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Case Report
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Severe Hypercalcemia in a Case of Rhabdomyolysis and AKI – Diagnostic and Therapeutic Dilemma

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Abstract

We report a case of 25-year-old male patient – with no comorbidities, having developed Rhabdomyolysis (RBD) - due to muscle injury following a fight and Acute Kidney Injury (AKI), who went on to develop severe Hypercalcemia during polyuric phase of AKI. Hypercalcemia in RBD is a relatively rare finding, with very few cases reported. Hypercalcemia is likely explained by systemic release of calcium phosphate salts deposited in the muscle following injury. Hypercalcemia can be very severe and symptomatic – as in present case and needs management on an urgent basis -especially to prevent arrhythmias and sudden death. It may need giving calcitonin, bisphosphonates, loop diuretics, aggressive hydration or hemodialysis – but is self-limiting, and in majority of cases - returns to normal within 8 to 10 days.

Case Presentation

A 25 Year Male patient without any comorbidity presented to emergency ward with complains of excessive nausea, vomiting, reduced appetite, oliguria and bipedal edema since last 4 days. There was no history of fever, flank pain, pyuria, hematuria, periorbital puffiness, any episode of upper respiratory tract infection in recent past, pain in upper or lower limbs. He was a habitual tobacco chewer, but did not have history of intravenous drug abuse and was not on any alternative medications.

General Examination revealed multiple abrasions and contusions over upper and lower back, which -on further probing were found to be due to alleged history of multiple blunt traumas over back- following a local fight.

Routine Laboratory investigations with CPK Total were sent (Figure 1 and Table 1).

Patient was subjected to hemodialysis immediately on admission in view of uremic features and severe acidosis on blood gas analysis. Patient remained anuric till 4th day post admission, with a total of 2 cycles of hemodialysis done till then, after which urine output gradually increased from 150 ml/day on 5th day post admission to 3 liters per day by day 15. Electrolytes were sequentially followed – except for serum calcium levels, other electrolytes were normal. There was mild hypokalemia during polyuric phase, which was corrected with oral potassium chloride. Initially there was mild hypocalcemia with S. Calcium of 7.7 mg/dl. By day 10, it was within normal limits 9.7 mg/dl. As polyuric phase of AKI progressed, patient began to develop hypercalcemia with S. Calcium reaching a level of 15 mg/dl by day 15, urine output at this time was about 3 liters per day. Serum phosphate levels were normal at 3.8 mg/dl. Intact parathormone levels were appropriately suppressed at this time with value of 17 units/ml. 25-Hydroxy Vitamin D was mildly low at 25 ng/ml. Both these reports ruled out possibility of primary hyperparathyroidism or hypervitaminosis D – which as such- was also expected to be the case, as calcium levels were mildly low at the beginning. Considering that the event was quite acute, malignancy also seemed less likely a possibility. Still, workup for multiple myeloma was done -which was negative. CT scan of thorax did not reveal prominent lymphadenopathy or mass lesion in thorax. Ultrasound examination of Whole Abdomen was also normal. One cycle of hemodialysis was done again on day 15 in view of severe symptomatic hypercalcemia and subcutaneous calcitonin and loop diuretics were given, which helped bring back calcium to a level of 10.7 mg/dl on discharge.

Discussion

Acute Kidney Injury (AKI) is seen in 15% to 50% of cases following Rhabdomyolysis (RBD).

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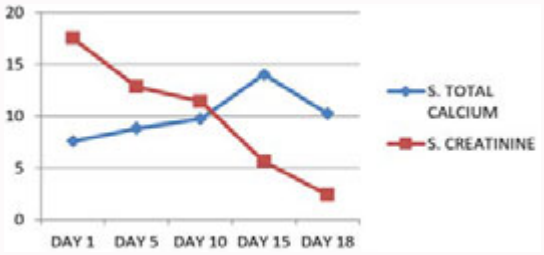

Figure 1: Course of serum calcium and creatinine values during indoor stay.

Table 1: Various laboratory parameters and their course during indoor stay.

Parameters	S. Creatinine	Urine Output	S. Calcium	PTH	CPK Total	SGOT	Vit D (25 Hydroxy)
DAY 1	17.5	0	7.6	1097	>10000	745	-
DAY 5	12.81	130	8.8	-	1220	59	-
DAY 10	11.4	2400	9.7	128	575	50	24
DAY 15	5.67	3000	14	17	698	44	-
DAY 18	2.38	3200	10.2	8.46	321	44	38

Serum calcium follows a biphasic pattern with an initial hypocalcemia seen in 60% in oliguric phase, followed by hypercalcemia seen in 20% to 30% during polyuric phase [1,2].

RBD can occur due to many causes like – ischemia, trauma, mycotoxins, myositis, extreme exertion, metabolic derangements as in severe hypophosphatemia or glycogen storage disorders. Physiologically, ionized calcium levels in sarcoplasm are 10,000 times lower than serum ionized calcium, and this is maintained by Ca - ATPase pump in sarcoplasmic reticulum and 2 Na/Ca exchanger on sarcolemma. Both these are energy intensive processes needing ATP for Ca mobilization. In RBD – muscle necrosis/ischemia leads to loss of ATP leading to increased cytosolic calcium in muscle, which triggers activation of cytosolic proteases that denatures muscle proteins and cell membrane leading to release of intracellular phosphate, potassium, myoglobin, creatinine and creatinine kinase [3,4].

AKI is likely due to release of these myoglobin's that precipitate in glomerular tubules and form casts that obstruct tubular lumen. Myoglobin also causes direct toxic effect on tubular epithelium, causing tubular necrosis [5]. RBD damages cell membrane of muscles and loss of Na/K ATPase pump - leading to increased permeability to fluids. Shift of large amount of sodium and intravascular fluid leads to muscle edema – which in severe cases can lead to Compartment Syndrome. This further leads to muscle ischemia – worsening the ongoing RBD. Depletion of intravascular volume is another factor leading to AKI [6].

After RBD, initially there is hypocalcemia during oliguric phase of AKI. This is due to calcium chelation by the released intracellular phosphate. Normally, 85% phosphate is in bones and teeth, 14% is present intracellularly and about 1% is in extracellular fluid [7]. RBD leads to release of large amount of phosphate which forms chelation salt with calcium and gets deposited locally leading to hypocalcemia. During the recovery phase of AKI, these sequestered salts are released back into the systemic circulation. This probably leads to hypercalcemia during polyuric phase. Case reports by Akmal and Bisop [8] as well as by Zerr and Durand [9] suggests elevated levels of Vitamin D, probably due to its extra renal production, and poor regulation in its synthesis by kidneys, as likely explanation of hypercalcemia.

Overall, very few cases have been reported with hypercalcemia following RBD and AKI. One of the studies by Olazo and Dolores in 2012 [1], as well as another study review by Lisa and Ali Sadjadi [2], suggested that only about 60 published cases of hypercalcemia following RBD were found till date since 1970. The highest level of hypercalcemia associated with rhabdomyolysis that has been published was 20 mg/dL [2,10].

Conclusion

AKI is a common complication of Rhabdomyolysis and in majority of cases, needs supportive treatment and hemodialysis – as and when required. But the present case shows that falling creatinine levels and rising urine output is not the end game. Vigilant monitoring of electrolytes and prompt intervention – especially during polyuric phase - is of utmost importance. It also shows that – hypercalcemia in such a clinical context – does not need to be over investigated in the initial 8 to 10 days of polyuric phase.

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