

Acute psychosis secondary to suspected hyperparathyroidism: A case report and literature review

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How to cite: Park S, Hieber R. Acute psychosis secondary to suspected hyperparathyroidism: A case report and literature review. *Ment Health Clin* [Internet]. 2016;6(6):304-7. DOI: 10.9740/mhc.2016.11.304.

Abstract

Introduction: Hyperparathyroidism begins as a benign disease that is often left undetected unless the patient presents with severe symptoms. Often, the first sign of hyperparathyroidism is elevation in serum calcium.

Case Description: A 38-year-old man presented with new onset acute psychosis. Laboratory testing revealed co-occurring untreated hyperparathyroidism.

Discussion: A literature search was performed using PubMed to identify articles published in English with the following key terms: “hyperparathyroidism,” “psychosis,” and “hypercalcemia.” A review of findings follows the case report. Despite a thorough literature review, any pathophysiological explanation for psychiatric manifestations of hyperparathyroidism remains hypothetical.

Keywords: psychosis, hyperparathyroidism, hypercalcemia

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Introduction

Hyperparathyroidism begins as a benign disease and is often undetected until the patient presents with severe symptoms. Parathyroid hormone is released by chief cells of the parathyroid glands in response to hypocalcemia. This hormone plays an important role in calcium homeostasis by increasing bone resorption rate and intestinal calcium absorption, and decreasing urinary calcium excretion.¹ The etiology of primary hyperparathyroidism is mostly idiopathic; whereas, secondary hyperparathyroidism is caused by decreased intake of calcium or an increase in calcium excretion. Most cases of hyperparathyroidism are detected because of the elevation of serum calcium level with little symptomatology.² See Table 1 for description of possible symptoms.

Chronic elevation in serum calcium level may lead to decreases in bone mineral density, nephrolithiasis, gastrointestinal effects, changes in mental status, and rarely symptoms of psychosis.² One study³ reviewing 441 patients with primary hyperparathyroidism found only 4 had psychosis (including hallucinations and paranoia), although 23% (102 of 441) of patients had psychiatric symptoms, most commonly depressive/anxious symptomatology. There can be several underlying causes of psychosis. However, certain medical conditions including hepatic encephalopathy, endocrine disorders, and neurologic disorders may also lead to the development of psychosis in patients. It is important to identify these underlying causes, as treatment plans may differ from those of patients with mental illnesses, and some symptoms may even resolve once the underlying medical condition is corrected.

The mechanism behind psychosis in hyperparathyroidism is unknown. It is thought that the changes in serum calcium level slow down nerve function and neurotransmission rate, inducing psychosis.⁴ Brown et al⁵ postulated

TABLE 1: Symptoms of hyperparathyroidism

Physical Symptoms	Psychiatric Symptoms
Commonly no signs	Disorientation
Fragile bones/osteoporosis	Delirium
Kidney stones	Confusion
Excessive urination	Paranoia
Abdominal pain	Hallucinations
Tiring easily/weakness	Forgetfulness
Bone/joint pain	Alteration in hunger/sexuality

that hypercalcemia causes higher concentrations of calcium in the extraneuronal environment, which triggers calcium influx into the neuron. This causes depolarization and release of the neurotransmitters into the synaptic cleft, which is manifested by various psychiatric symptoms including psychosis. Studies have reported that psychotic symptoms tend to be more closely associated with serum calcium levels than parathyroid hormone levels.⁵ Petersen⁶ performed a psychiatric evaluation of patients with hyperparathyroidism and hypercalcemia resulting from Boeck sarcoid or vitamin D intoxication. The authors found that personality changes and affective disturbances develop over years to several decades, whereas psychosis can have an acute onset. Patients who exhibited acute psychosis had a serum calcium level near 16 mg/100 mL, and all patients were able to regain their previous mental status after undergoing parathyroidectomy. The authors emphasize that psychosocial disturbances are closely related to hypercalcemia; however, hypercalcemia may not be the only contributing factor causing acute psychosis in patients with hyperparathyroidism. Because these studies are small, it is still unclear and controversial whether the degrees of psychotic symptoms are directly associated with hypercalcemia.

Patients with psychiatric manifestation of hypercalcemia may experience personality changes such as alterations in mood and increases in hunger and sexuality.² Other symptoms associated with hypercalcemia are lethargy and impaired memory and concentration.² With increased concentration of serum calcium, acute psychosis can occur, which may be manifested by disorientation, delirium, confusion, paranoia, and hallucinations. This article presents a case of psychotic symptoms suspected to have resulted from untreated hyperparathyroidism.

