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CASE REPORT

Severe Neuropsychiatric Symptoms Associated with "Mild" Primary Hyperparathyroidism: A Case Report

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Abstract

Neuropsychiatric manifestations are a well-known complication of primary hyperparathyroidism (PHPT) yet are often overlooked in patients with mild hypercalcemia [1]. Parathyroidectomy solely for the treatment of neuropsychiatric symptoms or signs of PHPT remains controversial [2]. We, herein, describe the case of a 66-year-old previously healthy woman with several months of severe depressive symptoms, including anhedonia, catatonia, hallucinations, and poor oral intake who was diagnosed with mild PHPT. After an extensive negative extensive workup for other causes of her neuropsychiatric symptoms, she underwent parathyroidectomy with a dramatic improvement in her symptoms shortly after surgery.

Introduction

Hypercalcemia is defined along a spectrum with mild hypercalcemia defined as a total serum calcium is between 10.5-12.5 mg/dL, and severe hypercalcemia can be acutely life threatening [3]. Generally, symptom severity can also be directly associated to the serum calcium as well.

Hypercalcemia secondary to HPTH is already well known in medical education and the existing literature. Neurocognitive manifestations of hypercalcemia are also already well-known complications: subjective symptoms include a loss of energy, depressed mood, neurasthenia, disorientation, memory problems, paranoia, and hallucinations [4].

Management of primary hyperparathyroidism centers around symptom necessity. The consensus gold standard for absolute treatment favors parathyroidectomy. However, no clear guidelines are set up for indication for early surgical, surveillance, or medical therapy in the setting of asymptomatic or minimally symptomatic patients. Moreover, there is less clarity regarding management patients with mildly elevated serum calcium because patients are typically asymptomatic [5]. Whereas, symptoms associated with severe hypercalcemia develop rapidly over days to weeks (Table 1).

Clinical guidelines for treatment of primary hyperparathyroidism were first published in 2002 calling for early parathyroidectomy or medical management for asymptomatic and minimally symptomatic patients. The management characterized neurocognitive symptoms as essential for diagnosis and treatment of PHPT. However, the recommendations are unclear

Table 1: Symptoms associated with degree of hypercalcemia.

Degree of Hypercalcemia	Serum Calcium (mg/dL)	Symptoms
Mild Hypercalcemia	10-12	**Constitutional symptoms:** Fatigue, constipation, nausea, vomiting, dehydration. **Neuropsychiatric symptom:** Depression, anxiety, insomnia, personality changes.
Moderate Hypercalcemia	12-14	
Severe Hypercalcemia	> 14	Confusion, somnolence, psychosis, delirium and coma.

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when considering cognitive and psychological symptoms as a criteria for parathyroidectomy [4].

Despite lack of clear guidelines, the existing literature describes a parathyroidectomy as the only definitive treatment of PHPT regardless of symptom severity. Although observation and pharmacological therapy are less invasive than surgery, observation and pharmacological therapy is less effective and less cost-effective than surgical intervention (ie-parathyroidectomy) [2]. Medical therapy also increases the risk of inducing chronic hypercalcemia which has its own potentially deleterious effect: Confusion, psychosis, coma, and overall decreased quality of life. However, some arguments for pharmacological treatment with centrally acting calcium channel blockers, gabapentin, and lamotrigine have been made [6].

The American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism strongly recommends parathyroidectomy as the preferred treatment for all cases with symptomatic PHPT or serum calcium greater than 1 mg/dL above the normal range regardless of the presence or absence of objective symptoms [2].

Case Presentation

A 66-year-old previously healthy woman with a remote history of GAD and MDD presented to the ED for progressive weakness, delirium, and slow but coherent speech. Of note, the patient was in her usual state of health until 6 months prior to admission when she started to experience muscle aches, generalized weakness, anxiety, constipation, muscle spasms, dysphagia/globus sensation, and depressive symptoms with suicidal ideation requiring an inpatient psychiatric admission. Given his constellation of symptoms and no obvious answer, this patient was ultimately admitted to the hospital for further workup.

On the day of admission, the patient was noted to be extremely slow responding to questions with long pauses between questions answered. Through a careful history and obtaining collateral from her family members, her initial history was impressive for a recent inpatient behavioral health admission for a suicide attempt after the patient's family confirmed that her mood and activity level drastically declined and had impressively worsened in only 6 months.

