Case Report

Hypercalcemic crisis treated with calcium-free hemodialysis with subsequent parathyroidectomy and postsurgical hypocalcemia

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Received 10 January 2014; accepted 9 June 2014
Available online 20 August 2014

Abstract

Hypercalcemic crisis is a rare but life-threatening condition defined by decompensation of hypercalcemia with significant disturbance to cardiac, renal, gastrointestinal and neurological function. Here we document the case of a 74-year-old gentleman with a parathyroid adenoma who presented to hospital after bloods revealed severe hypercalcemia (5.58 mmol/L). Rehydration with diuretics and bisphosphonate infusions failed to revert the hypercalcemia over 42 hours (5.58 mmol/L). Low calcium hemodialysis rapidly reduced calcium levels and allowed for further investigations. Computerised tomography (CT) scan and magnetic resonance cholangiopancreatography revealed associated acute pancreatitis. A parathyroid adenoma was discovered by ultrasound and removed surgically. Parathyroidectomy led to resistant hypocalcemia requiring multiple calcium infusions. Hypercalcemia may lead to nausea and vomiting, decrease oral fluid intake and nephrogenic diabetes insipidus. This in turn leads to volume depletion and hypovolemic acute kidney injury. In patients severe acute kidney injury leading to renal failure, aggressive fluid replacement may be detrimental and these patients may require correction by dialysis. Literature review returned 13 case reports/case series totaling 68 patients undergoing dialysis for hypercalcemia. These case reports found a rapid decrease in serum calcium levels post calcium free hemodialysis (CFHD). Mortality was observed in only one case report which was attributed to sepsis.1 Hemodialysis reportedly clears 682 mg/hr of calcium vs 82 mg/hr in saline diuresis.2 It offers a safe way of treatment in patients with cardiac and renal co-morbidities and results in rapid reduction in calcium levels and improvement in cognition.1,3,4

Keywords: calcium-free hemodialysis; hemodialysis; hypercalcemia; hypercalcemic crisis; parathyroid; parathyroidectomy; zolendronic acid

1. Introduction

Hypercalcemic crisis is a rare, but life-threatening condition defined by decompensation of hypercalcemia with significant disturbance to cardiac, renal, gastrointestinal, and neurological function.

We document the case of a 74-year-old gentleman with a parathyroid adenoma who presented to the hospital after blood work revealed severe hypercalcemia (5.58 mmol/L). Rehydration using intravenous fluids with diuretics and bisphosphonate infusions failed to improve the hypercalcemia over the course of 42 hours (5.58 mmol/L). Low-calcium hemodialysis rapidly reduced his calcium levels and allowed for further investigation. Computerized tomography (CT) and magnetic resonance cholangiopancreatography revealed associated acute pancreatitis. A parathyroid adenoma was discovered by ultrasound and removed surgically. Parathyroidectomy led to resistant hypocalcemia requiring multiple calcium infusions.

Hypercalcemia may lead to nausea and vomiting, decreased oral fluid intake, and nephrogenic diabetes insipidus. This, in turn, leads to volume depletion and hypovolemic acute kidney injury. In patients with severe acute kidney injury leading to renal failure, aggressive fluid replacement may be detrimental, and these patients may require correction by dialysis.

A literature review returned 14 case reports/case series totaling 74 patients undergoing dialysis for hypercalcemia.

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http://dx.doi.org/10.1016/j.jacme.2014.06.003
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These case reports found a rapid decrease in serum calcium levels after calcium-free hemodialysis. Mortality was observed in two case reports; one was attributed to sepsis and the other, to resistant hypercalcemia leading to ventricular fibrillation.\textsuperscript{1,2} Hemodialysis reportedly clears 682 mg/hour of calcium versus 82 mg/hour in saline diuresis.\textsuperscript{3} Hemodialysis offers a safe way of treatment in patients with cardiac and renal comorbidities and results in rapid reduction of calcium levels and improvement in cognition.\textsuperscript{1,4,5}

2. Case Report

A 74-year-old man presented to the hospital after a referral from his general practitioner. He had visited his general practitioner 2 days previously after his daughter reported slurred speech, difficulty walking, and collapse. At home, the patient was confused, aggressive, and unsteady. Prior to this, the patient had been cognitively intact and active for his age. Routine blood work was done, including a bone profile. His corrected calcium level was 5.58 mmol/L, and he was advised to report to the hospital immediately.

On arrival, the patient was confused, agitated, and disoriented. He had been well 2 days prior to admission until he had collapsed. A similar episode of hypercalcemia had occurred in 2006, and the patient had been admitted to intensive care but discharged himself after 5 days, prior to any further investigations.

Initial vital signs were recorded as blood pressure of 161/92 mmHg, heart rate of 88 beats/minute, respiratory rate of 14 breaths/minute, and oxygen saturation of 94% on room air. He was apyretic with a normal blood sugar. He was hallucinating, and examination revealed new onset atrial fibrillation, reduced skin turgor, and dry mucous membranes. A neurological examination was difficult to perform, but deep tendon reflexes remained intact.

A complete blood count revealed increased white blood cells of $21.5 \times 10^9$/L, neutrophils of $18.98 \times 10^9$/L, and hemoglobin of 154 g/L. Biochemistry revealed calcium of 5.58 mmol/L, urea of 11.7 mmol/L, creatinine of 161 μmol/L, potassium of 3.1 mmol/L, and C-reactive protein of 10.9 mg/L. Chest X-ray showed some minimal left side congestive changes, and an electrocardiogram showed a shortened QT interval, J waves in lead II, and new onset atrial fibrillation. A full septic screen was performed, but results later showed no bacterial growth in either urine or blood cultures; arterial blood gases were PO$_2$ 10.1 kPa, PCO$_2$ 6.07 kPa, pH 7.39, and base excess 4.5 mmol/L.

