

CASE REPORT

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Primary hyperparathyroidism presenting as subacute encephalopathy: A case report and review of literature

Dany Barrak, Romina Deldar, Chamilka Merle, Arthur Brannon III, Darren Jackson II, Jennifer E Rosen

ABSTRACT

Introduction: Altered mental status can be a reflection of any systemic disease. Endocrinopathies such as hypercalcemia and hyperparathyroidism are among those that may present with such neurologic symptoms. The aim of this case report is to emphasize that primary hyperparathyroidism (PHPT) should be considered as a possible diagnosis in patients who present with a decline in neurological function.

Case Report: Our case report details a patient with history of PHPT and breast cancer who presented with progressive neurocognitive decline, abnormal hyperkinetic involuntary movements, weight loss, and decline in functional status over the past year. Extensive workup including laboratory data, imaging, lumbar puncture, and gene panels were unremarkable. The patient underwent parathyroidectomy with improvement in her neurocognitive and functional status postoperatively.

Conclusion: Parathyroidectomy has favorable outcomes when performed early in elderly patients who present with hypercalcemic encephalopathy due to primary hyperparathyroidism. Hypercalcemia and primary hyperparathyroidism should be considered in the differential diagnosis of altered mental status, especially in the elderly population.

Keywords: Encephalopathy, Endocrine surgery, Parathyroidectomy, Primary hyperparathyroidism

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INTRODUCTION

Hyperparathyroidism is a benign disease that often goes undiagnosed until patients present with symptoms of hypercalcemia. Parathyroid hormone is released by the chief cells of the parathyroid glands in response to low serum calcium levels. This hormone plays a vital role in calcium homeostasis by multiple pathways: increasing bone resorption rate, intestinal calcium absorption, and decreasing urinary calcium excretion. Increased levels of serum calcium may present as confusion, paranoia, disorientation, delirium, and hallucinations. Although the pathogenesis of the neurologic symptoms in primary hyperparathyroidism (PHPT) remains unclear, calcium has been found to alter monoamine metabolism in the central nervous system (CNS), thereby altering neuro-signaling and resulting in mood and cognition variations seen in affected patients [1]. This article presents a case of subacute encephalopathy symptoms suspected to have resulted from untreated hyperparathyroidism.

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CASE REPORT

A 74-year-old female with history of PHPT, breast cancer, and osteoporosis presented to the MedStar Endocrine Surgery Clinic with a six-month history of rapid, progressive neurocognitive decline, abnormal hyperkinetic involuntary movements, and weight loss. The patient had progressive decline in functional status over the past year, initially with mild cognitive impairment which evolved into restlessness, irritability, abnormal involuntary movements, and a 70-pound weight loss. Extensive workup for infectious, paraneoplastic, neurodegenerative, autoimmune, psychiatric, and environmental causes were all negative. Chronic medical conditions, such as diabetes mellitus and hypertension, were ruled out. Brain magnetic resonance imaging showed punctate infarcts with subacute white matter changes likely related to a prior watershed infarct, and less likely related to her symptomatology. Computed tomography (CT) angiogram revealed no focal occlusions, electroencephalogram was normal, and CT chest, abdomen, and pelvis was unrevealing. Infectious workup was also negative. Gene panels for inherited neuromuscular disorders, such as Huntington's disease, were negative. Lumbar puncture was performed with unremarkable cerebrospinal fluid studies.

Several months prior to this hospitalization, the patient was found to have elevated calcium and parathyroid hormone (PTH) levels with no known secondary cause. Bone densitometry scan revealed osteopenia. Thyroid ultrasound at that time did not reveal an obvious focus. The patient did not undergo a Sestamibi scan as she was unable to tolerate it due to her neurocognitive deficits and hyperactivity. Prior to consideration of parathyroidectomy, the patient underwent three separate extensive neurologic evaluations, as it was unclear if her rapid cognitive decline was entirely due to PHPT.

Given the patient's presumed diagnosis of PHPT, a repeat thyroid ultrasound was obtained which demonstrated a focus inferior to the left thyroid lobe consistent with a left inferior parathyroid adenoma. In addition, her PTH level was elevated at 367 pg/mL and serum calcium level was markedly elevated at 12.6 mg/dL. Immediately after her outpatient clinical evaluation, the patient was admitted to the hospital with severe hypernatremia (serum sodium level of 179 ng/mL) and required free water supplementation over seven days to reach a near-normal level at 154 ng/mL. Workup again was consistent with PHPT, and no secondary causes for her hypernatremia or PHPT were identified.