Approximately 12 hours after the care team admitted her to the inpatient service, the patient exhibited a severe change in her baseline mental status that included not following commands, not responding to questioning, unable to keep her eyes open, and appearing generally weak without further localizing symptoms. At this point, differential diagnoses included acute hyperactive delirium, acute psychiatric decompensation of her existing psychiatric illness, and metabolic encephalopathy of unclear etiology, the care team ultimately decided to pursue a complete infectious, metabolic, and paraneoplastic encephalitis workup requiring a CSF sample through lumbar puncture. Acute stroke had been ruled out at admission.

Her admission lab results were significant for a serum calcium was 10.6 (normal: 8.6-10.2 mg/dL) with an ionized calcium of 5.6 (normal: 4.8-5.2 mg/dL). Serum PTH level was 84.9 (normal: 15-65 pg/mL). A confident diagnosis of hyperparathyroidism induced hypercalcemia was not made until hospital day 10 after further medical workup yielded unremarkable results. The patient was evaluated for a parathyroidectomy. CT neck and soft tissues revealed localized disease of the right neck: A 16 mm parathyroid adenoma.

Patient completed a parathyroidectomy on Hospital Day 12 with immediate improvement in depressive symptoms and anhedonia. On hospital day 14, the patient was finally discharged home in high spirits.

Approximately 2 months after discharge, the patient admitted to a 10-pound weight gain with improved appetite to her PCP after discharging with a weight of 122 pounds and height of 68 inches with a calculated BMI of 18.5 after an approximate 30-pound weight loss over 6 months prior to her admission.

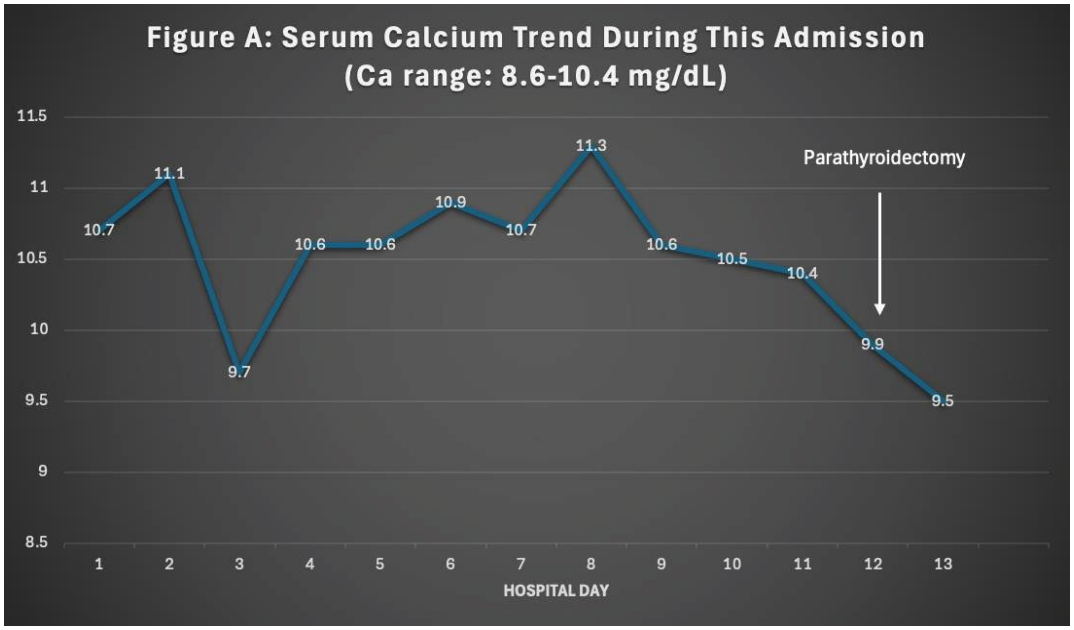
In summary, this patient's mental status deteriorated despite lack of a severe hypercalcemia. After extensive medical workup and discussion with the patient and the family, the patient underwent a parathyroidectomy with a dramatic improvement in her neuropsychiatric symptoms almost immediately following surgery. At 3 months follow-up, she continues to do well returning to her baseline mental status and functional ability (Figure 1).

