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Case Report

Urinary tract infection triggering hypercalcemic crisis in an asymptomatic patient with primary hyperparathyroidism

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Abstract

Hypercalcemic crisis (HC) is a rare and severe complication of primary hyperparathyroidism (PHPT), characterized by markedly elevated serum calcium levels and diverse clinical manifestations. PHPT is the primary cause of hypercalcemia and is often asymptomatic. The factors that trigger HC in PHPT are not fully understood. Here we report a patient who was diagnosed with HC resulting from previously undetected PHPT. Remarkably, the patient exhibited no symptoms of PHPT before the HC episode. The patient presented with neurological symptoms, including altered behavior and slurred speech, which were attributed to hypercalcemia. The probable trigger for HC in this case appears to be an acute febrile illness related to a urinary tract infection (UTI). The occurrence of an acute febrile illness or UTI as a precipitating factor for HC in PHPT is a rare and infrequently documented phenomenon in the existing medical literature.

Keywords: Hypercalcemic crisis, Hyperparathyroidism, UTI

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Introduction

A hypercalcemic crisis (HC) is an uncommon occurrence in individuals with primary hyperparathyroidism (PHPT) (1). During such a crisis, there is a significant elevation in serum calcium levels, typically exceeding ≥14 mg/dL or 3.5 mmol/L (2). These elevated calcium levels can adversely affect multiple organ systems, leading to a range of symptoms. The manifestations of HC in a patient can vary but may encompass symptoms like nausea, vomiting, severe weakness, cognitive impairments, drowsiness, acute kidney dysfunction, and cardiac arrhythmias (2).

PHPT is the leading underlying factor for hypercalcemia, whether or not it leads to a crisis (3). Typically, hypercalcemia in PHPT is of a chronic and mild nature, often displaying no noticeable symptoms. However, only a small fraction, approximately 1-2% of PHPT patients, experience a HC (1). This condition necessitates urgent hospitalization, and any delay in treatment could have life-threatening consequences for the patient (2). Nevertheless, it remains uncertain which individuals with PHPT face the highest likelihood of encountering a HC (3). Research has identified multiple scenarios in which HC could potentially be triggered in a PHPT patient. These circumstances encompass episodes of diarrheal illness, prolonged bouts of vomiting, the use of diuretics, post-major surgery recovery, periods of immobilization, excessive oral calcium salt consumption, and the rare occurrence of parathyroid carcinoma (4). The presence of nephrolithiasis in a patient with PHPT is also regarded as a risk factor for HC development (5).

Here we report a patient who was diagnosed with HC resulting from previously undetected PHPT. Remarkably, the patient exhibited no symptoms of PHPT before the HC episode. The patient presented with neurological symptoms, including altered behavior and slurred speech, which were attributed to hypercalcemia. The probable trigger for HC in this case appears to be an acute febrile illness related to a urinary tract infection (UTI). The occurrence of an acute febrile illness or UTI as a precipitating factor for HC in PHPT is a rare and infrequently documented phenomenon in the existing medical literature.

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Implication for health policy/practice/research/medical education

Healthcare providers should maintain vigilance for HC in patients with PHPT, even when asymptomatic, particularly when presented with neurological symptoms. Collaboration among specialists from neurology, endocrinology, and critical care is crucial for early hypercalcemic crisis diagnosis and management.

Case Report

The patient, a 56-year-old woman, has a known history of type 2 diabetes mellitus and cervical spondylosis. She presented to the emergency room with a complaint of altered behavior, slurred and nonsensical speech lasting less than one day. Additionally, she reported experiencing fever and fatigue for the past three days leading up to her visit. The patient had no other documented comorbidities and was solely taking oral hypoglycemic agents at the time of presentation; she was not on any diuretic therapy. Notably, there was no history of nausea, vomiting, photophobia, neck stiffness, seizures, lower urinary tract symptoms, constipation, or abdominal pain in her medical record.

During the examination, the patient displayed drowsiness but was responsive to commands. Her vital signs included a pulse rate of 106 beats per minute, a respiratory rate of 25 breaths per minute, a temperature of 101.4°F, oxygen saturation at 96% in room air, a blood pressure reading of 126/80 mm Hg, and a capillary glucose reading indicating a "high" value.

Upon examination, the oropharynx appeared normal without any signs of inflammation or exudates, and the neck was supple. Chest auscultation revealed equal and clear bilateral air entry, and the heart sounds exhibited normal characteristics with no murmurs detected. The abdomen was soft and non-tender. Pupillary examination revealed bilaterally equal, round pupils that were reactive to both light and accommodation. The patient presented with dysarthria, but displayed full movement in all four limbs, and there were no signs indicative of focal neurological deficits.

Upon admission, laboratory tests revealed a urea level of 43 mg/dL, creatinine at 1.13 mg/dL, a total white blood cell count of 10 000/mm^3, blood sugar measuring 532 mg/dL, HbA1c at 7.5%, and CRP at 203 mg/dL. A urine routine examination indicated the presence of 30-35 pus cells per high-power field and the presence of bacteria and urine culture showed growth of Escherichia coli extended-spectrum beta-lactamase (ESBL).

The patient was admitted with a provisional diagnosis of acute febrile illness attributed to a UTI and hyperglycemia. Treatment commenced with intravenous fluids (normal saline), intravenous antibiotics (meropenem), and intravenous insulin infusion. The plan included investigating the possibility of a central nervous system infection and performing a cerebrospinal fluid study if altered sensorium persisted after initiating antibiotics and correcting hyperglycemia.

