Case Report

RHABDOMYOLYSIS INDUCED ACUTE KIDNEY INJURY FOLLOWING PHYSICAL EXERTION AND SEVERE HYPERCALCAEMIA IN RECOVERY PHASE-A CASE REPORT

Nessa A[1], Hoque MF[2], Fakir MAH[3], Rahman AKMM[4]

Abstract

In military profession, acute kidney injury (AKI) due to rhabdomyolysis is not uncommon because of its nature of job. This life threatening condition needs early aggressive management in a specialized centre to restore normal renal function. Here we report a case of rhabdomyolysis due to physical exertion who developed acute kidney injury and required haemodialysis. Patient developed hypercalcaemia in his recovery phase which was successfully managed.

Key-words: Acute Kidney Injury, Rhabdomyolysis, Haemodialysis, Hypercalcaemia.

Introduction

Rhabdomyolysis is a skeletal muscle injury leading to loss of the cell membrane allowing leakage of intracellular contents like creatine kinase (CK), myoglobin, aldolase, potassium etc into the circulation leading to a spectrum of patho-physiological changes that may lead to acute kidney injury(AKI)[1,2]. Common triggering factors of rhabdomyolysis are physical exertion, muscle ischaemia, direct muscle injury, autoimmune disorders, drugs and toxins, infections, and potassium depletion[1]. Military personnel are more vulnerable to this potentially catastrophic condition as they routinely undergo extreme physical exertion as part of their training. Here we report a case of AKI due to rhabdomyolysis following physical exertion as a part of military training in a recruit who developed severe hypercalcaemia in recovery phase.It is the first reported case in Bangladesh to best of our knowledge.

Case Report

An 18 yrs old recruit of Ministry of Defense Constabulary (MODC) was received in Combined Military Hospital (CMH) Dhaka in semiconscious state with repeated convulsion and scanty high coloured urine. Detail history revealed that he performed 8 km run as part of physical training on that day. He joined into the training centre 01 month back and had febrile illness about 7 days back for which he was advised to take complete rest for 03 days prior to the day of incidence. Initially he was evacuated from ground to CMH Rajendrapur in a semiconscious state from where he was transferred immediately to CMH Dhaka.On admission into CMH Dhaka; he was semiconscious (GCS-7/15), had repeated generalized tonic clonic seizure, temp-101^{0}F, pulse-130/min, BP-100/60 mm Hg and had scanty high coloured urine. He was tachypnoeic (resp rate-40/min), lungs were clear, no external or internal bleeding manifestation, no features of compartmental syndrome or any signs of external trauma were observed. He had no neck stiffness or any lateralizing sign. Other systemic examination revealed no abnormalities. Immediately he was managed with intravenous (IV) phenobarbitone (100 mg IV bd), inj diazepam IV SOS, Inj calcium gluconate,Inj Meropenem,Inj Metronidazole , IV normal saline, oxygen inhalation and other supportive measures. But as convulsion was not controlled and patient couldn't maintain adequate oxygenation, he was put on mechanical ventilation and vigorous hydration was started along with urinary alkalinization (as per-

1. **Maj Azizun Nessa**, MBBS, Graded Med Spl, FCPS (Medicine), Trainee in FCPS (Nephrology), AFMI, Dhaka; 2. **Brig Gen Md Fazlul Hoque**, MBBS, FCPS (Medicine), Diploma in Nephrology, China. Chief Physician and Nephrologist,CMH Dhaka; 3. **Brig Gen Md Amzad H Fakir**, MBBS, FCPS (Medicine), FCPS (Nephrology-Pak), FRCP (Ireland) .Adviser Spl in medicine and Nephrologist, CMH Dhaka; 4. **Lt Col AKM Mijanur Rahman**, MBBS, FCPS (Medicine), FCPS (Nephrology).Graded Med Spl, and Nephrologist, CMH Dhaka.

rhabdomyolysis protocol). His laboratory investigations revealed markedly raised muscle enzymes like serum creatine phosphokinase (CPK), lactate dehydrogenase (LDH) and aldolase (Table-1). His CPK level was elevated upto 106120 U/L (nomal: 24-190 U/L). Serum creatinine was 2.9 mg/dl on admission which subsequently rose to 10.1 mg/dl. His serum myoglobin and urinary myoglobin were also positive. His serum calcium was low [6.8 mg/dl (corrected)] in initial few days as expected (Table-I).