Discussion

Primary hyperparathyroidism is a common condition characterized by over secretion of parathyroid hormone in patients with otherwise normal renal function. As is already known in the existing literature, hyperparathyroidism most often remains asymptomatic for years. However the sequelae of PHPT spans a spectrum of symptoms including fatigue, abdominal pain, hypertension, and mood disturbances. This case study specifically examined the neuropsychiatric disturbances associated with hyperparathyroidism induced hypercalcemia. More specifically, mild hypercalcemia leading to profound depression, personality changes, and anxiety.

It is already well-known that severe hypercalcemia can result in psychosis and coma. However, there may be insufficient evidence regarding the impact of mild hypercalcemia on overall quality of life. Advanced PHPT is already known to increase overall morbidity and mortality [4].

Neuropsychiatric sequelae of PHPT are also not well



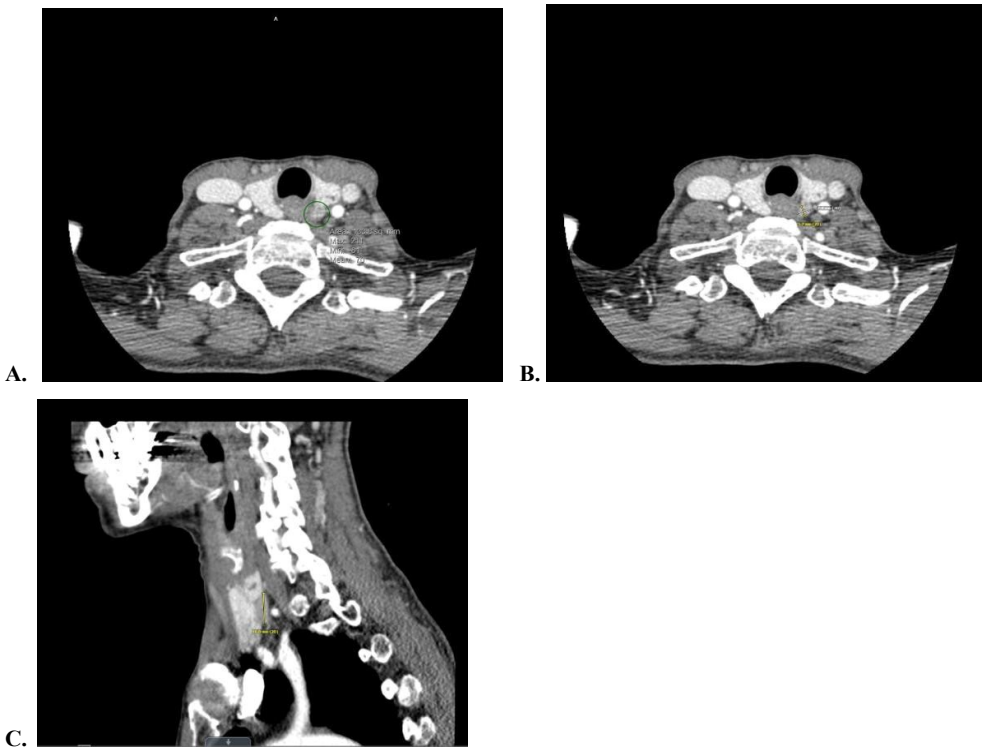


Figure 1: (A, B & C) CT images of the left sided 16 mm parathyroid adenoma.

described or understood in the medical literature - some studies suggest up to 25% of patients with PHPT have psychiatric symptoms. Most commonly these include: Fatigue, memory impairment, concentration difficulties, sadness, anxiety, and insomnia. Depressive states (75%) typically more common than delirium and psychosis (20-30%). Moreover, neuropsychiatric complaints are not an indication for parathyroidectomy despite RCTs demonstrating improvement in neuropsychiatric complaints weeks to months after surgery. However, some arguments for pharmacological centrally acting calcium channel blockers, gabapentin and lamotrigine have been made [6].

This case intends to educate readers about early management with parathyroidectomy may be necessary in patients with hypercalcemic neuropsychiatric disturbances. Moreover, this case illustrates the potential for neuropsychiatric disturbances stemming from PHPT associated with only mild hypercalcemia resolving after a parathyroidectomy [7-11]. Her dramatic response to parathyroidectomy adds to the increasing body of literature supporting surgical treatment in such cases when other causes of neuropsychiatric symptoms have been confidently ruled out.

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