



Depressive Disorder in Primary Hyperparathyroidism and Effects of Surgery in Elderly Patients: Case Series

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Case Report

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Abstract

Background: Patients with primary hyperparathyroidism (PHPT) often present nonspecific symptoms such as major depressive disorder and psychosis. Calcium plays a role in the pathogenesis of psychiatric symptoms by determining changes in monoamine metabolism in the central nervous system, thereby modifying neurotransmission and resulting in mood and cognitive alterations.

Case series: This report presents a case series of 3 patients; 70-year-old, 78 year-old and 94 year-old women with PHPT and severe depression symptoms and its response to parathyroidectomy. The patients were a poor historian. Results of preoperative laboratory tests showed an increased serum calcium level (11.15mg/dL, 10.9 mg/dL and 11.4 mg/dL- reference range 8.4-10.2 mg/dL). A repeat serum calcium test confirmed hypercalcemia with concurrent elevated intact parathyroid hormone level. Two patients were undergone at parathyroidectomy. A 94 year-old patient refuse surgical approach and was efficacy treated with a single dose of zoledronic acid. Therefore, the patients underwent parathyroidectomy two months after procedure had a clinical improvement on depressive symptoms. There was any recurrent laryngeal nerve injury or recurrent PHTP.

Conclusion: The presence of a long-standing depressive disorder unresponsive to medical therapy may suggest an organic disorder such as chronic hypercalcemia which may be secondary to PHPT. Surgical intervention in these selected cases can assist medical therapy in the improvement of depressive symptoms.

Keywords: Primary Hyperparathyroidism; Depression; Para Thyroidectomy; Surgical Outcomes

Abbreviations: PHPT: Primary Hyperparathyroidism; PTH: Parathyroid Hormone.

Introduction

Primary hyperparathyroidism (PHPT) is a common endocrinological disorder characterized by chronic

elevation of parathyroid hormone (PTH) and serum calcium concentrations. The incidence of PHPT is approximately 21 cases per 100,000 person/year, with the disorder typically caused by a solitary parathyroid adenoma [1]. PHPT is a disease with multisystemic and heterogeneous manifestations. The usual presentation is observed in less than 15% of PHPT cases [2], and neuropsychiatric symptoms



such as psychosis and, less commonly, depressive symptoms may occur [3-6]. Parathyroidectomy is the treatment of choice for patients with physically symptomatic PHPT. However, it remains unclear whether parathyroidectomy is indicated solely for its psychiatric manifestations [7].

The aim of this case series was to assess the role of surgery in management of primary hyperparathyroidism associated with psychiatric disorders in elderly. Written informed consent was obtained from all patients.

Case 1

A 70-year-old woman with depression was admitted to the Internal Medicine Unit due to worsening depression, characterized by catatonia, anorexia, mutism, dysphagia, constipation, weight loss, and lack of self-care. The patient was diagnosed with depressive disorder and was treated with antidepressants, but the response was unsatisfactory due to her refusal to take the therapy. Her medical history includes type 2 diabetes mellitus and sarcoidosis. The patient had several previous admissions to the emergency department for inappetence and dysphagia. Laboratory tests revealed increased serum calcium level (11.15mg/dL). A repeat serum calcium test confirmed mild hypercalcemia, which, in conjunction with the patient's elevated intact parathyroid hormone level of 101 pg/mL, strongly suggested PHPT. Subsequently, the patient underwent a CT-PET scan, which confirmed the presence of a hyperfunctioning right superior parathyroid. The patient then underwent parathyroidectomy, and histological examination confirmed the presence of an adenoma. Two months after the operation, she began to eat regularly and showed good compliance with psychiatric therapy.

Case 2

A 78-year-old female presented with depression was admitted to the Psychiatric Department due to worsening depression, anxiety and she was treated with antidepressants. She was diagnosed to have a depressive disorder and was treated with antidepressants. As a medical history she was a cured case of non-Hodgkin's lymphoma. Laboratory tests revealed an increased serum calcium level (11.9 mg/dL). A repeat serum calcium test confirmed mild hypercalcemia, which, in conjunction with the patient's elevated intact parathyroid hormone level of 135 pg/mL (reference range 16-87 pg/mL), strongly suggested PHPT. A small left sided neck lump was detected by CT head-neck scan. Subsequently, the patient underwent a non-invasive study with ^{99m}Tc-sestamibi scintigraphy, which confirmed the presence of a hyperfunctioning left inferior parathyroid. The patient then underwent parathyroidectomy, and histological examination confirmed the presence of an adenoma. A month after the

operation, she showed to resolve either the disturbance by calcium level and psychiatric symptoms.