Despite vigorous hydration and urinary alkalinization [100 ml 7.5% $NaHCO_3$ in 1000 ml normal saline at 2 ml/kg/hr to maintain urine output at least 2 ml/kg/hr and adjust according to central venous pressure (maintain CVP at 10-12 cm of H_2O)], his urine output was not adequate (20-30 ml/hr only) and he developed progressively increasing azotemia (raised s. urea and creatinine). So he required renal replacement therapy. After about nine sessions of haemodialysis (HD), his renal function improved and urine output was satisfactory. Interestingly this patient had normal level of serum potassium althrough unlike the usual features of rhabdomyolysis. He also had biochemical features of septicaemia and disseminated intravascular coagulation (DIC) as evidenced by severe neutrophilic leucocytosis and impaired coagulation parameter (Table-II).

Later on, patient developed culture proved UTI (? urinary catheter associated) which was successfully managed with sensitive antibiotic (Piperacillin+Tazobactum). During recovery phase, after about 04 weeks patient developed severe hypercalcaemia (serum calcium-16.1 mg/dl) which was also successfully managed by forced diuresis with normal saline, Inj frusemide, haemodialysis and Inj calcitonin (100 U S/C 12 hrly for 3 days).Patient was discharged after about 06 weeks of hospital stay without any residual disability. His serum creatinine (0.9 mg/dl) and all other physical and biochemical parameters were within normal limit during discharge. He was advised to report for follow up fortnightly for 01 month then monthly for next 03 months and was found to be clinically and biochemically healthy.

Discussion

Excessive and unaccustomed physical exertion and or injury along with some contributing factors like dehydration, infection, drugs, hot humid weather, ischaemia etc results in a state in which ATP produced cannot keep up with demand. Subsequently cellular energy supply exhausts and causes disruption of muscle cell membrane and release of intracellular enzymes into the circulation resulting in spectrum of pathophysiological changes clinically labelled as 'rhabdomyolysis[3,4].

