

CASE REPORT



An unusual case of severe hypercalcemia: as dehydrated as a bone

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ABSTRACT

Objective: Severe hypercalcemia is a medical emergency. Hyperparathyroidism, malignancy, vitamin D toxicity, infections such as tuberculosis, or systemic illness such as sarcoidosis are all possible etiologies. Among the less studied causes is dehydration. Our objective is to identify dehydration as an etiology of hypercalcemia.

Methods: Extensive literature review did not recognize dehydration as an etiology of hypercalcemia. We present a case of dehydration leading to severe hypercalcemia in a 60-years-old female with a presentation of altered mental status and corrected calcium level of 19 mg/dL in the absence of parathyroid abnormality, vitamin D toxicity, systemic disease, or malignancy.

Results: Dehydration caused hypercalcemia which led to a feed-forward mechanism and caused further worsening dehydration, worsening kidney function, and severe hypercalcemia. The patient responded very well to intravenous fluid and at the time of discharge had a serum calcium of 9.8 mg/dL with improved mental status back to the baseline.

Conclusion: Our literature review demonstrated many causes of hypercalcemia, with dehydration being exceptionally rare. It is our hope that this case report may serve as evidence of one such instance, allowing providers to keep a working differential of dehydration in severely elevated calcium levels.

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1. Background

Hypercalcemia is an elevation of serum calcium and may lead to significant clinical consequences. Clinical manifestations of hypercalcemia include hyporeflexia, shortened QT interval leading to arrhythmias like ventricular fibrillation, altered smooth muscle contraction, and many others [1]. There are many causes of hypercalcemia which include primary hyperparathyroidism, malignancy, and vitamin D toxicity [2–4], as well as other less common causes including but not limited to the use of calcium beads in orthopedic surgery, certain infections such as tuberculosis, or other systemic diseases such as sarcoidosis [5–7].

Furthermore, the magnitude of elevation of serum calcium is not always dependent on etiology, however, trends are noticed. For instance, the amount of elevation seen in primary hyperparathyroidism is usually in the ballpark of 11 mg/dL [8]. Hypercalcemia of malignancy and vitamin D toxicity leads to frequently higher levels of elevation of more than 12–14 mg/dL. The highest we found in a literature review was 23.08 mg/dL [8,9,10].

Using PubMed.gov with NCBI search terms of ‘severe hypercalcemia’ with parameters set for full text, and dating from 2010 to 2020, 1029 results

were generated. To emphasize the rarity of our case, of the first five results generated, one discusses vitamin D intoxication, one discussed inherited familial hypocalciuric hypercalcemia, and the other three discuss malignancy as the culprit. None of the first 50 results was due to dehydration as a primary culprit. There was mention of acute kidney injury and chronic kidney disease leading to elevated calcium levels; however, there were no reported cases of dehydration being the primary etiology. In a review of the literature, dehydration was not found to be associated with being the primary etiology in causing hypercalcemia [7–11]. We report a case of a 60-year-old female with a serum calcium level of 18 mg/dL (corrected for albumin was 19 mg/dL) due to dehydration.

2. The case

A 60-years-old female with a past medical history of chronic anemia, decompensated liver cirrhosis, hepatic encephalopathy, diabetes mellitus type 2, hypertension, depression, hypothyroidism, and restless leg syndrome presented to the hospital with a one-week history of depressed level of consciousness associated with poor oral intake and few episodes of nonbloody

nonbilious vomiting on the day of presentation. The patient was accompanied by her husband who reported that the patient was discharged from another hospital a few weeks ago where she was treated medically for hepatic encephalopathy. The husband denied fever or a change in bladder and bowel habits, and noncompliance with medications but mentioned that the patient had exhibited no interest in eating and drinking and had been sleeping most of the week. Patient's home medications included albuterol meter dosed inhaler, aspirin 81 mg daily, calcium carbonate 650 mg twice daily, cholecalciferol 1000 units daily, cyanocobalamin 5000 µg daily, enalapril 20 mg daily, folic acid 1 mg daily, insulin glargine 30 units nightly, sitagliptin 100 daily, lactulose 30 g twice daily, levothyroxine 50 µg daily, mirtazapine 50 mg nightly, oxybutynin 10 mg daily, pramipexole 0.125 mg daily, and rifaximin 550 mg twice daily. The husband denied a recent changes in her home medicines like the introduction of diuretics.