Case Report

The patient is a 38-year-old male veteran who presented to the emergency department (ED) complaining of chest tightness and shortness of breath over the last 3 to 4 days. The patient had a past medical history of vitamin D

deficiency and osteoarthritis. He did not have any history of cardiovascular disease, and his electrocardiogram was normal. On admission, the patient appeared to be very anxious and reported having an anxiety attack the day before his ED visit. This attack was accompanied by tinnitus, profuse sweating, and syncope. The patient also reported decreased appetite and 5 lbs unintentional weight loss. Upon examination, his vitals were unremarkable, except for slightly elevated blood pressure (141/78 mm Hg). The patient's current medications were cholecalciferol 2000 IU daily for vitamin D deficiency and naproxen 500 mg twice daily as needed for osteoarthritic pain. Because of his acute anxiety, the patient was admitted to the mental health unit for stabilization. Upon admission, the patient was treated for acute psychosis with haloperidol 5 mg every 6 hours as needed for agitation and lorazepam 1 mg every 6 hours as needed for anxiety. Trazodone, 50 mg at bedtime, was used for insomnia.

A mental health care provider first saw the patient in 2011 for depressed mood and low energy. Because of low symptom severity, no medications were initiated at that time. In 2015, the patient was started on sertraline 25 mg daily for depressive symptoms triggered by loss of his mother. However, sertraline was discontinued after 2 doses because of intolerable severe diarrhea, and no other medication was prescribed. Since this time, and for nearly 4 months prior to his seeking treatment, the patient reported intense fear and paranoia regarding biker gangs who he believed were following him. He reported several incidences of threats, which his wife denied hearing or seeing. The veracity of such reports was questionable. Both his wife and the patient denied previous psychotic symptoms. He presented with both positive and negative symptoms, which were manifested by delusions and social withdrawal/depression. The patient also lost his job, which indicated some extent of social dysfunction. However, the patient maintained healthy social relationships and stable relationships with his wife and 2 children. Considering that the patient was 38 years old, a diagnosis of schizophrenia was unlikely as most patients with schizophrenia are diagnosed in late adolescence to early 20s.⁷ Other causes of psychosis, such as late-onset schizophrenia and a depressive disorder with psychotic features, cannot be completely ruled out based on the patient's presentation. However, because of the co-occurrence of acute psychosis and significantly elevated parathyroid hormone, the patient's current symptoms were suspected to be related to his hypercalcemia secondary to hyperparathyroidism.

Laboratory tests indicated high levels of serum calcium and parathyroid hormone, which increased throughout the patient's admission (see Table 2 for description of laboratory parameters). Serum albumin level was obtained, and the results were normal. Based on the

TABLE 2: Laboratory measurements¹³

Laboratory Parameter (Normal Value Range)	Time of Blood Draw	Result
Calcium (9–10.5 mg/dL)	Hospital day 1	11 mg/dL
	Hospital day 2	11.8 mg/dL
Parathyroid hormone (10–65 pg/mL)	3 days prior to admission	106 pg/mL
	Hospital day 2	141.7 pg/mL
1,25 (OH) ₂ D (15–80 ng/mL)	Hospital day 2	9 ng/mL

patient’s mental health history and current symptoms, he was diagnosed with major depressive disorder with psychotic features. Risperidone 1 mg and clonazepam 0.5 mg were ordered to treat current acute psychotic and anxious symptoms. The patient’s 25-hydroxy vitamin D level was noted to be low at 9 ng/mL despite being treated with a maintenance dose of cholecalciferol. With current psychotropic medications, his mood stabilized over 5 days during his hospitalization, and he was discharged.

Upon follow-up, an outpatient psychiatrist saw the patient 10 days after discharge, and his primary care physician was notified regarding the abnormal laboratory results. Despite prompting for further testing and treatment, the patient refused to leave his home because of his fear of gangs, indicating continued symptoms of paranoia. The patient is being followed via telehealth and will not come in to the hospital or clinic. As a result, he is unable at this time to undergo further testing or have other interventions to treat his possible hyperparathyroidism. He continues to be prescribed risperidone at this time.

Literature Review and Discussion

A literature search was performed using PubMed to identify articles published in English with the following key terms: “hyperparathyroidism,” “psychosis,” and “hypercalcemia.” The search was not limited to year of publication to ensure comprehensive results were obtained. All identified articles were included in the literature review.

