

Primary Hyperparathyroidism With Pancreatitis, Nephrocalcinosis And Chronic Kidney Disease: When Hypercalcemia Is The One To Blame

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Abstract

A 53 year-old woman with a history of nephrolithiasis was admitted to the hospital with acute pancreatitis. Hypercalcemia, high intact parathyroid hormone levels (PTH)i, nephrocalcinosis, and renal failure were also present. The patient denied alcohol consumption and abdominal ultrasound excluded gallstones. Biochemical levels of triglycerides were normal. Other etiologies of chronic kidney disease were excluded.

In the following months, the kidney function remained stable as the high PTHi levels (2355-4157 pg/mL, normal range 12-88 pg/mL). Primary hyperparathyroidism (PHPT) was suspected and confirmed by radionuclide scintigraphy and ultrasonography of parathyroid glands. Parathyroidectomy was performed and histology confirmed parathyroid adenoma.

Due to chronic kidney disease stage 5, the patient started haemodialysis thirteen months after the first admission. She has not presented any new pancreatitis episodes since then.

We report an unusual case of PHPT with classical features that are rare today: acute pancreatitis, symptomatic nephrolithiasis, and nephrocalcinosis leading to end stage renal disease.

INTRODUCTION

The most common cause of elevated serum calcium level in ambulatory patients is PHPT. Most cases of hypercalcemia are asymptomatic. Presently, the majority of PHPT patients in developed countries are asymptomatic and symptomatic PHPT with classical skeletal, renal, abdominal and neuropsychiatric manifestations have become exceedingly rare.

Even if the association of PHPT with acute pancreatitis is controversial, renal manifestations of PHPT, such as nephrolithiasis, nephrocalcinosis, and chronic kidney failure are widely recognized.

The patient we describe had a classical presentation of PHPT with acute pancreatitis, nephrocalcinosis, and chronic kidney failure being the first manifestations of PHPT. This case intend to increase awareness of classical manifestations of PHPT among clinicians, since they become rare as first presentation of PHPT in developed countries.

CASE PRESENTATION

A 53 year-old woman was admitted to a district general hospital for uncontrollable vomiting and epigastric abdominal pain with dorsal irradiation. She had a history of nephrolithiasis and had been submitted to lithotripsy 25 years ago but without regular medical follow-up. Laboratorial results showed renal impairment (creatinine: 7.5 mg/dL; urea: 471 mg/dL); raised serum amylase and lipase levels (1860 IU /L; normal range 28-100 and 1960 IU/L; normal range 22-51 respectively); leucocytosis (30720 UI/L); neutrophilia (88.5%); an elevated alkaline phosphatase of 303 UI/L (normal range 38-126 UI/L); normal serum gamma-glutamyl transferase and serum transaminases. Hypercalcemia (serum calcium level of 10.9 mg/dL), serum phosphorus in normal range (4.5 mg/dL, normal range 3.5-5.1 mg/dL) and a raised PTHi of 2100 pg/mL were also present at that time. Other signs secondary to hypercalcemia, such as polyuria, constipation, muscle

weakness, myalgia, arthralgia or peptic ulcer were absent.

Abdominal axial computed tomography confirmed oedematous pancreatitis, excluding gallstones. The patient denied alcohol consumption and hypertriglyceridemia was excluded. Renal ultrasonography revealed bilateral nephrolithiasis and small hyperechoic kidneys, suggesting chronic kidney disease. Renal axial computed tomography confirmed the diagnosis of bilateral nephrocalcinosis and nephrolithiasis.

Intravenous (IV) crystalloids were provided; analgesics (tramadol and alphenitanil) were administered for pain relief.

She was discharged after 20 days, asymptomatic, with improvement in kidney and pancreatic function (creatinine: 3.6 mg/dL; urea: 83 mg/dL; lipase: 306 IU/L; amylase: 298 IU/L). She was referred to Nephrology consultation.

In the following months, kidney function did not improve and PTHi remained high (PTH: 2355-4157 pg/mL), with calcemia in the upper limit of normal (serum calcium level of 10 mg/dL). Cinacalcet (30 mg/day), a calcimimetic, was started with no reduction in PTHi levels. A radionuclide scintigraphy and ultrasonography of parathyroid glands were performed and revealed a parathyroid adenoma projected below the lower pole of the left lobe of the thyroid gland (Figure 1).

Lower left parathyroidectomy was performed after location of hyper functioning parathyroid through scintigraphy. Scintigraphy excluded ectopic parathyroid tissue. PTHi was measured pre surgery (2641.2 pg/ml) and intraoperative at time zero (972.7 pg/ml), 5, and 15 minutes after parathyroidectomy (8536.1 and 375.5, respectively). The histology of the surgical specimen confirmed parathyroid adenoma.

Due to chronic kidney disease stage 5, haemodialysis was started in May 2013.