In the emergency department, the rectal temperature was 37°Celsius, heart rate was 71 bpm, blood pressure was 181/75 mmHg, respiratory rate was 17 per min, and oxygen saturation was 99% on room air. On the physical examination the patient was lethargic, with Glasgow Coma Scale 13/15. The mucus membranes were extremely dry. The abdomen was soft, nontender, and no ascites were present. Deep tendon reflexes were 2+ bilaterally. She was oriented to self only. The lab work revealed hemoglobin 11.1 gm/dL, platelet count $128 \times 10^3/\mu\text{L}$, serum sodium of 144 mmol/L, potassium 2.7 mmol/L, magnesium 1.1 mg/dL, blood urea nitrogen (BUN) of 23 mg/dL, creatinine 2.04 mg/dL, calcium 18.0 mg/dL with corrected calcium level of 19.0 mg/dL, serum albumin 3.2 g/dL, lactate 1.3 mmol/L, and ammonia 31 µg/dL. The comparison of the blood work from a week ago suggested hemoconcentration with acute kidney injury (Table 1). The Electrocardiogram demonstrated sinus rhythm, left axis deviation

without ST-segment changes. Chest X-ray did not reveal perihilar lymphadenopathy, acute infiltrates, or effusion. CAT scan of the head without contrast demonstrated no evidence of intracranial pathology or mass. The patient was given 2-g intravenous magnesium sulfate, 80 mEq oral potassium, and 10 mg intravenous potassium chloride, and 200 units intramuscular calcitonin. The patient was admitted to the telemetry floor where she was started on normal saline infusion at the rate of 125 mL/hr.

The patient's serum calcium was out of proportion to the degree of acute kidney injury, so the secondary cause of hypercalcemia was sought out. About 25-OH Vitamin D was 107 ng/mL (30–100 ng/mL), 1,25-OH Vitamin D was 59 pg/mL (19.9–79.3 pg/mL), parathyroid hormone level was 10 pg/mL (15 to 65 pg/mL), parathyroid hormone-related peptide less than 2 pmol/L (less than 2 pmol/L), Thyroid Stimulating Hormone (TSH) 0.216 µIU/mL (normal 0.350–3.7 µIU/mL), free T4 1.18 ng/dL (0.76–1.46 ng/dL). The serum protein electrophoresis and immunofixation revealed normal alpha-1, alpha-2, beta and gamma globulin levels, and no monoclonal M spike. Urine electrolytes revealed urine sodium 66 mmol/L, and urine specific gravity 0.015 (0.010–0.025). The renal ultrasound revealed normal-sized kidneys, normal, and no hydronephrosis.

Due to the patient's poor oral intake, a lactulose enema was started. Aggressive intravenous hydration was continued. On day three, the mucous membranes were noted to be moist. On day four, the serum calcium level had improved to 10.6 mg/dL, and the calcitonin and intravenous fluid were stopped (Table 2). There was also gradual improvement in her mental status. On day five, the patient was awake and oriented to time, place, and person. On day six the patient's mental status, oral intake, and physical activity were back to the baseline and she was discharged home. During follow up visit a week following discharge, her mental status was at her baseline, with a good appetite

Table 1. Comparison of labs on the day of presentation vs a week before. (Reference range in bracket.)

	Day of presentation	7 days before presentation
Sodium: (136–145 mmol/L)	142 mmol/L	137 mmol/L
Potassium: (3.5–5.1 mmol/L)	2.7 mmol/L	4.2 mmol/L
Chloride: (98–107 mmol/L)	103 mmol/L	108 mmol/L
Bicarbonate: (21–32 mmol/L)	32 mmol/L	21 mmol/L
Blood Urea Nitrogen: (7–18 mg/dL)	23 mg/dL	15 mg/dL
Creatinine: (0.55–1.30 mg/dL)	2.04 mg/dL	0.99 mg/dL
Glucose: (74–106 mg/dL)	105 mg/dL	445 mg/dL
Calcium: (8.5–10.1 mg/dL)	18 mg/dL	8.1 mg/dL
e Glomerular Filtration Rate: (>60 mL/min)	25.9 mL/min	>60 mL/min
Aspartate Aminotransferase: (15–37 U/L)	57 U/L	38 U/L
Alanine Aminotransferase: (12–78 U/L)	38 U/L	26 U/L
Alkaline phosphatase: (50–136 U/L)	145 U/L	85 U/L
Total Protein: (6.4–8.2 g/dL)	6.8 g/dL	4.5 g/dL
Albumin: (3.4–5.0 g/dL)	3.2 g/dL	2.1 g/dL
Total Bilirubin: (0.2–1.0 mg/dL)	2.5 mg/dL	1.0 mg/dL
White blood cells: (4.5–12.5 $\times 10^3/\mu\text{L}$)	$6.5 \times 10^3/\mu\text{L}$	$4.9 \times 10^3/\mu\text{L}$
Hemoglobin: (12–16 g/dL)	11.1 g/dL	7.8 g/dL
Hematocrit: (36%–48%)	32.8%	24.5%
Platelets: (150–450 $\times 10^3/\text{microliter}$)	$128 \times 10^3/\text{microliter}$	$80 \times 10^3/\text{microliter}$

Table 2. Lab values during the patient’s stay and post-discharge follow up.

