CASE REPORT

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Hypercalcemia in a Patient with Rhabdomyolysis. A Case Report and A Literature Review

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ABSTRACT

Calcium kinetics can be challenging during the different phases of rhabdomyolysis. In this case report we illustrate an unusual biphasic calcium behavior in a 27-year-old male patient who was diagnosed with septic shock and rhabdomyolysis complicated with acute kidney injury and oliguria. Initially he had hypocalcaemia but as rhabdomyolysis improved, his calcium levels started to rise to above normal levels despite intermittent dialysis sessions. Hypercalcemia later on responded to denosumab and cautious hydration after his urine output improved.

In conclusion, hypercalcemia can complicate the recovery phase of rhabdomyolysis. Careful monitoring of calcium levels and management are warranted.

Keywords

Rhabdomyolysis; Hypercalcemia; Acute kidney injury

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INTRODUCTION

Rhabdomyolysis is a serious condition characterized by muscular breakdown frequently resulting in multiple biochemical abnormalities such as acute kidney injury and hypocalcaemia. Calcium levels however can vary at the different phases of rhabdomyolysis[1]. We herein report a case of severe hypercalcemia refractory to hemodialysis following a period of hypocalcaemia that developed in a patient with rhabdomyolysis.

CASE REPORT

A 27-year-old previously healthy gentleman and not on any regular medications was admitted to the intensive care unit with a three-day-history of fever and repeated attacks of tonic-clonic seizures at the day of admission. Upon presentation his level of consciousness was impaired, and he was hypotensive. He was intubated and mechanically ventilated. On examination he was an obese patient with a body mass index of 39.5. He was febrile and blood pressure was maintained on inotropic support. Glasgow coma scale of 4/15 off sedation. Initial laboratory work up revealed evidence of acute kidney injury with rhabdomyolysis. His creatinine was 219 µmol/L (53-115), urea was 8 mmol/L (2.5-6.4). Creatine kinase (CK) was significantly high above assay range. His Troponin-I was 1.84 ug/L. Corrected calcium was 1.82 mmol/L (2.12- 2.52), phosphate was 0.48 mmol/L (0.81-1.58), potassium was 2.4 mmol/L (3.5-5.1). Liver enzymes were also mildly high. A brain computerized tomography scan showed evidence of brain edema. Lumbar puncture was performed but after starting antibiotics as the patient initially had contraindications to the procedure. It revealed evidence of mildly elevated white cell counts.

Collectively the evidence was suggesting meningoencephalitis with acute kidney injury and rhabdomyolysis. He required intermittent sessions of hemodialysis and antibiotics therapy which were both initiated since the first day of admission. His in-hospital course was complicated with multiple nosocomial infections, critical illness myopathy along with multiorgan failure. However, his initial hypocalcaemia did not require intravenous or enteral supplements.

By day 13 post admission, his corrected calcium was normalized and his CK started to drop. By day 16 following presentation, he started to gradually develop hypercalcemia (Fig. 1).

Initially, it was 2.73 mmol/L and in another 10 days it was 3.39 mmol/L and reached a maximum of 3.90 mmol/L despite the intermittent dialysis sessions which were not free of calcium at the beginning but later on they were calcium free and K0 dialysate. Over that time, his renal functions were stable and the patient's urine output started to actually improve despite concurrent respiratory and urinary sepsis. From null per day, urine output improved reaching up to 500 ml/day then gradually increased to a normal range and dialysis sessions were spaced further. His CK also gradually improved and decreased to 2274 and the following week 719 IU/L.

With this hypercalcemia, parathyroid hormone (PTH) was supressed at 0.62 Pmol/L. The clinical impression was PTH independent hypercalcemia and the work up for that was initiated. A com chest, abdomen and pelvis did not reveal any suspicious masses, lytic bone lesions, organomegaly or lymphadenopathies. His acid-fast bacilli stain and culture were both negative. His chest imaging did

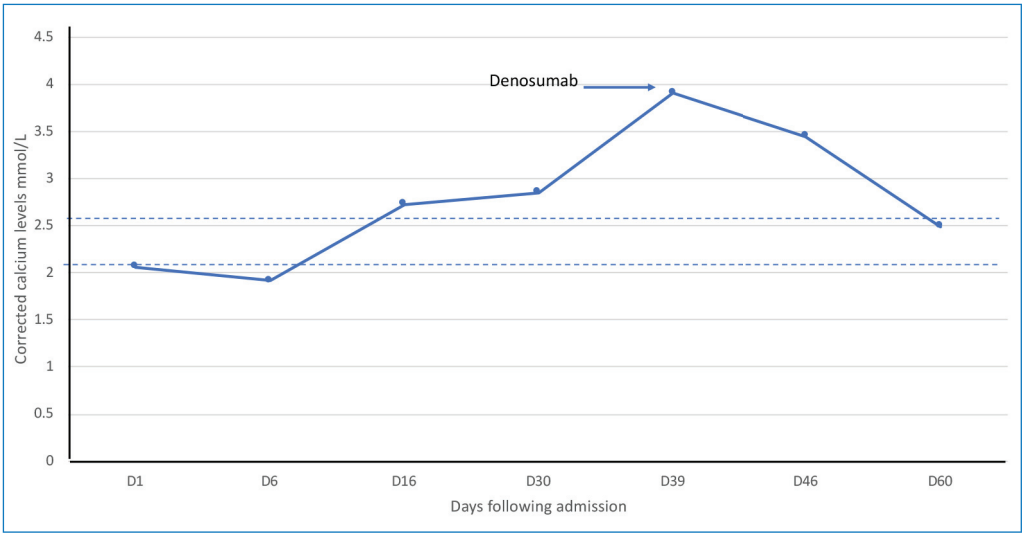

FIGURE 1.
Variation of serum calcium levels during hospitalization. Timing of Denosumab administration is indicated with arrows. The dotted lines indicate the normal range of calcium.

not show any interstitial lung disease findings to suggest sarcoidosis. Thyroid stimulating hormone was normal and random cortisol was 339.2 nmol/l with albumin 20g/L. HIV 1,2 serology came back negative.