Eight months after surgery, PTHi levels remained high (2000-2500 pg/mL). A new radionuclide scintigraphy of parathyroid gland and thorax was performed and showed no remaining adenoma tissue. So, a bone biopsy was performed and revealed high turnover, normal mineralization, and an increased bone volume (TMV classification), suggesting the diagnosis of fibrosis osteitis. Since January 2014, PTHi levels have slowly decreased after re-introduction of cinacalcet and vitamin D analogues. In April 2015 PTHi

reached its lowest - 85 pg/mL. She did not present any new pancreatitis episodes.

Figure 1

Radionuclide scintigraphy and ultrasonography of parathyroid glands revealing a parathyroid adenoma projected below the lower pole of the left lobe of the thyroid gland.



DISCUSSION

PHPT is the third most common endocrine disorder [1] with an incidence of 25 per 100,000 people per year. PHPT commonly appears in the fifth and sixth decades of life. The male to female ratio is 1:3. Pathological lesions responsible for PHPT include solitary adenomas (>80%); multigland hyperplasia (15%); double adenomas (2-3%); and carcinoma (2%). As shown in histology, this patient had a solitary parathyroid adenoma, so other possible parathyroid diseases related to PHPT were excluded.

Concerning pancreatitis, some studies have shown that pancreatitis is associated with primary hyperparathyroidism in 1.5 to 7% of cases [ii],[iii]. A recent meta-analysis has shown a higher rate of pancreatitis among patients with PHPT than in general population [1]. The mechanism by which PHPT is associated with acute pancreatitis is unclear. Some published literature suggested that elevated serum calcium level is responsible for the development of pancreatitis in patients with PHPT. Elevated serum calcium

levels lead to premature activation of pancreatic protease resulting in acute pancreatitis [2].

Our patient had an onset of acute pancreatitis revealed by clinical symptoms, laboratorial findings and imagological changes. The patient had no alcohol consumption and gallstones were excluded by abdominal ultrasound. Biochemical levels of triglycerids were normal. PHPT seemed to be responsible for acute pancreatitis in this patient.

PHPT has also some renal manifestations, including hypercalciuria, nephrolithiasis, nephrocalcinosis, chronic kidney disease, and renal tubular dysfunction. One study reported that only 19 (7%) of the 271 patients with mild PHPT had renal stones [14]. Nevertheless, the presence of renal stone categorizes PHPT as symptomatic and is an indication for parathyroid adenomectomy. Nephrocalcinosis is a generalized increase in the concentration of calcium and the deposition of calcium salts in the renal parenchyma. This condition differs from kidney stones by the formation of calculi in the excretory tract. The increase in calcium content in the kidneys occurs in three phases (chemical, microscopic and macroscopic) with different kidney damage severity.

In a cross-sectional survey of 294 PHPT patients, an estimated glomerular filtration rate below 60 ml/min/1.73 m² was found in 17% of the patients, indicating that renal impairment was a common finding in PHPT [15]. Development of renal insufficiency in PHPT was related to the degree and duration of hypercalcemia.

In this case, we present a female patient with end stage renal disease, a past of nephrolithiasis, submitted to lithotripsy 25 years ago. She also had macroscopic nephrocalcinosis revealed by renal ultrasonography and renal axial computed tomography. Other frequent causes of chronic kidney disease such as diabetes, hypertension, hereditary diseases and use

of nephrotoxic drugs were excluded. Chronic kidney disease seemed to be related to PHPT and consequent nephrocalcinosis.

Two particular features of this case report suggest a probable superimposed secondary hyperparathyroidism (SHPT): on the one hand, hypercalcemia was always only slightly elevated (maximum 10,9 mg/dL) or in the upper limit of normal values; on the other, even after parathyroidectomy, PTH levels remained high and re-introduction of cinacalcet was needed. SHPT occurs most commonly associated to chronic kidney disease and the use of calcimimetics in SHPT is well described in literature. Tertiary hyperparathyroidism (THPT) was excluded since that, in THPT, the hyperplasic glands function autonomously despite withdrawal of calcium and calcitriol therapy. Additionally, in patients with THPT, medical treatment is not curative and, generally, not indicated.

In conclusion, in this case report, hypercalcemia due to PHPT seems to be the "one to blame" considering pancreatitis and chronic kidney disease development.

References

1. Beattie GC, Ravi NR, Lewis M, Williams H, Blair AW, Campbell IW, et al. Rare presentation of maternal primary hyperparathyroidism. *Br Med J* 2000; 321: 223-224
2. Bai HX, Giefer M. The association of primary hyperparathyroidism with pancreatitis. *J Clin Gastroenterol*. 2012;46:656-661
3. Khoo TK, Vege SS, Abu-Lebdeh HS, Ryu E, Nadeem S, Wermers RA. Pancreatitis and primary hyperparathyroidism: a population- based study. *J Clin Endocrinol Metab*. 2009; 94:2115-2118
4. Suh JM, Cronan JJ, Monchik Jm. Primary hyperparathyroidism: Is there an increased prevalence of renal stone disease? *AJR Am J Roentgenol*. 2008; 191:908-911
5. Tassone F1, Gianotti L, Emmolo I, Ghio M, Borretta G. Glomerular filtration rate and parathyroid hormone secretion in primary hyperparathyroidism. *J Clin Endocrinol Metab*. 2009;94:4458-4461

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