Case Report

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2022.46.007397

Primary Hyperparathyroidism and Psychosis: A Case Report and Review of the Literature

Serif Damadoglou Ekrem[1], Arvaniti Aikaterini[1,2]*, Tzikos Anthimos[1,2], Tsirmpinis Pantelis[1], Tsiouprou Ioanna[3] and Samakouri Maria[1,2]

[1]*Department of Psychiatry, University General Hospital of Alexandroupolis, Greece*

[2]*Department of Psychiatry, Medical School, Democritus University of Thrace, Greece*

[3]*Medical School, Aristotle University of Thessaloniki, Greece*

***Corresponding author:** Aikaterini Arvaniti, Department of Psychiatry, Medical School, Democritus University of Thrace, Alexandroupolis, Greece

ARTICLE INFO

Received: October 12, 2022

Published: October 20, 2022

Citation: Serif Damadoglou Ekrem, Arvaniti Aikaterini, Tzikos Anthimos, Tsirmpinis Pantelis, Tsiouprou Ioanna and Samakouri Maria. Primary Hyperparathyroidism and Psychosis: A Case Report and Review of the Literature. Biomed J Sci & Tech Res 46(4)-2022. BJSTR. MS.ID.007397.

ABSTRACT

Primary hyperparathyroidism (PHPT) is one of the most common endocrine disorders and is characterized by hypercalcemia and elevated or marginally normal levels of parathyroid hormone (PTH). Most patients are asymptomatic at the time of diagnosis. Nevertheless, an association between PHPT and neuropsychiatric signs and symptoms is well known. This article presents a unique case of a senior woman, who presented at the emergency department with psychotic symptoms that led to a diagnosis of PHPT resulting from a parathyroid adenoma. Unlike the initial treatment with antipsychotics, which was unsuccessful, surgical excision of the adenoma led to a total and long-term remission of the psychiatric symptoms. PHPT should be included in the differential diagnosis of elderly patients who suffer from neuropsychiatric symptoms, since an early diagnosis could be extremely beneficial to them.

Keywords: Primary Hyperparathyroidism; Psychosis; Psychiatric Manifestations; Parathyroid Adenoma

Introduction

It is widely known that primary hyperparathyroidism (PHPT) is one of the most common endocrine disorders. Its' prevalence is approximately 0.2% to 1.3% in iodine-sufficient parts of the world [1]. The incidence of PHPT increases with age and is higher in women and African Americans in comparison with men and other racial groups [2]. It is mainly diagnosed in postmenopausal women. This disorder results from excessive secretion of parathyroid hormone (PTH) from one or more of the parathyroid glands and is mainly characterized by hypercalcemia and elevated or marginally normal levels of PTH. Some patients are normocalcemic despite increased serum PTH and others are hypercalcemic whereas serum PTH levels are normal [3]. Although the etiology of primary hyperparathyroidism varies, a solitary parathyroid adenoma is responsible for 80% of all cases of PHPT [2]. The diagnosis is based on laboratory findings. Psychotic symptomatology is a rare manifestation of PHPT and hypercalcemia is included among the organic causes of psychosis [4]. The purpose of this article is to present a unique case of primary hyperparathyroidism in a 66-year-old woman who developed psychotic symptoms as initial signs of the disease and to review current literature.

Case Report

A 66-year-old woman, a retired farmer, presented to the emergency department with confusion and persecutory delusions. She was accompanied by her daughter, who reported that her mother presented a continuously worsening condition during the last six days. Her complains included fatigue, nervousness, insomnia, memory and concentration problems. She expressed occasionally a strong belief that she had COVID-19 despite the lack of laboratory findings of SARS-COV-2. The patient had been diagnosed with mixed anxiety and depressive disorder 10 years ago. As a result, the patient visited the emergency department of a district hospital daily over the past six days. Despite her frequent visits to the emergency department, general practitioners solely performed a daily thorough physical examination, which was normal and then discharged her with instructions for daily medication (escitalopram, sertraline). Because of her psychiatric history, they also advised her to consult her private psychiatrist in case of worsening. She has been on 20 mg escitalopram once a day for the last 5 years, which she has tolerated well so far. Her daughter reported that she had also been under regular psychiatric supervision by a private psychiatrist. Addition of 50 mg of sertraline once a day due to the worsening symptoms of depression during the preceding 3 weeks had no effect on the patient. There was no history of other medical conditions, medication, or hospital admissions. No family history of hypercalcemia or major medical or mental illnesses was reported. Upon arrival at the emergency department, she was confused and disoriented to time and place. She was sluggish, hostile, and reported that her daughter's husband was planning to kill her. She was convinced that he tried to murder her several times during the past days, but she managed to save herself. Physical examination was unremarkable. No signs of tics, stereotypic movements or cognitive disorders were noted.

