Diclofenac-Induced Rhabdomyolysis - A Great Masquerader

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Abstract
We report herein a patient who developed diclofenac-induced acute rhabdomyolysis and hypovolemic shock. Timely recognition and management led to rapid recovery. Awareness of this potentially life-threatening side-effect is very important to encourage sparing and selective use of this drug in clinical practice.

Introduction
Rhabdomyolysis is a life threatening condition and the full-blown form presents with the triad of severe myalgia, muscle weakness, and tea colored urine.¹ These symptoms eventually lead to life threatening hypovolemia, disseminated intravascular coagulation, acute kidney injury, hyperkalemia, metabolic acidosis, arrhythmia and cardiac arrest.² The mildest form of this disorder is characterized by non-specific myalgias and elevated muscle enzymes.³ A high index of clinical suspicion is needed for early diagnosis. Prompt intervention is lifesaving. We describe here a patient with rhabdomyolysis who presented with hypovolemic shock and acute renal failure after a single intramuscular dose of Diclofenac sodium.

Case Report
50 year old male, with childhood poliomyelitis of left lower limb, presented to our casualty with giddiness and tachypnoea. On examination he was hypotensive (BP 70/40 mm of Hg), had tachycardia (pulse 150/min) and was tachypnoeic (respiratory rate 36/minute). Temperature was normal. Patient did not have any features of cardiac failure. Intravenous saline was rushed into in through wide bore cannula for volume repletion and the systolic blood pressure increased to 100 mm of Hg. On review of a detailed history he informed us that he had joint pains and had received an intramuscular injection (details not available at admission) three days ago. Subsequent to the diclofenac injections patient developed severe myalgias in both lower limbs and had became acutely ill 6 hours prior to admission. He denied any history suggestive of skin rash, arthritis or involvement of muscles innervated by cranial nerves. He last voided urine 8 hours ago but had not noticed any alteration in urine color. ECG showed only sinus tachycardia without any ischemic changes. In view of the hypovolemic shock and history of severe myalgias, rhabdomyolysis was suspected clinically. Investigations showed neutrophilic leucocytosis (Total count 24000 per cu mm with 90% polymorphs), elevated blood urea (165 mg/dl), creatinine of (6.2 mg/dl) and elevated serum potassium of (5.8 mEq/L) severe metabolic acidosis with serum bicarbonate of 8 mmol/l. CPK was 1256 U/L (normal value: 22-198 U/L) and LDH was 1800 U/L (normal value:140-280 U/L). After obtaining blood culture, a single dose of antibiotic was given. Ultrasound examination of the abdomen showed normal sized kidneys and this suggested that the renal failure was acute. After correction of hypovolemia with IV fluids, the patient became normotensive but remained tachypnoeic and so was referred to a tertiary centre, in case he needed dialysis. However in the tertiary centre he showed improvement with just hydration and IV antibiotics and was discharged after 2 days when his creatinine came down to 1.6 mg/dl. He was investigated in the tertiary centre for underlying vasculitis (ANA, C-ANCA, P-ANCA were negative) and serum complement was normal. The elevated muscle enzymes returned to normal as well. At follow-up in our hospital 2 weeks after discharge, he had fully recovered and renal functions were normal. The patient’s relatives brought the first prescription and the injection he had received from the private practitioner was diclofenac.

Discussion
The classical triad of symptoms of acute rhabdomyolysis namely myalgias, muscle weakness and tea-colored urine² is seen in only 10% of affected individuals.³ Our patient presented with hypovolemic shock and severe myalgias without fever and the severe myalgia in the absence of fever was the symptom that pointed to the diagnosis. Rhabdomyolysis can occur due to a multitude of other causes such as trauma, crush injury, adverse effects of drugs (antipsychotics and statins) abuse of drugs (cocaïne) extremes of body temperature (heat stroke), inflammatory myopathies (dermatomyositis, polymyositis and inclusion body myositis), infectious causes (Pyomyositis, legionella infection), viral infections (Epstein Barr virus, herpes simplex virus, Coxsackie virus, parvo virus, influenza virus and adenovirus).³ Viral illnesses can produce severe myalgias but patients with viral fever generally are febrile. Our case had hypovolemic shock without preceding blood loss or gastroenteritis and this along with Severe myalgias was the clue to the diagnosis. The possibility of sepsis was considered and so a blood culture was obtained and this was reported as sterile. However the neutrophilic leucocytosis along with shock mandated the use of IV antibiotics. He made a rapid and gratifying recovery with just hydration and IV antibiotics and did not need dialysis presumably because of early correction of hypovolemic shock. The common conditions which cause rhabdomyolysis like hypokalemia and autoimmune disorders were ruled out in our patient and the only cause we could identify was the intramuscular injection of diclofenac which he had received 2 days earlier. Sequelae and
consequences of rhabdomyolysis such as hypovolemic shock, DIC and acute renal failure ensue 12-72 hours after the acute insult as seen in our patient. In rhabdomyolysis, hypovolemic shock is attributed to influx of fluid from the extracellular space into the necrotic and inflamed skeletal muscle and third space effect. Acute renal injury as seen in our patient is due to a multiplicity of pathophysiological factors such as nephrotoxic effects of myoglobin, tubular obstruction, hypovolaemia and DIC.

The drugs causing rhabdomyolysis include statins, antipsychotics, antidepressants, antihistamines, antiepileptic agents, sedative and hypnotic agents. Diclofenac induced rhabdomyolysis was first reported by Delrio ET all in 1996. A review indicates that diclofenac is next only to statins in inducing rhabdomyolysis. It has been suggested on the basis of epidemiological surveys that the adverse effect of diclofenac on the skeletal muscle may be exacerbated by co-administration of pantoprazole. The mechanism for the diclofenac induced rhabdomyolysis had been postulated to be because of the effect on the cation exchange proteins. Even though initial reports of diclofenac associated rhabdomyolysis seemed to suggest that large cumulative parenteral doses may be important, later reports described this problem even after a smaller oral dose of the drug. In a child with diclofenac associated rhabdomyolysis the problem proved fatal and cautious use of diclofenac in children is recommended. In one patient diclofenac induced rhabdomyolysis occurred along with angioedema of the pharynx.

Our report highlights a rare but serious side effect of diclofenac. Where paracetamol will suffice for fever and body-aches practitioners should avoid using diclofenac as tablets or injections. Awareness of this potential serious side effect after use of this drug will lead to early recognition of the problem.

References