CASE REPORT

The forgotten electrolyte, when hypercalcaemia manifest as gait instability and altered mental status

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SUMMARY

An altered mental status presents a diagnostic challenge for many clinicians. Described here is a case of primary hyperparathyroidism not initially suspected until after a thorough neurological and infectious cause were excluded. A 60-year-old woman presented with altered mental status and gait instability. Her family noticed progressive gait instability and mood swings for the past 4 months. Initial imaging and laboratory values were unable to explain her symptoms. On transfer out of the intensive care unit, her corrected calcium was found to be 13.3 mg/dL with an elevated parathyroid hormone. Her hypercalcaemia was refractory to medical management. Ultrasound found a 2 cm nodule, which was surgically removed and found to be a parathyroid adenoma. Her calcium normalised and neurological deficits subsided. Hypercalcaemia can lead to a constellation of symptoms that include the classical 'stones, bones, abdominal moans and psychic groans' and electrolyte derangements should be considered in the differential of altered mental status.

BACKGROUND

Altered mental status is a broad term that encompasses changes in personality, mood and recall ability. Patients can sometimes be described as delirious, bizarre or confused. The spectrum of diseases that can cause someone to become altered is broad. When developing a differential diagnosis for altered mental status, a detailed history and physical examination are important to help and guide the diagnostic work-up.

Reported here is a case report of primary hyperparathyroidism (PHPT) associated with nephrolithiasis requiring ureteral stent placement and progressive altered mental status that was refractory to the medical management. Her symptoms were also refractory to the medical management. Given her degree of hypercalcaemia that did not respond to adequate hydration, furosemide, calcitonin, initial bisphosphonates and her associated altered mental status with nephrolithiasis, it was decided to surgically remove a solitary parathyroid adenoma localised on imaging.

CASE PRESENTATION

A 60-year-old African-American woman presented to the emergency department (ED) with an altered mental status and gait instability for 3 days. She had arrived from a Caribbean cruise vacation the day prior. While on vacation, her family noticed

difficulty walking with frequent falls and episodes of confusion. When the cruise arrived back to port, she was unable to walk and her family noticed worsening of her mental status and brought her to the ED for further evaluation. She denied ever having similar symptoms in the past. She felt subjective fevers for the past 3 days but denied having any headaches, neck pain, regional numbness or weakness, constipation, focal weakness, weight loss, nausea or vomiting.

On physical examination in the ED, she was noted to be somnolent. She had significant difficulty with short-term and long-term recall. When ambulated, she had a wide gait and required almost full assistance. Her cardiac, pulmonary and abdominal examinations were unremarkable. No rashes or skin changes were noted.

INVESTIGATIONS

On laboratory investigation (table 1), she presented with a neutrophilic predominant leucocytosis of $19.5 \times 10^9/L$, blood urea nitrogen of 20 mg/dL, creatinine of 1.85 mg/dL and a calcium of 12.3 mg/dL.

She had a CT of her head and lumbar puncture, which were normal. Given she developed a fever of 100.4°F and generalised myalgia the day after admission, she underwent MRI of her brain and PCR for herpes simplex virus 1 and 2 which were negative. No infectious aetiology was found and all blood, urine and cerebrospinal fluid cultures were negative. She did not develop a fever again during the rest of the hospitalisation. During her hospital course her calcium increased to 13.3 mg/dL. A renal ultrasound revealed a partially obstructing 0.9 cm left proximal ureter calculus that was causing mild hydronephrosis for which a left ureteral stent was placed. Her parathyroid hormone (PTH) was elevated at 630 pg/mL, which suggested hyperparathyroidism. A 24-hour urine calcium was <200, which was thought to be secondary to a low-vitamin D level of 5.9 ng/mL. Her serum PTH was higher than expected given her degree of vitamin D deficiency and acute kidney injury which lead to a suspicion of PHPT. After adequate hydration, she continued with a persistently high calcium. During her hospitalisation, she was treated with calcitonin, cinacalcet and furosemide. Given her poor response, she was given zoledronic acid, which lowered calcium to 12.3 mg/dL. Sestamibi scan (figure 1) showed an increased uptake on the right consistent with hyperparathyroidism, which also correlated with an ultrasound of the neck which

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Table 1 Laboratory investigations on admission

Variable	On admission	Reference range, adult
Haemoglobin (g/dL)	12.1	12.0–16.0
Haematocrit (%)	38.8	37.0–47.0
Platelet (109/L)	196	150–450
WCC (10 ⁹ /L)	19.51	4.80–10.80
Differential count (%)		
Neutrophils	76.8	42–75
Lymphocytes	8.5	16–45
Monocytes	14.0	2–12
Eosinophils	0.0	0–5
Basophils	0.2	0–2
Lactic acid (mmol/L)	0.9	0.4–2.0
Glucose (mg/dL)	175	74–106
BUN (mg/dL)	20	7–18
Creatinine (mg/dL)	1.85	0.55–1.02
Calcium (mg/dL)	12.3	8.5–10.1
Albumin (g/dL)	2.7	3.4–5.0
CSF		
Colour	Colourless	Colourless
Turbidity	Clear	Clear
Xanthochromia	None	None
RCC (cells/μL)	7	0–5
Total nucleated cells (cells/μL)	0	0–5
Glucose (mg/dL)	106	40–70
Protein (mg/dL)	26	15–45

Corrected calcium=(0.8x(4–albumin))+serum calcium.
BUN, blood urea nitrogen; CSF, cerebrospinal fluid; RCC, red cell count; WCC, white cell count.

showed a 2.2 cm vascular nodule on the right thyroid gland (figure 2).