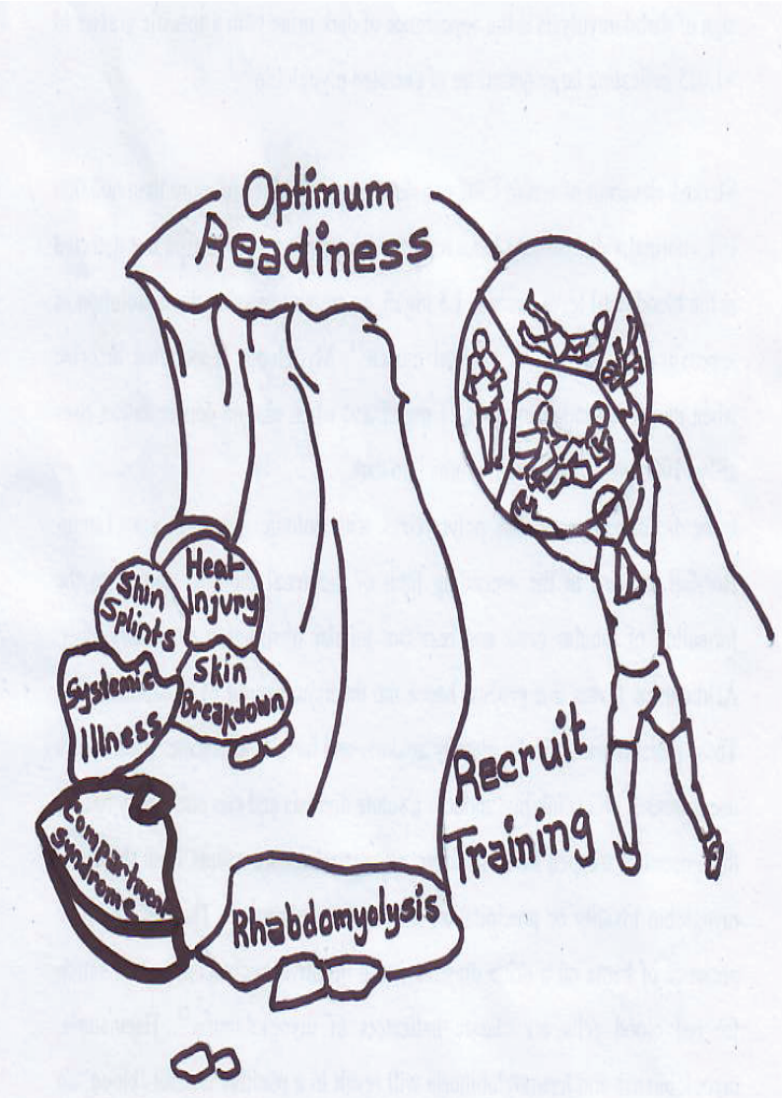

Fig-1: A diagram representing the goal of recruits training: optimum readiness without injury. Training that exceeds physical limitations can result in a variety of injuries, some of which are depicted here.

Table-I: Biochemistry reports

Investigations (unit)	On admission (09/07/12)	10/07/12	15/07/12	21/07/12	01/08/12	12/08/12 (on discharge)
S.CPK(U/L) (normal value:24-190 U/L)	54,600	106120 (peak level)	3566	153	142	112
S. Aldolase(U/L) (normal value: <7.6 U/L)	-	219	195	-	64	-
S. Myoglobin(mg/dl) (normal value :0-85 mg/dl)	-	329	25	12	-	-
S. LDH(U/L) (normal value 208-460 U/L)	3890	7260	1854	896	420	356
S. sodium(mmol/L) (normal value :136-148 mmol/L)	150	148	143	134	136	146
S. potassium(mmol/L) (normal value :3.5-5.2 mmol/L)	4.7	3.9	4.2	4.1	4.0	4.8
S. urea(mg/dl) (normal value:15-50 mg/dl)	81	97	113	94	46	39
S. creatinine(mg/dl) (normal value:0.6-1.4 mg/dl)	2.9	5.4	5.2	10.0	1.4	0.8
S. calcium(mg/dl) (corrected) (normal value:8.1-10.4 mg/dl)	8.0	6.8	7.4	9.8	16.1 (peak level)	8.1
S. albumin(gm/L) (normal value:36-62 gm/L)	33	36	30	38	38	36
S. magnesium(mg/dl) (normal value:1.6-2.3 mg/dl)	-	1.9	2.4	1.0	0.7	1.4
S. PTH(i)(U/L) (normal value:16-80 U/L)	-	-	-	-	17 (04/08/12)	-
S. i phosphate(mg/dl) (normal value:2.7-4.5 mg/dl)	-	2.6	3.2	3.6	3.0	3.7
S. bil(mg/dl) (normal value:0.1-1.0 mg/dl)	0.6	0.4	2.2	1.8	0.9	1.0
S. ALT(U/L) (normal value: upto 45 U/L)	160	214	449	2082	56	42
S. amylase(U/L) (normal value: upto 220 U/L)	3890	7260	134	120	104	108