	D-0 (2053)	D-1 (0425)	D-1 (0839)	D-1 (1441)	D-2 (0517)	D-3 (0528)	D-4 (0606)	D-5 (0543)	D-6 (0432)	D-14
BUN (mg/dL)	23	25	26	25	31	43	45	39	33	15
Cr (mg/dL)	2.04	1.79	1.82	1.97	2.41	2.87	2.61	2.25	2.09	1.26
Ca (mg/dL)	18.0	14.8	14.3	14.0	12.8	11.6	10.6	10.2	9.8	10.1

BUN: Blood Urea Nitrogen; Cr: Creatinine; Ca: Calcium

and oral intake. Serum calcium level was 10.1 mg/dL, BUN 15 mg/dL, creatinine 1.26 mg/dL and e Glomerular Filtration Rate (eGFR) were >60 mL/min.

3. Discussion

The calcium homeostasis is tightly regulated by various mechanisms. Normal lab ranges are typically around 9.4 mg/dL or 2.4 mmol/L with small percentage leeway in either direction [1]. The dietary gastrointestinal (GI) ingestion of calcium is around 1000 mg daily. However, only 350 mg of calcium is absorbed from the gastrointestinal tract daily which is facilitated by Vitamin D, and the remainder is excreted in feces. The human skeletal system is made of over 1,000,000 mg of calcium and serves as the largest store of total body calcium [1]. PTH increases the serum calcium by bone resorption, increasing gastrointestinal absorption, and decreasing renal excretion [1]. These mechanisms serve to increase and decrease calcium levels depending on the body’s total calcium stores which are primarily measured via calcium-sensing receptors in the parathyroid and renal tubules [1].

Hypercalcemia is a common hospital problem and has multiple causes. Mild hypercalcemia of less than 12 mg/dL may be asymptomatic or mild symptoms of constipation, fatigue, depression [12]. Some of the common manifestations are depressed neuronal functions such as hyporeflexia, as well as decreased appetite, and constipation, likely from decreased gastrointestinal smooth muscle activity [1]. At a level of over 12 mg/dL, rare but serious cardiac manifestation includes decreased QT interval, falsely elevated ST segments, and arrhythmias like ventricular fibrillation can occur [13]. Calcium levels greater than 15 mg/dL usually manifest in marked severe symptoms such as lethargy stupor or even coma and levels above 17 mg/dL may precipitate calcium phosphate crystals and lead to coma as well [1,12]. Though no specific symptoms can be defined solely based on calcium level, the severity of potential morbidities is correlated to the level of elevation (Table 3).

To the best of our knowledge, the highest levels of hypercalcemia reported to be in association with dehydration was in a case of colonic ischemia and septic shock that secondarily lead to dehydration and

Table 3. The degree of hypercalcemia and the associated symptoms.

Degree of Hypercalcemia	Symptoms
< 11.5 mg/dL	<ul style="list-style-type: none"> • Usually asymptomatic • If levels rise from baseline quickly, may present as polyuria, polydipsia, fatigue, depression.
11.5–14 mg/dL	<ul style="list-style-type: none"> • Fatigue, apathy, muscle weakness, anorexia, nausea, constipation.
>14 mg/dL	<ul style="list-style-type: none"> • The above symptoms persist and become more severe in nature at this level. • Dehydration, abdominal pain, vomiting, EKG changes such as QT prolongation, obtundation, and even coma may occur.

hypercalcemia which reported a level of 17.7 mg/dL [14]. The highest total level found in a literature review was 23.08 mg/dL which was a result of severe vitamin D toxicity in which a patient received over 6,000,000 international units of Vitamin D intramuscularly within 2 weeks [9].

It is well known that hypercalcemia causes a nephrogenic diabetes insipidus which may lead to dehydration. There is also evidence hypercalcemia can cause natriuresis and subsequent dehydration [11]. We propose that an initial insult such as dehydration leading to hypercalcemia can precipitate further dehydration as a result of hypercalcemia interfering with the kidney’s ability to concentrate urine. This sets up a vicious loop whereby dehydration leading to hypercalcemia becomes worsened by decreasing renal function and worsening hypercalcemia. This patient being dehydrated allowed for such a dramatic rise in serum calcium. The degree hypercalcemia was out of proportion of kidney injury, and furthermore normalization of serum calcium did not correlate with normalization of kidney function. Therefore, we assumed that the hypercalcemia was due to dehydration and the feedforward mechanism which worsened both dehydration and hypercalcemia.

In a patient with normal kidney function and after ruling out primary or secondary hyperthyroidism, malignancy, multiple myeloma, Vitamin D toxicity, Vitamin D secreting conditions corrected serum calcium level of 19 mg/dL because of dehydration and causing acute kidney injury is so far not reported, which makes our case extremely rare. It is our hope that this case report will allow the providing providers to keep a broad differential and be mindful that dehydration may lead to such severe hypercalcemia.

4. Conclusion

Severe hypercalcemia is a life-threatening medical emergency. So far dehydration has not been identified as an etiology of severe hypercalcemia in a patient with normal kidney function. It is very important to keep severe hypercalcemia in the working differential when encountering a confused and dehydrated patient, especially the elderly.

Disclosure statement

No potential conflict of interest was reported by the authors.

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