There are several case reports of acute psychiatric symptoms associated with hypercalcemia and hyperparathyroidism. Watson and Marx⁸ published a case of a 63-year-old man with a new onset of psychosis, which was completely reversed with a parathyroidectomy. The patient presented to the hospital with homicidal and suicidal behavior and was found to have elevated serum calcium and parathyroid hormone levels (10.8 mg/dL and 127 pg/mL, respectively). His symptoms were significantly reduced with normalization of his serum calcium level with intravenous fluids and diuretics. He eventually received a parathyroidectomy owing to recurrent episodes

of psychosis and hypercalcemia. After the surgery, the patient remained asymptomatic and returned to his normal functioning state.

Baber and Alemzadeh⁹ describe a case of a 17-year-old adolescent boy with acute psychosis and hypercalcemia. The patient presented with difficulty sleeping, hallucinations, and delusional ideations. Upon examination, markedly elevated serum calcium (16.5 mg/dL) and parathyroid hormone (315 pg/mL) levels were noted. The patient was treated with intravenous fluids and calcitonin but was unable to achieve a normal serum calcium level. Eventually, he received a parathyroidectomy. The patient’s psychiatric symptoms gradually resolved over 2 to 3 months, and he received psychiatric care for 6 months after the surgery.

Papa and colleagues¹⁰ report about a 72-year-old man with acute psychosis, particularly delusional persecutory ideations with severe hypercalcemia. Initially, noninvasive methods to decrease the serum calcium concentrations were attempted, including saline infusion, furosemide, and calcitonin. After day 5, with little improvement, a parathyroidectomy was performed with resolution of hypercalcemia and neuropsychiatric symptoms. The authors suspected a direct correlation with serum calcium levels and psychotic symptomatology, though this is not corroborated by other publications.

Alarcon and Franceschini¹¹ published a case of a 53-year-old woman with acute psychosis and hypercalcemia. With a delay in diagnosis of hyperparathyroidism, she was treated unsuccessfully with antipsychotics for 3 weeks, at which time a proper diagnosis was made, and a parathyroidectomy was performed. It is notable that her paranoid delusions disappeared by the third postoperative day with no antipsychotic treatment, although auditory hallucinations continued until her discharge. Upon follow-up 2 months post discharge, she no longer reported hallucinations.

The 4 case reports above clearly show reversibility of psychotic symptoms with a parathyroidectomy and corrected serum calcium levels. These cases have many features in common: acute psychosis, no prior history of mental illness, and elevated serum calcium and parathy-

roid hormone levels. The differences were in age and severity of hypercalcemia. The age range was from 17 to 72 years, and the youngest patient had a significantly higher serum calcium level than those who were older. As mentioned earlier, it is still unclear whether the degree of psychotic symptoms is directly proportional to the severity of hypercalcemia. It is also possible that elderly patients have a lower tolerance to changes in serum calcium levels and thus present with more severe symptoms at smaller alterations in serum calcium levels.

The 38-year-old male veteran presented in this case report had significant elevations in serum calcium and parathyroid hormone levels. The patient was an otherwise healthy young man with a past medical history of depression, vitamin D deficiency, and osteoarthritis. He was diagnosed with major depressive disorder with psychotic features and his symptoms were well managed with an antipsychotic and a benzodiazepine. Owing to the co-occurrence of acute onset of psychosis and a sudden increase in serum calcium level, hypercalcemia may be a potential underlying cause of his psychosis. Mental changes associated with hyperparathyroidism may take years to develop.³ The patient's low 25-hydroxy vitamin D level could be the body's compensatory mechanism for chronic hypercalcemia secondary to hyperparathyroidism. Further diagnostic testing such as bone mineral density, bone turnover markers, and 24-hour urine calcium level may be helpful in this patient to determine the etiology of his current disease state. Unfortunately, he did not follow up as an outpatient, highlighting the difficulty in treating a patient with paranoid symptomatology.

Conclusion

This literature review indicated a paucity of data regarding the relationship between psychotic symptoms and hyperparathyroidism. However, in all the cases found, there was a clear reversal of symptoms after parathyroidectomy. Any pathophysiological explanation for psychiatric manifestations of hyperparathyroidism remains hypothetical. There are many disease states and conditions that can cause psychosis in patients.^{1,3} Ideally, each patient should be thoroughly evaluated to determine possible treatable underlying causes instead of solely treating the symptoms.¹² This case illustrates the need for a deeper

understanding between the relationship of psychosis and hyperparathyroidism.

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