

## Case Report

# Primary Hyperparathyroidism Presenting as Major Depression; The Surgical Treatment of a Psychiatric Disorder; A Case Report and Review of the Literature

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## Abstract

Primary hyperparathyroidism is common disorder that is nowadays diagnosed in 0.7% of the general population with increased incidence in postmenopausal women. The patients suffering from primary hyperparathyroidism can either be completely asymptomatic or present clinical manifestations from multiple systems. The most commonly affected organs are the bones and the kidneys, while neuropsychiatric symptoms come third in rate of incidence. Symptoms from the gastrointestinal system, the cardiovascular system, the eyes or the skin are even less common. We present a rare case of a 50-year-old woman who was initially diagnosed with major depression, but laboratory workup and imaging studies revealed primary hyperparathyroidism. As a result, the patient was subjected to parathyroidectomy leading to complete remission of her psychiatric symptoms and discontinuation of her antidepressant drugs.

**Keywords:** Hyperparathyroidism; Depression; Organic psychosyndrome; Hypercalcemia

## Case Presentation

A 50-year-old Caucasian female patient presented herself at our department with an established diagnosis of primary hyperparathyroidism. She was originally diagnosed with major depression one year ago with symptoms of sadness, anhedonia, loss of appetite, insomnia and fatigue for which she was introduced to systemic anti-depressant medication. Specifically, she was administered p.os. tb olanzapine 5 mg 1x1, p.os. tb escitalopram 20 mg 1x1, p.os. tb mirtazapine 30 mg 1.5x1 and p.os. tb alprazolam 5 mg occasionally. The patient did not present symptoms from any other organs that are usually affected at a higher incidence in cases of primary hyperparathyroidism, such as the kidneys and the bones. Her past history was unremarkable. However, during a routine laboratory evaluation, the patient was found to suffer from mild hypercalcemia with a serum calcium level of 10.5 mg/dl (normal range 8.2-10.2 mg/dl). Thus, the patient was subjected to PTH level testing, which revealed a value higher than 15 pmol/L (normal range 1.06-6.04 pmol/L). As a result, the diagnosis of primary hyperparathyroidism was established. The patient was afterwards subjected to imaging testing with the ultrasound cervix scan revealing an enlarged (diameter: 28.6 mm) and heterogeneously hypoechoic, well circumscribed mass attached to the left superior parathyroid gland (Figure 1) and the Tc-99m sestamibi scan displaying increased uptake in the superior left parathyroid gland, findings compatible with parathyroid adenoma. Thus, the patient was subjected to upper left parathyroidectomy with the intra-operative biopsy revealing an abnormal parathyroid gland and the quick PTH test showing a radical decrease of the PTH serum level (6 pmol/L). The patient had an uneventful recovery and was discharged on the second post-operative day. The final histopathological examination validated the diagnosis of parathyroid adenoma. The patient's follow-up three months later demonstrated a remarkable reduction to half

of the therapeutic dose of antidepressants required by the patient. Six months after the operation, the patient was advised to discontinue the medication, due to lack of symptoms. The patient, one year later, has not experienced any psychiatric symptom.

## Discussion and Conclusion

Primary hyperparathyroidism is a common endocrine disorder with an overall prevalence of 0.2-1% in the U.S. and usually affects patients over 65 years old and postmenopausal women (2.1-3.4%) [1]. The disease is normally characterized by hypercalcemia with elevated PTH levels and it is the major cause of hypercalcemia in the general population [1]. The most common cause of primary hyperparathyroidism is a solitary adenoma (80%) as in our case, 15% of the cases are caused by parathyroid gland hyperplasia, 3% are due to double adenoma and a very rare cause is parathyroid carcinoma [2].

When Fuller Albright first described primary hyperparathyroidism in the 1930s over two-thirds of the patients had renal involvement in the form of nephrolithiasis or nephrocalcinosis, while the typical skeletal abnormality, osteitis fibrosa cystica, was found in almost one-third of the patients [3]. Psychiatric, neurological, gastrointestinal and cardiovascular symptoms were also frequently encountered in these patients [3]. However, throughout the past decades a shift has happened in the presentation of primary hyperparathyroidism and nowadays more than 80% of the patients are diagnosed incidentally by discovering hypercalcemia in routine laboratory testing [4,5]. Symptomatic patients with renal involvement consist of 10-25% of the cases and bone disease is encountered in 10-20% among patients with primary hyperparathyroidism [6].

A review of the literature indicates that psychiatric symptoms



**Figure 1:** Image of the ultrasound scan showing the presence of a 28.6 mm mass behind the upper left lobe of the thyroid gland.

occurred in approximately 4.2% of 405 patients suffering from primary hyperparathyroidism [7]. These symptoms vary from sleep disturbance, loss of appetite, vague muscle aches and fatigue to major depression, psychosis and delirium [8]. However, the severity of the psychiatric symptoms does not always correlate with the increase in serum calcium [9], as in our case where the patient suffered from major depression with only a mild hypercalcemia. This phenomenon can be explained by the fact that PTH itself causes psychiatric symptoms since it affects the levels of monoamine metabolites acting as neurotransmitters in the cerebrospinal fluid [7]. According to a study conducted by Wilhelm et al on 360 patients suffering from primary hyperparathyroidism from 1994 to 2002, 10% of them met the Diagnostic and Statistical Manual of Mental Disorders IV-Text Revision (DSM IV-TR) criteria for major depression, with 37% of them requiring antidepressant medication [10].

The role of parathyroidectomy in treating the patients with depression caused by primary hyperparathyroidism has been well advocated in the literature. Wilhelm et al reported that 90% of the patients subjected to parathyroidectomy stated a significant reduction of depressing symptoms postoperatively leading to an improvement of their quality of life, while 27% discontinued their preoperative antidepressant medication and another 27% reduced their dose. In another major cohort study performed by Espiritu et al, out of the 169 patients with primary hyperparathyroidism who participated, 31.4% of them were diagnosed with major depression using the PHQ-9 test and 19.5% of them were on antidepressant medication [11]. In this study, 88 participants were subjected to parathyroidectomy resulting in a decrease of patients with clinically significant PHQ-9 score from 43.2% to 7% and 7.6% at 1 month and 1 year, respectively, postoperatively [11]. Among the 81 patients who were not subjected to surgery no change was reported in those with clinically significant PHQ-9 scores [11].

Depression is common among patients in primary care setting, making up for 10% to 14% of all reasons for a visit [12]. Our case report

emphasizes the fact that depression as a primary psychiatric disorder must be a diagnosis of exclusion. Serum calcium level must always be evaluated in cases of psychiatric disorders and if the diagnosis of primary hyperparathyroidism is established, parathyroidectomy is the treatment of choice since it leads to a quick resolution of the symptoms.

The fact that surgical treatment still remains the only successful treatment of primary hyperparathyroidism has led to a rapid development in minimal access parathyroidectomy and minimally invasive parathyroidectomy giving rise to groundbreaking and extremely promising techniques, such as unilateral neck exploration, focused parathyroidectomy, endoscopic and minimally invasive endoscopic parathyroidectomy, minimally invasive videoscopically assisted parathyroidectomy and minimally invasive radio-guided parathyroidectomy [13].

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