The patient was initially treated for hypercalcemia, sepsis of unknown source, and acute kidney injury. Zolendronic acid intravenous infusion, rapid rehydration with normal saline, and cefuroxime as per microbiology guidelines were started. The patient was prescribed 5 L of fluid over 24 hours, catheterized for strict fluid input/output, placed on cardiac telemetry, and had daily blood work. A CT scan of his brain showed no acute pathology.

The following day, the patient had a deteriorated mental state and reduced responsiveness although observations showed that his condition remained stable. Intravenous furosemide was prescribed, and he was given a further 5 L of fluid over the course of the day.

After 42 hours, the patient had had a total of 7200 mL of fluid input with 7075 mL total output. He remained confused and agitated. His condition deteriorated, and the patient became septic requiring 3 L of oxygen via nasal cannula. His calcium level remained high with three consecutive readings all >5 mmol/L during the first 42 hours. Inflammatory markers were elevated with neutrophils of $28.14 \times 10^9$/L and C-reactive protein 289 mg/L. The patient was started on teicoplanin and gentamicin for presumed chest sepsis. A bridled nasogastric tube was inserted to provide nutrition and prevent hypophosphatemia.

The patient was immediately transferred to the dialysis ward for 2 hours of hemodialysis with low calcium/high potassium dialysate via a femoral line. His postdialysis calcium was 3.13 mmol/L with rapid improvement in cognition (Glasgow Coma Scale 14) and attempts made at communication.

Further reduction of calcium was attempted by rehydration with 4 L of normal saline daily and adjuvant furosemide. Once stabilized, CT of the chest/abdomen/pelvis showed acute pancreatitis (amylase, 58 μ/L), and follow-up magnetic resonance cholangiopancreatography showed no evidence of gallstones. The patient’s admission parathyroid hormone was 1.9 pmol/L but had risen to 120 pmol/L 10 days after admission. A nuclear medicine parathyroid scan was clear, but a follow-up parathyroid ultrasound revealed a 1.7 cm × 1.6 cm × 3.5 cm parathyroid adenoma at the inferior pole of the left thyroid. Owing to ongoing hypercalcemia, the patient required two more zolendronic acid infusions and a second course of low calcium hemodialysis.

After parathyroidectomy, the patient suffered hypocalemia (1.7 mmol/L) and required multiple calcium infusions of 40 mL of 10% calcium gluconate and adcal D3. Unfortunately, the patient discharged himself with resistant hypocalemia (1.87 mmol/L) and failed to attend follow-up outpatient appointments.

3. Discussion

Calcium homeostasis is maintained mainly by parathyroid hormone, which acts by aiding conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D in the kidney and stimulates calcium reabsorption in the ascending loop of Henle.\textsuperscript{6} The vast majority of the body’s calcium is within the bones and can be accessed by osteoclast activation. Only a very small percentage of total body calcium contributes to serum calcium levels, and it is protein bound and not biologically active.

Hypercalcemia affects multiple organs and often presents as polyuria and polydipsia, nausea, vomiting, and diarrhea, tiredness, and headache.\textsuperscript{7} In severe hypercalcemia termed “hypercalcemic crisis”, patients can present with oliguria and have psychological disturbances or coma. The most common causes of hypercalcemic crisis are primary hyperparathyroidism and malignancy.\textsuperscript{8} Hypercalcemia is a presenting feature in up to 5%
of patients with malignancies and is a poor prognostic marker. Parathyroid hormone or its related peptide can be directly released by cancer cells or have local osteolytic affects. Treatment consists of aggressive rehydration therapy aiming for input of 200–500 mL/hour depending on age, calcium level, and comorbidities. Furosemide is still widely used in view of its ability to increase diuresis although its use in treatment of hypercalcemia lacks evidence. Bisphosphonates, particularly zoledronic acid, have been shown to be superior to pamidronate at lowering calcium levels and providing reductions in calcium levels over the course of 48 hours. During the first 48 hours, a rapid reduction in calcium can be provided by calcitonin although its use is limited to this period. Hemodialysis is indicated for resistant hypercalcemia and those with hypercalcemic crisis and renal failure.

The definitive treatment is surgery in those patients with parathyroid hormone-related hypercalcemia. Patients must be adequately hydrated prior to and after surgery, and strict monitoring of postsurgical calcium levels is essential. Hypercalcemic crisis remains one of the few indications for urgent parathyroidectomy, and appropriate resection can keep patients eucalcemic in the long term. It is important to note that patients presenting in hypercalcemic crisis are more likely to be male and have related pancreatitis and significant alteration of mental state than those presenting with mild to moderate hypercalcemia.

Currently, the use of hemodialysis in hypercalcemia is often reserved for those with renal failure or comorbidities that contraindicate aggressive fluid management. There are currently no guidelines for when dialysis should be considered, but the common consensus is when the glomerular filtration rate falls below 10–20 mL/minute. This case is an example of the use of low calcium hemodialysis in a hypercalcemic crisis with preserved renal function.

In summary, calcium-free hemodialysis is extremely effective in treating hypercalcemic crisis, with a rapid reduction in serum calcium. It is safe in patients with both cardiac and renal comorbidities as well as those with preserved renal function. In patients with prolonged hypercalcemia and hyperparathyroidism, parathyroidectomy can lead to resistant postsurgical hypocalcemia.

Conflicts of interest

The authors above are the sole contributors for this manuscript. As this is a case report there are no directly comparable manuscripts, case reports for low calcium hemodialysis in cases of severe hypercalcemia do exist and can be found in the literature review of this article. The authors express no conflicts of interest.

References