Table-II: Haematology reports

Investigations	09/07/12	13/07/12	18/07/12	01/08/12	12/08/12
Blood CBC-	13.8	10.4	10.0	11.8	12.0
Hb%(gm/dl)	21	7.3	15.8	8.6	9.8
TLC($X10^9$/L)	87	90	72	76	65
N (%)	160	40	405	420	380
PC($X10^9$/L)	Not seen	Not seen	Not seen	Not seen	-
MP	21	21	22	16	-
PT(sec)(patient)	1.78	1.78	1.87	1.34	-
INR	70	37	48	33	-
APTT(sec)(patient)	>5<20	>5<20	>5<20	<5	-
FDP/D-Dimer(µmol/L) (Normal value:<5)	178	185	188	210	-
Fibrinogen(mg/dl) (Normal value:200-400mg/dl)	Not seen	Not seen	Not seen	Not seen	-

Table-III: Urine analysis

Urine examination	10/07/12	12/08/12
Colour	Coffee brown	Amber
P^H	7.0	6.0
Protein	+	Nil
Glucose	-	-
WBC	10-12/HPF	1-2
RBC	Nil	Nil
Cast	Nil	Nil
Myoglobin	Present	-

Rhabdomyolysis has been documented in military recruits, professional and amateur athletes, weight lifters, firefighters and law enforcement agencies that are prone to intense physical exercise[5]. Our patient joined the training centre one month back, had febrile illness for 7 days and had 3 days rest prior to the incidence. These probably worsened his clinical scenario. Sinert et al[6] found nearly half of the hospital admissions for rhabdomyolysis were exercise induced. A retrospective cohort analysis by Josua et al[7] found the rate of acute rhabdomyolysis in military trainees was 22.2 cases /lac/yr and recurrence rate is 0.08%/person/yr. Early manifestations of rhabdomyolysis may be limited to muscle weakness and tenderness, generalized malaise, lethargy and nausea which needs high index of suspicion[1]. Most commonly the initial clinical sign of rhabdomyolysis is the appearance of dark urine indicating large quantities of excreted myoglobin[8]. Serum CPK was markedly elevated (106120 U/L) in our patient (normal value:50-200 U/L).Normally myoglobin is not detected in blood until level exceeds 1.5 mg/dl, an amount equal to the dissolution of approximately 100 gm of skeletal muscle[9]. Myoglobin is excreted in urine, when its concentration exceeds 21 mg/dl and when plasma concentration rises above 100 mg/dl, urine quickly turns dark. Serum myoglobin concentration in our patient was 329 mg/dl and he had myoglobinuria .In acidic urine, myoglobin polymerizes with anionic mucoproteins in ascending limb of the renal tubules leading to the formation of tubular casts and resultant tubular obstruction to urinary flow and ultimately renal failure[9]. Acidic urine favours this process hence the theoretic benefit of bicarbonate use. Metabolic acidosis in rhabdomyolysis is due to combination of increase in lactic acid, uric acid, phosphate, sulphate and potassium in the circulation which was not evident in this patient, may be due to early alkalinization, hydration and diuresis. Low urinary pH (<5.6) not only facilitates formation of casts but also promotes the dissociation of myoglobin into cytotoxic components which are aggravated by hypovolemia and subsequent renal vasoconstriction. Therefore keeping both urine volume (150-300 ml/hr) and pH high are important components of rhabdomyolysis therapy[10,11]. Alkalinization of urine is achieved by adding sodium-bicarbonate to intravenous crystalloid infusion. Mannitol can be given to promote diuresis and to prevent formation of casts in the tubules but it increases osmolar gap and may worsen AKI[10]. If the fluid and sodibicarb are insufficient to maintain brisk urine output, frusemide can be added to the regimen but it may acidify urine[10]. When the kidneys do not respond to these interventions, emergency haemodialysis is necessary for the management of oliguria, persistent electrolyte imbalance, resistant metabolic acidosis, uraemic encephalopathy and fluid overload[12]. Some researchers suggest that renal replacement therapy by continuous veno-venous haemofiltration dialysis is equally effective[13]. In our patient, nine sessions of haemodialysis was given, after which urine output and biochemical parameters were satisfactory after few days of polyuric phase. Upto 33% of patients with rhabdomyolysis progress to acute renal failure[1]. In fact rhabdomyolysis accounts for 7%-15% of all cases of acute renal failure in United States of America[1].

