RHABDOMYOLYSIS

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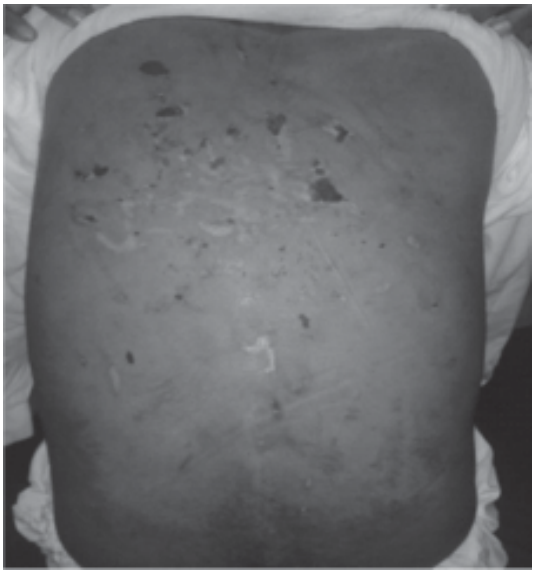
CASE HISTORY

A sixty year oldgentleman, presented with body aches, pain, weakness and bilateral pedal edema for last 6 days.8 days before admission he remained in the custody of law enforcement agencies and was subjectedto physical torture.No previous history of hypertension, diabetes, renal, cardiac, liver or respiratory problems.



PHYSICAL EXAMINATION

Conscious, oriented, pale looking elderly gentleman, pulse 80/min regular.B.P150/70 mm Hg, bilateral pitting edemapitting pedal edema. Chest had bilateral basal crepts,on back there were marks of violence all over the back and on limbs in the form of bruises lacerations. Cardiovascular, nervous and abdominal examination was unremarkable. Investigations showdLow Hb of9.5 g%,highTLC of 12600/mm3(80% neutrophils),Platlets=345000/mm^{3}grossely deranged ranal functions with Urea=227 mg/dl and creatinine=8.7 mg/dl.

Liver function tests were also abnormal with ALT 242 IU/L.

Na=136mmol/l, K=7.5mmol/l,Cl=112mmol/l.

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RBS=91mg/dl.ProthrombinTime =15(control=14), APTT = 34 (control = 34).Hepatitis B,C =Negative,Urine R/E shows dark colour urine, no albumin and sugar Pus cells=2-3/HPF.CPK was very high 5000.

On the basis of history (physical violence), examination, deranged renal functions and very high CPK diagnosis of Rhabdomyolysis with acute renal failure was made.He was dialysed 3 times and the renal functions became normal.

LITERATURE REVIEW; RHABDMYOLYSIS

Rhabdomyolysis — literally, the dissolution of skeletal muscle is characterized by the leakage of muscle-cell contents, including electrolytes, myoglobin, and other sarcoplasmic proteins (e.g., creatine kinase, aldolase, lactate dehydrogenase, alanine aminotransferase, and aspartate aminotransferase) into the circulation 1, 2

CAUSES

1. Trauma…..crush syndrome
2. Exertion…strenuous exercise, seizures, alcoholwithdrawl syndrome
3. Muscle hypoxia…limb compression during immobalisation or artery occlusion
4. Genetic defects.

   Disorders of glycolysis or glycogenolysisi. ephosphorylase kinase

   Disorders of lipid metabolism.i. ecarnitinepalmtoyltransfarase 2.

   Mitochondrial dossorders.. i.e succinate dehydrogenase.
5. Infections…

   Influenza A & B, coxsakievirus, EBV, HIV, strep, pyogene, staphaureus, clostridium.
6. Body temp changes..heatstroke, malignanthyperthermia, NMS,hypothermia.
7. Metabolic& electrolyte disorder… hypokalemia, hypocalcemia, hypophosphatemia, DKA, HONK.
8. Drugs&toxins.. statins, fibrates, heroin, cocaine, alcohol.
9. Idiopathic.. sometimes recurrent.