Subsequent tests revealed an ionized calcium level of 1.4 mmol/L (normal range: 1.16-1.31), followed by serum calcium and serum phosphate levels of 14.1 mg/dL (normal range: 8.5-10.2) and 1.6 mg/dL (normal range: 2.5-4.9), respectively. Additionally, the intact parathyroid hormone (iPTH) level was measured at 449.9 pg/mL (normal range: 15-65), and a neck ultrasound (ultrasonography, USG) confirmed the presence of an intrathyroidal parathyroid adenoma at the lower pole of right lobe of the thyroid inseparable from the thyroid gland. Abdominal imaging results came back negative for nephrocalcinosis and nephrolithiasis.

The patient received a diagnosis of HC attributed to PHPT. Treatment was initiated with hydration, involving intravenous normal saline (IV NS) at a rate of 250 mL/h. Additionally, the patient was administered intravenous calcitonin at a dosage of 200 mg every 6 hours for one day, later reduced to every 12 hours for the subsequent 3 days. Concurrently, a surgical consultation was sought, leading to the scheduling of a right hemithyroidectomy and right parathyroid excision. As the patient's serum calcium levels decreased, her sensorium and speech improved. Serum calcium was reduced to 9.9 mg/dL prior to the surgery. The procedure was performed successfully, and the postoperative period transpired without complications. Serum calcium levels further decreased to 8.1 mg/dL on the third postoperative day, and the patient experienced symptomatic relief. Pathological examination of the resected specimen confirmed the presence of a parathyroid adenoma within the thyroid gland. Subsequently, the patient was discharged and prescribed calcium tablets for follow-up care.

Discussion

PHPT arises from a primary dysfunction within the parathyroid tissue, resulting in the inappropriate secretion of parathyroid hormone (PTH) (3). In our case, the diagnosis of PHPT was confirmed through laboratory assessments. PHPT is characterized by two distinctive biochemical markers: consistently elevated serum calcium levels in conjunction with an increased iPTH concentration. In our specific case, the serum calcium level exceeding 14 and an iPTH value exceeding 400 strongly indicated HC in the context of PHPT. This provisional diagnosis was corroborated by a neck ultrasound (USG), which revealed the presence of a parathyroid adenoma.

The definitive treatment for PHPT is parathyroidectomy, which is the sole curative option. This surgical procedure involves the removal of the overactive parathyroid gland or glands, resulting in a reduction of PTH release into the bloodstream and consequently lowering serum calcium levels. In cases of HC, parathyroidectomy is an

urgent intervention, often recommended during the same hospital admission. Alternatively, other approved therapies for managing hypercalcemia include the use of calcitonin or bisphosphonates to reduce calcium levels before surgery. In this particular case, we administered intravenous calcitonin in a tapering dosage over a span of 3 days, successfully bringing the calcium levels within the normal range. This intervention significantly improved the patient's neuropsychiatric symptoms prior to undergoing surgery.

While the established treatment for HC, involving hydration followed by surgery, has proven efficacy, there exists a notable gap in the literature regarding strategies to prevent HC in patients with PHPT. Certain factors that may aid clinicians in anticipating HC include preoperative calcium levels, a Charlson Comorbidity Index (CCI) score equal to or greater than 4, and PTH levels (4).

Notably, previous case reports have discussed PHPT manifesting as recurrent UTIs. However, these recurrent UTIs have typically been attributed to nephrolithiasis or nephrocalcinosis resulting from prolonged asymptomatic hypercalcemia associated with PHPT (5,6). In our patient's case, there was no history of recurrent UTIs, and imaging conducted during admission did not reveal nephrolithiasis. Structural urinary tract abnormalities induced by hypercalcemia in PHPT have been documented in some prior case reports, leading to the colonization of the urinary tract by atypical bacteria such as non-typhoidal Salmonella (Salmonella Group D) (7). It is noteworthy that in our case, the isolated bacterium from the urine culture was *E. coli* ESBL.

At present, there is limited literature available regarding the precipitating factors of HC in patients with parathyroid adenoma. Dehydration and immobilization are recognized triggers for HC in PHPT (3). However, our patient had no history of conditions that typically lead to dehydration, such as diarrheal illnesses or vomiting, and she was not undergoing diuretic therapy. Furthermore, there was no prolonged immobilization preceding her presentation. Additional potential causes of HC encompass parathyroid carcinoma or parathyroid hemorrhage, both of which were ruled out in the pathological examination of the resected specimen in this case. The patient's history primarily included a two-day episode of fever and fatigue before developing neuropsychiatric symptoms indicative of hypercalcemia. Therefore, it is noteworthy that the sole antecedent event leading to HC in our patient was an acute febrile illness resulting from a urinary tract infection caused by *E. coli*.

Conclusion

This case report underscores the importance of considering hypercalcemia as a potential diagnosis when a patient presents with neurological symptoms such as altered sensorium and slurred speech, especially in the context of dehydration or an acute febrile illness.

Authors' contribution

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Writing–review & editing: Faiz mohamed, Pichen Shihabudheen, Mohammed Javad Kotta Veluthedathu, Muhammed Unais Thattaril, Nalakath Arakkal Uvais.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

This case report was conducted in accordance with the World Medical Association Declaration of Helsinki. The patient has provided written informed consent for publication as a case report. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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