CASE REPORT

Severe hypercalcaemia and colon ischaemia: dehydration as an unusual cause?

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SUMMARY

Hypercalcaemia is an emergency with severe consequences. Dehydration can be an uncommon cause of hypercalcaemia, as seen in this case. A 63-year-old woman with type 2 diabetes mellitus, hypothyroidism and osteoporosis, was admitted to the emergency room with abdominal distension and vomiting for 24 h. Initial evaluation was Hg 18.5 g/dL, Htc 56.2%, creatinine 2 mg/dL, metabolic acidaemia, lactate 8.3 mmol/L, anion gap 19, total Ca^{2+} 17.7 mg/dL and PO_4 6.6 mg/dL. CT revealed colonic distension without obstruction or ischaemia. Renal replacement therapy and pamidronate were initiated. The patient's clinical condition deteriorated with septic shock in the context of toxic megacolon and she underwent an emergency subtotal colectomy (10 kg). Hypercalcaemia was corrected in 24 h with aggressive fluid replacement (8 L NaCl 0.9% first 12 h), with a reduction of total Ca^{2+} to 8.2 mg/dL. Other causes of hypercalcaemia were excluded. 'Hypercalcaemic crisis' secondary to severe acute dehydration is not mentioned in the literature.

BACKGROUND

Calcium is a vital cation and its metabolism is determined by intestinal absorption and renal excretion controlled by parathyroid hormone (PTH) and vitamin D.¹

Hypercalcaemia is usually caused by primary hyperparathyroidism or malignancy and a number of other conditions that correspond to less than 10% of cases.²

Some patients have been described with rare and unusual causes of hypercalcaemia.³ In these cases, clinical investigation might improve our knowledge about normal metabolism of calcium, namely the real importance of hydration in serum calcium levels, and the underlying humoral and cellular processes in the pathogenesis of hypercalcaemia.³

Concerning the most common aetiologies, hypercalcaemia associated with primary hyperparathyroidism is typically less than 11 mg/dL and it is most often due to a parathyroid adenoma with subsequent PTH-mediated intestinal calcium absorption and activation of osteoclasts leading to increased bone resorption.⁴ Hypercalcaemia of malignancy (HCM) is usually a moderate hypercalcaemia (12–14 mg/dL) and it can be a consequence of different mechanisms: secretion of PTH-related protein (PTH_{rp})—humoral HCM; direct osteolytic metastases with the release of local cytokines and secretion of 1,25-dihydroxy vitamin D (calcitriol).⁵

Among the less frequent causes of hypercalcaemia reported, with serum calcium level range of

11.5–14.5 mg/dL, are granulomatous diseases, milk-alkali syndrome, PTH_{rp} secretion with benign clinical conditions such as systemic lupus erythematosus diseases and vitamin A intoxication. Some reports of hypercalcaemia were published because of the unusual clinical circumstances, but have no presumed mechanism defined.³

We report a case of unusual high serum calcium level with a presumed mechanism not described before. We present this case to emphasise the importance of early diagnosis and the identification of the real cause of hypercalcaemia, to achieve the correct treatment. The association between dehydration and hypercalcaemia is poorly understood and there are no reported cases in the literature.

CASE PRESENTATION

A 63-year-old woman was admitted to the emergency room with abdominal distension, vomiting and nausea, for 24 h. She had a medical history of type 2 diabetes mellitus, hypothyroidism, osteoporosis and bipolar disorder. Her current medication was: cloxazolam 2 mg/day; metformin 500 mg/day; sitagliptin 100 mg; aspirin 150 mg/day; levothyroxine 25 µg/day; quetiapine 150 mg/day; topiramate 300 mg/day; pantoprazole 40 mg/day; strontium ranelate 2 g/day; calcium carbonate and vitamin D 500 mg+200 UI/day.

The patient presented with lethargy and signs of dehydration. She was afebrile and non-icteric. Her blood pressure was 106/80 mm Hg, heart rate 120 bpm and SpO_2 was 96% (FiO_2 21%). The physical examination revealed marked abdominal distension without bowel sounds and generalised tenderness with no signs of peritonitis. Nasogastric tube drainage (500 cc) in the first hour showed no faecaloid content. The examination of the heart, lungs and central nervous system showed no abnormalities.

Initial laboratory evaluation showed haemoglobin 18.5 g/dL, haematocrit 56.2%, white cell count of $33\,700/\text{mm}^3$ (91.8% neutrophils), serum albumin of 2.7 g/dL, serum urea of 109 mg/dL, creatinine 2 mg/dL, metabolic acidaemia with pH 7.24, HCO_3^- 11.7 mmol/L, anion gap 19, lactate 8.3 mmol/L, a total serum calcium (Ca_2) level of 17.7 mg/dL (normal range 8.4–9.7 mg/dL), ionised calcium level of 1.95 mmol/L (normal range 1.15–1.29 mmol/L) and phosphorus (PO_4) 6.6 mg/dL (normal range 2.7–4.5 mg/dL).

Abdominal CT showed a massive colic distension without obstruction or signs of ischaemia (figure 1).

The patient was admitted to the intensive care unit with the diagnosis of severe hypercalcaemia

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Figure 1 Abdominal CT: massive colic distension without obstruction or signs of ischaemia.

without an obvious cause; she was started on dialysis and pamidronate.