The laboratory results showed white blood count of 12,350 cells/mm^3. Mild anemia was detected, and the total serum calcium was elevated with a value of 16 mg/dL (reference range: 8.1 – 10.5 mg/dL). Albumin was 4 g/dL (normal 3.5 – 5.5 g/dL) and phosphorous was 2.2 mg/dL (normal 2.5 – 4.5 mg/dL). Signs of extensive osteoporosis of the bony structures were discovered in a chest x-ray. Consequently, the patient was admitted to an inpatient psychiatric unit with a provisional diagnosis of acute psychosis. Further investigation revealed elevated serum alkaline phosphatase and parathyroid hormone levels, consistent with PHPT. Urinary calcium was increased in 24-hour collections. A diagnosis of vitamin D deficiency was also set. Glomerular Filtration Rate (GFR), electrolytes, thyroid hormone screening and vitamin A levels were normal, as were the urinary phosphorus, creatinine, and cyclic AMP. Afterwards, neck ultrasound along with Tc-99 sestamibi scintigraphy were used. An enlarged parathyroid gland appeared homogeneously solid and markedly more hypoechoic than the adjacent thyroid tissue. The sestamibi scan indicated an increased uptake at the level of the left thyroid lobe, where the ultrasound localized the parathyroid lesion. Therefore, parathyroidectomy was recommended by a group of surgeons. Unfortunately, the COVID -19 pandemic had a harmful impact on emergency surgery services. Additionally, she was several times admitted, due to medical conditions, in internal medicine departments and the surgery was repeatedly postponed. There was a critical delay in providing a surgical therapy. Because of the excessively high calcium levels, the patient was initially treated with saline infusion and intravenous bisphosphonates. She was also given oral risperidone at 0.5 mg b.i.d. to target her psychotic symptoms and tolerated a gradual increase to a total of 2 mg per day with no significant change in her mental status and the antidepressants were discontinued. While waiting for the surgery, the therapeutic effort focused on regulating and restoring calcium and parathyroid hormone levels.

Achieving the above along with the removal of initial psychiatric treatment led to a complete remission of psychotic symptoms. She was afterwards treated with mirtazapine due to symptoms of depression and anxiety with predominant insomnia which worsened due to prolonged waiting and complications of long-term hospitalization. A minimally invasive partial left parathyroidectomy was performed without complications three weeks later. A large parathyroid adenoma at the left lower pole of the thyroid was found and excised. Histologic analysis showed that it was a chief-cell adenoma with no features of malignancy. At her outpatient psychiatric appointment, the patient's daughter reported that she was "completely back to normal" and no unusual behavior was noted. The patient remained under psychiatric surveillance for six months after surgery and there was no remission of psychotic symptoms. Serum calcium levels remained within normal range on six-month routine follow-up.

Discussion

Psychosis may be the first manifestation of endocrine abnormalities such as hyperthyroidism, hypothyroidism, Cushing's syndrome and exceptionally primary hyperparathyroidism [4]. Currently only a few patients exhibit the classic clinical manifestations of PHPT (renal stones, decrease of bone mineral density, skeletal fragility and neuromuscular weakness) [5]. Neuromuscular, cardiovascular, cognitive and also psychiatric symptoms and signs may appear [5-7]. An association between hyperparathyroidism and the development of neuropsychiatric signs and symptoms was initially reported in 1942 by Eitinger, who found such symptoms in seven of fifty patients with hyperparathyroidism [8]. It was primarily believed that there were three types of psychiatric manifestations of hyperparathyroidism:

confusional psychosis, psychosis along with severe depression, violent behavior and paranoid delusions and a pseudoneurotic form consisting of fatigue, irritability, anxiety, anorexia and mood alteration [9]. Other symptoms such as apathy, sleep disturbances and anxiety were later added to the list [7]. This symptomatology is frequently reversible.

A study of the literature on this subject indicates that there is a wide range of the age of the patients who suffer from psychiatric symptoms (from 17 to 72 years) [10]. Serum calcium levels also vary. However, psychiatric symptomatology does not bear a direct relationship to the serum calcium level. However, studies show that symptoms that are related to hypercalcemia are associated with severity of parathyroid dysfunction, pre-existing comorbidities and polypharmacy [11]. Research suggests that elderly patients have a lower tolerance to changes in serum calcium levels [10]. The underlying pathophysiology of the development of psychiatric manifestations remains unclear [12,13]. It is believed that hyperparathyroidism is associated with modification in the central nervous system metabolism of monoamines of possible importance for the psychiatric symptoms [14]. PHPT is often an incidental diagnosis during screening laboratory tests and studies show that more than 80% of all patients present as asymptomatic in the USA and Western Europe [2,11]. Diagnosis of hypercalcemia on routine testing is frequently the initial step to set the hypothesis of primary hyperparathyroidism. Further investigation includes the determination of PTH level, bilateral neck exploration and biochemistry and imaging tests to determine the type of hyperparathyroidism and possible underlying causes. It is also important to distinguish PHPT from the familial hypocalciuric hypercalcemia [3].

Undoubtedly the only definite treatment of PHPT is parathyroidectomy, which is recommended not only for patients with symptoms but also for asymptomatic ones at risk of progression or with subclinical evidence of end-organ effects [2,15]. Patients who do not fulfill the criteria for surgical treatment should undergo conservative treatment. Bisphosphonates, cinacalcet, estrogen and thiazides are frequently used in order to normalize serum calcium and PTH levels or to increase BMD [2]. Further research is needed to evaluate the effect of surgical and conservative treatment on the elimination of nonclassical manifestations of PHPT such as cognitive and psychiatric symptoms [5,6]. This article presents a case of primary hyperparathyroidism because of a parathyroid adenoma in a 66-year-old woman. The diagnosis was set following an acute psychotic episode in combination with elevated serum calcium and parathyroid hormone levels. The patient's low vitamin D level could possibly be the compensatory mechanism for chronic hypercalcemia. Unfortunately, the initial treatment with risperidone was ineffective. The surgical excision of the parathyroid adenoma resulted in a complete and long-term reversal of psychotic symptoms, but the symptoms of the emotional disorder remained.

Conclusion

PHPT should be considered in individuals who present with neuropsychiatric symptoms at the emergency department. This case alerts physicians to use routine serum calcium testing as a screening tool among elderly patients since it could lead to an early diagnosis of this unique entity and possibly achieve better control and a reversal of the symptoms.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2022.46.007397

Arvaniti Aikaterini. Biomed J Sci & Tech Res

Submission Link: https://biomedres.us/submit-manuscript.php