Case 3

In the last case our patient an elderly lady (94 year-old) was admitted to the Internal Medicine Unit with catatonia, haziness and weight loss due to appetite reduction. A collateral history from personal documentation revealed hypertension, no alcohol consumption and no pertinent family history. Investigations revealed raised level of serum calcium (16.1 mg/dL), raised Parathyroid Hormone (PTH) (402 pg/ml). From this result PTH was suspected and hypercalcemia was treated with intravenous isotonic saline and furosemide, with low response. Chest X-ray and CT head-neck were normal. A sestamibi scintigraphy scan was conclusive of a hyperfunctioning left inferior parathyroid. After patient's refusal surgical treatment due to the persistent hypercalcemia, on decided to treat her with intravenous infusion of zoledronic acid (4 mg). After a single dose of zoledronic acid had transient effects, serum calcium levels progressively decreased. At 1 month of follow-up. Currently, at 40 days after treatment calcium serum level was growing slowly.

Discussion

Primary hyperparathyroidism (PHPT) is a complex endocrinopathy involving parathyroid glands which produces high amounts of parathyroid hormone and consequently high calcium serum level. Classic manifestations of PHPT include renal and skeletal disorders that are associated with significant depletion in bone mineral density. Elderly patients are particularly susceptible to bone-related diseases and the risk of fractures. In cases of "fragile patient" with PHPT, non-specific complaints are reported; among these, depression is a common psychiatric manifestation, found in about 33% of PHPT sufferers. Although the pathogenesis of psychiatric disorders in PHPT is unclear, it appears that calcium plays a central role in the onset of disorders by interacting with monoamine metabolism, thereby modifying neurotransmission and resulting in mood and cognitive alterations [8]. We concur with several studies indicating that patients with PHPT who undergo parathyroid surgery could experience improvements in mood and neuropsychological functioning [2,3,5,9-13]. When serum parathyroid hormone levels are lowered, a decrease in severe depressive symptoms is noted [3]. A systematic review published in 2023 by Desai et al. explored the results of 1227 patients from 11 studies; 833 patients suffered from hyperparathyroidism, and the remaining were from control groups. Of the 1227 patients, 499 were reviewed for the improvement of neuropsychiatric symptoms after parathyroidectomy and 334 were reviewed for the effects of increased PTH on their neurocognitive

behaviours. They concluded that there is a significant correlation in patients with hyperparathyroidism between high serum calcium level, high serum parathyroid hormone level, high serum alkaline phosphatase level, and depressive symptoms [3]. The presence of a long-standing depressive disorder unresponsive to medical therapy should suggest an organic disorder such as chronic hypercalcemia, which may be secondary to PHPT. Surgical intervention in these selected cases can assist medical therapy in the improvement of depressive symptoms. This is in accordance with Liu JY, et al. [14] who in 2020 published a comparative study of 244 patients who underwent parathyroidectomy and 161 who underwent thyroidectomy. They observed improvement in neuropsychiatric symptoms after parathyroidectomy (6.2 [5.0-7]).

The diverse neuropsychiatric manifestations observed in patients with Primary Hyperparathyroidism (PHPT) could potentially lead to a high rate of misdiagnosis. Increasing awareness of this correlation could facilitate earlier diagnosis of PHPT. There is a need for more randomized controlled trials to evaluate the effectiveness of treatments for depression in patients with hyperparathyroidism.

Our case series on elderly patients above show reversibility of psychiatric symptoms with correction serum calcium levels by parathyroidectomy and transient effect on noninvasive treatment. As already described in some reports, it is still unclear whether the degree of psychotic symptoms is directly proportional to the severity of hypercalcaemia. It is also possible that elderly patients have a lower tolerance to changes in serum calcium levels and therefore present more severe symptoms in the presence of small changes in serum calcium levels. The prevalence of primary hyperparathyroidism (PHPT) increases with age. They are more likely to present with vague neuropsychiatric complaints, which can be mistakenly attributed to their age rather than PHPT. The only cure for PHPT is surgery, but referral for parathyroidectomy in patients over the age of 70 is often limited due to comorbidities and perceived surgical risks. However, the cure rate in the elderly, as measured by surgical success, has been shown to be equivalent to that of younger patients, with minimal increased risk of postoperative complications. As the life expectancy of the population increases, elderly patients with PHPT are at an increased risk of developing sequelae from this disease. In conclusion, we described three cases of PHPT in elderly. A consideration by our case series, as described in similar reports, patient age should not be the reason for abstaining from a surgical referral in cases of PHPT. Surgery remains an effective treatment to prevent PHPT-associated complications and improve the quality of life for symptomatic patients.

In addition, when dealing with elderly patients presenting with recent complaints of depressive or psychiatric disorder, hypercalcemia must be considered among the causes of the symptoms presented.

Appropriately designed future studies are needed to confirm these findings and definitively compare outcomes to conservative approaches

Authors' Contributions

GB-AS wrote the manuscript. AS supervised the project. AM, DP, ST, and FB critically revised the manuscript. LZ external endocrinological revision. All authors read and approved the final manuscript.

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