On the first day, the patient developed toxic megacolon with septic shock. Intra-abdominal pressure (IAP) was 17 mm Hg. Invasive ventilation and vasopressor support were initiated, maintaining dialysis with continuous venovenous haemofiltration.

Owing to the clinical course, raised IAP with septic shock, it was decided to perform an emergency laparotomy. Intraoperative abdominal examination revealed necrosis of the entire colon, 5000 cc of liquid stools were removed and a subtotal colectomy and ileostomy (± 10 kg) were performed.

After the surgery, a transient urticarial rash (figure 2) was noticed, interpreted as secondary to severe hypercalcaemia. The rash vanished in a couple of hours.

Serum calcium levels were corrected in the first 24 h, after intensive hydration (8 L NaCl, 0.9% for 12 h), with final serum calcium levels of 8.2 mg/dL and haemoglobin 15.3 g/dL.

Other laboratory tests were performed on the day of admission in order to establish the cause of the hypercalcaemia: thyroid stimulating hormone 2.86 IU/mL (normal range 0.41–4.5 IU/mL); PTH intact 17.3 pg/mL (normal range 15–65 pg/mL); PTH_{rp} 0.3 pg/dL; 1,25-dihydroxyvitamin D 33.0 nmol/L (normal range 75–250 nmol/L) and 24 h urinary calcium 256.55 mg (normal range 100–300 mg/24 h). Chest X-ray was normal. Abdominal CT revealed no underlying malignancy.

Figure 2 Transient urticarial interpreted as secondary to severe hypercalcaemia.

Other causes of hypercalcaemia such as vitamin A and D intoxication, chronic renal failure, parathyroid disease, sarcoidosis, multiple myeloma, milk-alkali syndrome, adrenal insufficiency as well as thiazides, diuretics and lithium ingestion, particularly in this patient with bipolar disorder, were excluded on the basis of laboratory and clinical data. Other causes of acute kidney injury (AKI), such as urinary tract infection, were also excluded.

The patient showed clinical improvement. On the second day, vasopressor support was suspended and enteric diet was started, with functional ileostomy. Sedation and dialysis were also suspended, and the patient was weaned from mechanical ventilation successfully with extubation on the fifth day of stay in the unit.

The pathological anatomy revealed ischaemic lesions with non-specific inflammatory infiltrate, negative for malignancy.

The patient was discharged to the intermediate care unit in the surgery department on the sixth day with a total serum calcium (Ca^{2+}) level of 8.6 mg/dL. She was discharged home after 28 days of hospital stay.

One year later, the patient maintains treatment with calcium carbonate supplement and preserves her previous renal function, without new episodes of hypercalcaemia (11/2014: Ca^{2+} 9.4 mg/dL; creatinine 1.02 mg/dL; clearance creatinine 80.2 mL/min; urea 19 mg/dL).

DISCUSSION

Hypercalcaemia is a relatively common clinical problem with many clinical manifestations and consequences related to serum calcium levels. It can be asymptomatic or lead to coma or cardiorespiratory arrest, usually when calcium levels are as high as 15–18 mg/dL.^{1 2} In this case, calcium levels were almost 18 mg/dL, and because of the initial mild acute symptoms, the condition was considered critical and immediately addressed.

There are many causes of hypercalcaemia. They are divided into PTH-dependent and PTH non-dependent causes.^{2 3} The most frequent are primary hyperthyroidism (adenoma, hyperplasia, carcinoma) and malignancy (tumours secreting PTH_{rp}; ectopic production of vitamin D substrates; metastatic/lytic bone lesions; haematological cancers).^{6–8}

Natriuresis and water loss associated with hypercalcaemia cause acquired nephrogenic diabetes insipidus leading to dehydration. In this case, the patient presented with septic shock and toxic megacolon with severe hypovolaemia due to acute bowel sequestration, and secondary pre-renal AKI. As a result, electrolyte homeostasis was disrupted, affecting calcium balance, since glomerular filtration is responsible for excretion of 60% of serum Ca^{2+} .⁹

The aggressive rehydration with NaCl 0.9% was preferred since Ca^{2+} reabsorption in the proximal tube and thick ascending limb of Henle's loop is passive and paracellular and electromechanical forces driving it are dependent directly and indirectly on sodium (Na^+) reabsorption. Conversely, in more distal segments of the nephron, Ca^{2+} reabsorption is through active and transcellular mechanisms, some of them by Na^+ - Ca^{2+} exchange.⁹

The immediate and aggressive correction of serum Ca^{2+} levels achieved after intensive hydration obviated the need for urgent parathyroidectomy. The patient's evolution endorsed the hypothesis of severe acute dehydration as the primary cause for severe hypercalcaemia, since serum Ca^{2+} remained normal without therapy.

Besides control of the cause, the goals of treatment of hypercalcaemia are: optimise glomerular filtration rate with hydration, increase the filtered load of calcium by using loop diuretics and

inhibit calcium reabsorption. Bisphosphonate therapy should also be initiated as soon as hypercalcaemia is diagnosed.¹⁰

Learning points

- ▶ Hypercalcaemia is a rare but potentially fatal medical emergency if unrecognised.
- ▶ In a patient with hypercalcaemia, the identification of the cause is determinant for correct treatment.
- ▶ Being viewed mainly as a consequence, dehydration has not been contemplated as a potential cause of hypercalcaemia. Dehydration should be considered one of the direct causes and it can be easily controlled.

Competing interests None.

Patient consent Obtained.

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