Considering the significant hypercalcemia which was refractory to hemodialysis and the difficulty to hydrate him aggressively with impaired kidney function despite the improvement in urine output, he received Calcitonin 500 IU BID for three days and denosumab 120 mg SC in order to control the hypercalcemia. Along with the aforementioned management, cautious intravenous hydration was initiated when his urine output improved further, and hemodialysis was discontinued. Within one week after denosumab therapy, serum corrected calcium decreased to 3.07 mmol/L. After another week, corrected calcium reached 2.53 mmol/L and four days later normalized to 2.49 mmol/L.

After ruling out the common differential of PTH independent hypercalcemia, and from the diuretic phase the patient went through with concomitant hypercalcemia following hypocalcaemia, it was concluded that the cause of hypercalcemia was rebound hypercalcemia following rhabdomyolysis recovery.

DISCUSSION

In this report we highlight a case of rebound severe hypercalcemia complicating the diuretic or the recovery phase of rhabdomyolysis. The prevalence of rhabdomyolysis- associated hypercalcemia is estimated to be 9.2% based on case series[2].

The pathogenesis of calcium metabolism disturbances associated with rhabdomyolysis is likely multifactorial. Hypocalcaemia usually manifests at the early, oliguric phase of rhabdomyolysis. The underlying mechanism of hypocalcaemia is likely related to the development of acute kidney injury, hyperphosphatemia and skeletal resistance to PTH. Calcium deposition in the injured muscles was also demonstrated in a few reports[3].

During the recovery phase of rhabdomyolysis, renal function starts to improve and the patients usually undergo a diuretic phase with normalization of calcium level. Rarely, such as in the patient in our report, calcium levels at the recovery phase will exceed normal limits. This biphasic pattern of hypocalcemia followed by gradual hypercalcemia can infrequently complicate the rhabdomyolysis course.

The pathophysiology of the hypercalcemia observed in the recovery phase is not fully understood but might be due to several mechanisms including mobilization of calcium from injured muscles. This was supported by previous case reports that utilized technetium-99m diphosphonate imaging and provided evidence of muscular calcium deposition during the oliguria phase of rhabdomyolysis. Following the recovery from acute kidney injury, there was dissolution of these deposits[4]. Another theory related the hypercalcemia to the elevated levels of 1,25 dihydroxy vitamin D that developed during the initial phase as a corrective response to the hypocalcemia[5,6].

Management of hypercalcemia in this setting often follows the usual algorithms for such calcium levels. In the reported similar cases, the hypercalcemia resolved with calcium free hemodialysis and bisphosphonates therapy[5-7]. There was also a report of a response to hydration only[4]. In our case, hypercalcemia was initially refractory to hemodialysis, but later on responded to Denosumab therapy and low dose intravenous hydration and subsequently hemodialysis was stopped. Hypertensive emergency was described along with Hypercalcemia and rhabdomyolysis in one of the case reports[8]. Hypercalcemia can also be associated with abnormal electrocardiographic test as reported in a patient who had rhabdomyolysis, hypercalcemia and findings similar to Brugada syndrome[9].

In conclusion, rebound hypercalcemia following hypocalcemia can complicate the course of rhabdomyolysis-induced kidney injury. Cautious calcium management and thorough monitoring are warranted during follow up.

Conflict of Interest

The author has no conflict of interest.

Disclosure

The author did not receive any type of commercial support either in the form of compensation or finances for this study. The author has no financial interest in any of the products devices, or drugs mentioned in this article.

Ethical Approval

Obtained.

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ارتفاع مستوى الكالسيوم لدى مريض انحلال الربيدات: تقرير حالة و مراجعة الأدبيات العلمية

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المستخلص.

حركية الكالسيوم خلال الأطوار المتعددة لانحلال ربيدات العضلات المخططة قد تشكل تحديا طبياً، في تقرير هذه الحالة نستعرض سلوكاً ثنائي الطور لمستوى الكالسيوم لدى مريض يبلغ من العمر ٢٧ عاماً، والذي تم تشخيصه بصدمة جرثومية وانحلال الربيدات، والذي ترتب عليه اصابته باعتلال كلوي حاد وانحسار تدفق البول، في البدء كان يعاني من هبوط في مستوى الكالسيوم، ولكن مع تحسن انحلال الربيدات بدأ مستوى الكالسيوم في الارتفاع حتى تخطى المستوى الطبيعي، بالرغم من الغسيل الكلوي المتقطع ، كما استجاب ارتفاع الكالسيوم بعد ذلك لعقار دينوسوماب مصاحبا لتروية حذرة بعد أن تحسن تدفق البول.
ويتلخص الموضوع في أن ارتفاع الكالسيوم يمكن أن يعقد طور التعافي من مرض انحلال الربيدات وينبغي المراقبة الحذرة لمستوى الكالسيوم وطريقة علاجه.