OUTCOME AND FOLLOW-UP

Given the difficult to control hypercalcaemia associated with nephrolithiasis and altered mental status, surgery was recommended. A 3 g mass from the right parathyroid (figure 3) was removed, and pathology confirmed it to be a hyperfunctioning right inferior parathyroid adenoma.

Figure 1 Technetium (99mTc) sestamibi scan showing increased uptake on the right.

Figure 2 Thyroid ultrasound showing exophytic vascular nodule.

Her calcium decreased to 9.8 mg/dL the following day. After the hypercalcaemia was treated, her gait instability and altered mental status subsided and patient was discharged the following day. She followed up a week later with the urologist for the removal of her ureteral stent. Preoperative and postoperative serum calcium levels continued within the normal range.

DISCUSSION

Hypercalcaemia due to PHPT can lead to a constellation of symptoms that include the classical ‘stones, bones, abdominal moans and psychiatric overtones.’¹ An infectious aetiology was initially considered because the patient presented to the ED with subjective fevers and altered mental status with recent travel to the Caribbean islands. Altered mental status is a common presentation to the emergency room and accounts for up to 10% of admissions.² A detailed history, physical examination and laboratory values can point you to an endocrine cause, which accounts for 5% of cases.²

Neuropsychiatric manifestations of PHPT present in up to 23% of patients.³ Our patient had gait difficulty, confusion and difficulty with memory recall, which are unusual for her level of hypercalcaemia. Hypercalcaemia of malignancy was low in the differential because her PTH was elevated and the patient exhibited no other symptoms to suggest an underlying malignancy. The nephrolithiasis, serum calcium elevation 1 mg/dL above the upper limit of normal and decreased estimated glomerular

Figure 3 Hypercellular parathyroid tissue consistent with parathyroid adenoma.

Figure 4 Serum calcium and calcium-lowering interventions.

filtration rate qualified our patient for the surgical removal of the parathyroid adenoma based on the Fourth International Workshop on Asymptomatic Primary Hyperparathyroidism guidelines.⁴ Her symptoms mildly improved with conservative medical treatment but ultimately required the removal of the hypersecreting parathyroid gland to obtain complete resolution of her neuropsychiatric symptoms.

There are many reported cases of refractory hypercalcaemia that are mainly associated with malignancy and most commonly associated to elevated PTH-related protein or multiple bone metastasis.^{5–7} PHPT tends to respond better to medical management, and our patient was refractory to appropriate medical management which included adequate hydration, furosemide, bisphosphonates, calcitonin and cinacalcet. A timeline of calcium-lowering interventions are listed in figure 4. Case reports describe concomitant causes of hypercalcaemia with PHPT and multiple myeloma as possible associations.^{7–9} Given elevated calcium, creatinine and anaemia on admission, she was evaluated for multiple myeloma with monoclonal immunoglobulin proliferation and Bence-Jones protein, both of which were not detected. A 24-hour urine calcium was <200. It was thought to be secondary to a low-vitamin D level of 5.9 ng/mL. Familial hypocalciuric hypercalcaemia (FHH) was considered but FHH

does not tend to cause nephrolithiasis and serum calcium levels above 13 mg/dL.

In conclusion, PHPT can pose a challenging work up in the hospital given symptoms may be vague and prone to an extensive work-up. PTH closely regulates calcium and phosphate homeostasis. In PHPT, there is an increase in serum calcium from bone resorption, intestinal calcium absorption and decreased urinary calcium excretion. Hypercalcaemia can cause dysfunction in multiple organs that can lead a clinician to suspect different diseases before investigating the parathyroid. Most cases can be managed in an ambulatory setting but some are refractory to the medical management and require more aggressive intervention. Adenomas account for the majority of cases of PHPT and surgical removal may alleviate symptoms of hypercalcaemia.

Contributors All authors have directly participated in the planning and execution of this case report in medicine. IU and MBS were the internal medicine physicians responsible for the care of the patient during the hospitalisation in advisement with AC as the intensive care physician. SO was the pathologist who contributed to the diagnosis of parathyroid adenoma. All authors contributed to the content and revision of the final manuscript. Figures and tables were created by IU and he was responsible for explaining the consent to publish to the patient during her hospitalisation.

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Patient's perspective

The patient did not wish to provide a personal perspective. However, she emphasised that it was important to her that she be described as an African-American woman in the case report. She hoped that case reports include race so that scientific inquiry into racial correlations continue to be explored.

Learning points

- Primary hyperparathyroidism (PHPT) can present as altered mental status with gait instability.
- The most common cause of PHPT is due to a solitary parathyroid adenoma.
- PHPT and multiple myeloma can be associated findings in patients with hypercalcaemia.
- Surgical removal is indicated for parathyroid adenomas if the serum calcium is 1.0 mg/dL above the upper limit of normal, bone mineral density T-score is 2.5, vertebral fracture, creatinine clearance <60 mL/min, 24 hours urine calcium >400 mg/day and increased risk of stone, the presence of nephrolithiasis or age <50 years.

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