   The mechanisms involved in the pathogenesis

of rhabdomyolysis are direct sarcolemmic injury (e.g., trauma) or depletion of ATP within the myocyte, leading to an unregulated increase in intracellular calcium 3, 4. Sarcoplasmic calcium is strictly regulated by a series of pumps, channels, and exchangers that maintain low levels of calcium when the muscle is at rest and allow the increase that is necessary for actin–myosin binding and muscle contraction. Depletion of ATP impairs the function of these pumps, resulting in a persistent increase in sarcoplasmic calcium that leads to persistent contraction and energy depletion and the activation of calcium-dependent neutral proteases and phospholipases; the result is the eventual destruction of myofibrillar, cytoskeletal, and membrane proteins, followed by lysosomal digestion of fiber contents. Ultimately, the myofibrillar network breaks down, resulting in disintegration of the myocyte 2. In the case of patients with rhabdomyolysis caused by trauma, additional injury results from ischemia reperfusion by neutrophils that infiltrate damaged muscle. 5

Acute kidney injury as a complication of rhabdomyolysis is quite common, representing about 7 to 10% of all cases of acute kidney injury in the United States 4. The outcome of rhabdomyolysis is usually good provided that there is no renal failure. Among patients in the intensive care unit, the mortality has been reported to be 59% when acute kidney injury and 22% when it is not present6, 7.

PATHOGENESIS OF KIDNEY INJURY IN RHABDOMYOLYSIS

Myoglobinuria occurs only in the context of rhabdomyolysis. Although the exact mechanisms by which rhabdomyolysis impairs the glomerular filtration rate are unclear, experimental evidence suggests that intrarenal vasoconstriction, direct and ischemic tubule injury, and tubular obstruction all play a role 8. Myoglobin becomes concentrated along the renal tubules, a process that is enhanced by volume depletion and renal vasoconstriction, and it precipitates when it interacts with the Tamm–Horsfall protein, a process favored by acidic urine 9. Tubule obstruction occurs principally at the level of the distal tubules, and direct tubule cytotoxicity occurs mainly in the proximal tubules.

Renal Manifestations of Rhabdomyolysis

Patients with acute rhabdomyolysis usually present with pigmented granular casts, reddish-brown urine supernatant, and markedly raised serum creatine kinase. Myoglobinuria can be inferred if urinary dipstick testing shows a positive result for blood when there are no red cells in the sediment. This false positive result for blood occurs because the dipstick test is unable to distinguish between myoglobin and hemoglobin. The test has a sensitivity of 80% for the detection of rhabdomyolysis 10. Other causes of pigmented urine should be taken into consideration. Acute kidney injury associated with rhabdomyolysis often leads to a more rapid increase in plasma creatinine than do other forms of acute kidney injury. Similarly, a low ratio of blood urea nitrogen to creatinine is often seen in patients with rhabdomyolysis. Rhabdomyolysis-induced acute kidney injury frequently causes oliguria and occasionally causes anuria. Another characteristic feature of rhabdomyolysis-induced acute kidney injury that is different from the manifestation of other forms of acute tubular necrosis is the frequent, but not universal, presence of a low fractional excretion of sodium (<1%), perhaps reflecting the primacy of preglomerular vasoconstriction and tubular occlusion rather than tubular necrosis 11. The electrolyte abnormalities that can occur with rhabdomyolysis include hyperkalemia (which can be rapidly increasing), hyperphosphatemia, hyperuricemia, high anion-gap metabolic acidosis, and hypermagnesemia mainly when renal failure is present. Hypocalcemia is a common complication of rhabdomyolysis and usually results from calcium entering the ischemic and damaged muscle cells and from the precipitation of calcium phosphate with calcification in necrotic muscle.

Treatment and Prevention

1. Check for extracellular volume status, central venous pressure and urine output.
2. Measure serum creatinine kinase level, and other muscle enzymes i.e myoglobin, aldolase, LDH, ALT, AST.
3. Measure level of serum and urine creatinine, potassium, sodium, BUN, total and ionized calcium, magnesium, phosphorus, uric acid and albumin. Evaluate acid-base status, blood cell count and coagulation.
4. Perform urine dipstick test and examine the urine sediment.
5. Initiate volume repletion immediately with normal saline at a rate of approximately 40 ml per hour.(200-1000 ml per hour depending upon the severity).monitor cvp.
6. Target urine output of 3ml per kg body weight per hour.
7. Check serum potassium level frequently.
8. Correcthypocalcemia only when symptomatic, or if severe hyperkalemia occurs.
9. Check urine pH, if it is less than 6.5, alternate each litre of normal saline with 1 litre of 5% dextrose plus 100 mmol of bicarbonate.avoid potassium and lactate containing solutions.
10. Consider treatment with mannitol(upto 200 g per

day, total 800 g), check for plasma osmolality and osmolalgape. Discontinue if diuresis >20ml per hour is not established.

11. Maintain volume repletion until myoglobinuria is cleared(urine dipstick negative for blood).

12. Consider renal replacement therapy if there is resistant hyperkalemia of >6.5 mmol/l that is symptomatic, rapidlyrisisngpotassium, oliguria (<0.5 ml urine per kg per hpur for 12 hours), anuria, volume, or resistant metabolic acidosis pH<7.1

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