may also be tubular obstruction by myoglobin itself or uric acid crystals. Another hypothesis is that the release of vasoconstrictive mediators (angiotensin-II, catecholamines, vasopressin, and intrarenal thromboxane) secondary to renal ischemia may play a major role.\(^7\) Risk factors of acute renal failure in the setting of rhabdomyolysis include hypovolemia, extreme elevation of serum CK concentration, and a low urine pH.\(^3,9\) Some authors suggest all acutely ischemic patients are groups at high-risk for renal complication.\(^6\)

Adequate hydration and urine alkalization is essential for treatment of rhabdomyolysis combined with acute renal failure. In fact, under such treatment, our patient did initially recover from renal failure. Regarding treatment of rhabdomyolysis secondary to reperfusion injury, controversy exists. A previous report showed that inhibitors of oxygen free radicals limit the generation of arachidonic acid products following ischemia.\(^10\) In addition, scavengers of free radicals have been investigated. These agents include mannitol (which also promotes osmotic diuresis and may be appropriate for acute renal failure) and allopurinol.\(^7\) However, effects are difficult to assess because the severity of crush syndrome is unpredictable; for example, it does not appear to be related to the size of the area involved or the duration of compression.\(^2,7\) Other inhibitors of free radicals, such as superoxide dismutase, catalase, iron chelating agents and calcium channel blockers, have been shown to be effective in animal models.\(^8\) However, these scavengers need to be administered as early as possible during reperfusion in order to prevent irreversible cell damage. Amiloride, a potassium-sparing diuretic decreasing intra-cellular sodium concentration and inhibiting sodium-hydrogen exchanger in many tissues, is reported to markedly improve the contractile and metabolic recovery during post-ischemic reperfusion.\(^3\) Benzamil, an amiloride analogue with a stronger ability to block sodium-calcium exchanger, is more protective against the calcium-paradox than amiloride.\(^3\) Our patient was hyperkalemic after the onset of rhabdomyolysis, therefore, usage of these potassium-sparing agents seemed to be inappropriate. Fasciotomy will be performed if compartment syndrome develops.\(^3,7\) To save life from extension gangrene, amputation is suggested if fasciotomy treatment is not effective.\(^6\) The lack of definitive therapy for rhabdomyolysis together with the numerous clinical problems in this lady prevented us from saving her life from the lethal sequela after the bypass surgery.

REFERENCES

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