Hypocalcaemia is common in rhabdomyolysis as calcium sequestrate in the damaged muscle. But calcium administration should be avoided unless patient had symptomatic hypocalcaemia or severe hyperkalaemia. Our patient also had hypocalcaemia (corrected serum calcium-6.8 mg/dl).He had repeated episodes of seizure, which was not controlled with anticonvulsant like intravenous phenobarbitone and also calcium

supplement. As he had also features of hypoxaemia, we had to put him on mechanical ventilation for about 26 hrs. In 30% of patients, hypercalcaemia develops in recovery phase of rhabdomyolysis induced renal failure[1]. This is due to mobilization of calcium from muscle deposits[1]. Our patient developed severe hypercalcaemia (16.1 mg/dl) on day 21 after admission (in recovery phase) which was managed with normal saline (2-4L/day), IV loop diuretics (frusemide) after volume expansion (60 mg 6 hrly), IV hydrocortisone (200 mg 6 hrly) and Inj calcitonin (100 IU s/c 12 hrly). Although overall survival after rhabdomyolysis is approximately 77% but it is higher in cases of exertional rhabdomyolysis and risk of recurrence is also low[7]. When treated early and aggressively, it has an excellent prognosis with no residual renal impairment.

Conclusion

With increasing emphasis on physical fitness and training, rhabdomyolysis is likely to become more frequent. The most important preventive measure is gradual conditioning and adequate hydration. Adequate knowledge of this disease process will help our physicians to prevent, suspect, diagnose and intervene early to avoid the potentially life threatening complication of renal failure.

References

1. Visweswaran P, Guntupalli J. Rhabdomyolysis. Crit Care Clin 1999; 15(2): 415-28.

2. F.Y.Khan.Hypercalcaemia:Review of literature. The Journal of Medicine, Netherlands. Oct 2009;67(9)272-83.

3. Moghtader J, Brady WJ, Bandai W. Exertional rhabdomyolysis in an adolescent athlete. Pediatric Emerg care 1997; 13: 382-5.

4. Santos J Jr. Exertional rhabdomyolysis, potentially life threatening consequence of intense exercise. JAAPA, 1999: 12 (7): 46-9.

5. Walsworth M, Kessler J. Diagnosing exertional rhabdomyolysis- a brief review and report of two cases. Mil Med 2001; 166: 275-7.

6. Sinert R, Kow L, Rainone T, Scalea. Exercise induced rhabdomyolysis. Ann Emerg Med 1994; 23: 1301-6.

7. Joshua P, Alpeis MD, lyellk, Jones Jr MD. Natural history of exertional rhabdomyolysis- A population based analysis, 2010; 42 (4): 487-91.

8. Slater MS, Mullins RJ. Rhadomyolysis and myoglobinuric renal failure in trauma and surgical patients- a review .J Am coll surg 1998; 189:693-716.

9. Wise JJ, Fortin PT. Bilateral exercise induced thigh compartment syndrome diagnosed as exertional rhabdomyolysis. A case report and review of the literatures. Am J. Sports Med 1997; 25: 126-9.

10. Abassi A, Hoffman A, Better D. Acute renal failure complicating muscle crush injury. Semin Nephrol 1998; 18: 558-65.

11. Graham DJ, Staffa JA, Shatin D et al. Incidence of hospitalised rhabdomyolysis in patients treated with lipid lowering drugs. JAMA 2004, 292; 2585-90.

12. Amzad HF, Mostafi M, Rabiul H, et al. Rhabdomyolysis complicated with acute renal failure due to multiple wasp bite - A case report and review of literatures. BAFMJ 2002; Vol 29: 57-9.

13. Vanholder R, S.ever M, Erek E, Lameire N. Rhabdomyolysis. J Am Soc Nephrol 2000; 11: 1553-61.