After extensive discussion with the family, the patient was taken to the operating room and underwent a parathyroidectomy. Intraoperative findings consisted of a very small thyroid gland, normal soft 3 × 4 mm light tan left superior parathyroid gland, normal soft 3 × 4 mm light tan right superior parathyroid gland, a normal small 3 × 4 mm ovoid right inferior parathyroid gland, and a 1 × 1.2 cm ovoid dark brown firm left inferior parathyroid gland which was resected. The intraoperative PTH

(ioPTH) levels were drawn from the internal jugular vein and results were as followed: ioPTH from left internal jugular vein prior to resection was 367 pg/mL (normal 15–64 pg/mL), ioPTH from left internal jugular vein immediately after resection was 192 pg/mL, ioPTH from left internal jugular vein at 10 minutes after resection was near normal at 70.9 pg/mL. The specimen was sent to pathology which confirmed a hypercellular parathyroid tissue without evidence of carcinoma. Postoperatively, her PTH levels and serum calcium levels normalized. Her mental status, involuntary movements, and overall mood significantly improved over the next few days. Upon discharge, the patient's mini-mental status examination was scored as 23 (she was unable to complete examination prior to surgery). The patient was seen one month later in clinic and displayed no neurocognitive symptoms. Her PTH levels remained normal.

DISCUSSION

Increasing severity of hypercalcemia is usually associated with worse clinical presentations. Mild hypercalcemia (10.5–11.9 mg/dL) commonly manifests as anxiety or depression, moderate hypercalcemia (12–13.9 mg/dL) as cognitive dysfunction, and severe hypercalcemia (>14 mg/dL) is associated with lethargy, confusion, stupor, or even coma [2]. The abrupt rise in calcium levels reflects the severity of the neurologic manifestation such that a sudden rise in calcium levels would present with more severe neurologic dysfunction compared to chronic hypercalcemia [3, 4]. Interestingly, some studies have reported neuropsychiatric disturbances in cases of mild hypercalcemia due to otherwise asymptomatic PHPT, which was the case in our patient [5]. The elderly population appears to be more susceptible to psychiatric symptoms secondary to hypercalcemia, and these symptoms can be inappropriately attributed to comorbidities such as vascular or Alzheimer's dementia and can be misdiagnosed for extended periods of time [6]. The proposed mechanisms for the neurologic effects of hypercalcemia are reversible cerebral vasospasm and vasogenic edema. This hypothesis is thought to be responsible for symptoms of encephalopathy and seizures associated with hypercalcemia. It may also cause vasospasm by promoting actin-myosin coupling leading to activation of vascular smooth muscles [7].

When our patient initially presented to the emergency room, she did not present with typical symptoms of hyperparathyroidism. Usually, when hypercalcemia is detected, levels of intact parathyroid hormone, ionized calcium, or total serum calcium corrected for albumin level, and serum 25-hydroxyvitamin D level can be ordered to investigate the cause of the hypercalcemia and diagnose hyperparathyroidism accordingly [8]. The poor quality of life associated with the neuropsychiatric symptoms in PHPT, even with mild hypercalcemia, makes it imperative that treatment for PHPT be followed

through [9]. To our knowledge, this is the first case report of a patient who presented with solely neuropsychiatric and neurologic symptoms of PHPT which improved after parathyroidectomy.

Evidence on the use of anti-psychotics in this population is limited, but treatment may be required initially for symptom control until normalization of serum calcium levels. Moreover, psychiatrists should be aware of the neuropsychiatric manifestations of hyperparathyroidism, especially early on in the course of treatment. This case highlights the potential benefit of screening for high serum calcium levels at presentation to aid a prompt diagnosis and minimize future complications.

CONCLUSION

Hypercalcemia and primary hyperparathyroidism should be considered in the differential diagnosis of altered mental status, especially in the elderly population. The neuropsychiatric symptoms must be addressed in a timely and multi-disciplinary fashion to solidify a plan and improve patients' quality of life.

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Author Contributions

Dany Barrak – Analysis of data, Drafting the work, Revising the work critically for important intellectual

content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Romina Deldar – Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Darren Jackson II – Acquisition of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Jennifer E Rosen – Conception of the work, Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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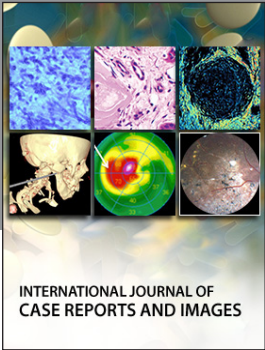
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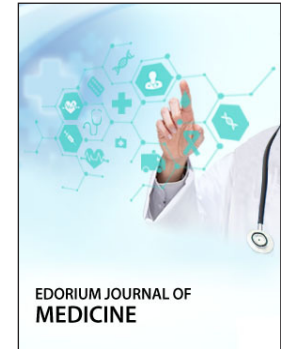


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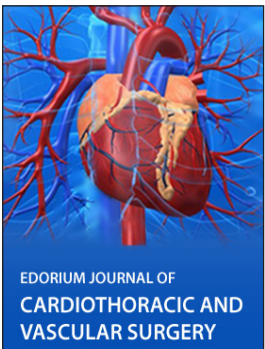


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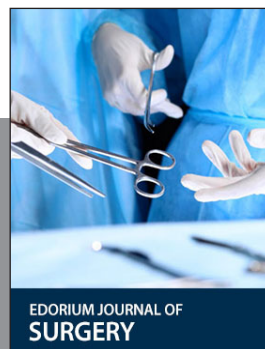
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