

CASE REPORT

Multiple organ dysfunction caused by parathyroid adenoma-induced primary hyperparathyroidism

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Abstract

We present a 27-year-old male with multiple organ dysfunction caused by parathyroid adenoma-induced primary hyperparathyroidism (PHPT). Initially, the patient experienced a sudden onset of gastrointestinal symptoms, polyuria, polydipsia, bone pain, renal dysfunction, nephrolithiasis, and acute pancreatitis, symptoms associated with hypercalcemia. Biochemical findings suggested PHPT. Renal biopsy showed an acute tubular injury and massive calcium deposits in the tubular epithelial cells and tubular lumina. Moreover, neck ultrasonography suggested the possibility of a parathyroid tumor. We excised his right parathyroid gland. Histopathological analysis revealed features of a parathyroid adenoma. Post-operatively this patient had normal serum calcium concentration, but was renally insufficient. A recent repeat biopsy showed chronic renal tubular injury. Our findings illustrate the complications of various systems that can occur in patients with PHPT caused by a parathyroid adenoma.

Key words: Hypercalcemia, parathyroid adenoma, parathyroid hormone, primary hyperparathyroidism

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Introduction

Parathyroid adenoma is the most frequent cause of primary hyperparathyroidism (PHPT). To date; however, there have been no reports of multiple organ dysfunction caused by parathyroid adenoma-induced PHPT. Here, we describe a male patient with renal dysfunction, nephrolithiasis, bone disorders, and acute pancreatitis (AP) associated with hypercalcemia caused by parathyroid adenoma-induced PHPT.

Case Report

A 27-year-old man presented with a 10-day history of nausea, vomiting, and abdominal distension and a 7-day history of thirst, polydipsia, nocturia, and flank pain. His previous medical history included an appendectomy for acute appendicitis 1 year earlier, with a serum calcium concentration of 2.8 mmol/L (normal range 2.2-2.7 mmol/L)

and a subsequent subarachnoid hemorrhage (SAH), from which he recovered completely. His physical examination was unremarkable. Urine output was an average 3000 ml/day.

Initial laboratory examinations showed renal dysfunction (serum creatinine 205 $\mu\text{mol/L}$), but his urinalysis was normal. His serum calcium concentration was exceedingly high (4.72 mmol/L), although his urinary calcium excretion and serum phosphate concentration were normal. Abdominal ultrasonography showed normal liver, gallbladder, pancreas, and spleen while a large renal mass with an unclear structure due to extensive blood loss and left renal stones. Renal biopsy showed severe acute tubular injury. His tubular epithelial cells and tubular lumina contained deposits of royal purple crystals [Figure 1] and were positive for van-Cossa-staining [Figure 2], confirming the presence of calcium crystals. No significant histological

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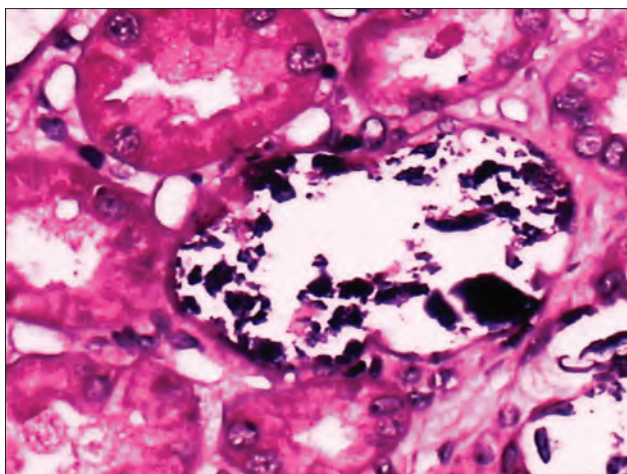


Figure 1: HE-stained section showing royal purple crystal deposits in tubular epithelial cells and tubular lumina. (Original magnification $\times 400$)

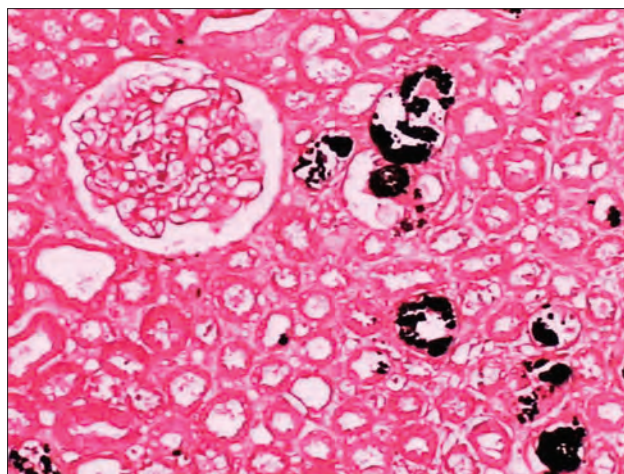


Figure 2: Van Cossa-stained section showing calcium (black) in tubular epithelial cells and tubular lumina. (Original magnification $\times 100$)

lesions were found in the glomeruli and vascular spaces. Immunofluorescent staining of the biopsy samples was negative. He was initially diagnosed with hypercalcemia, acute kidney injury and left renal stones.

This patient was treated with rehydration, diuresis and glucocorticoids to decrease his serum calcium concentration. However, he suffered episodes of fatigue, dizziness, anorexia; abdominal distension; constipation; bone pain in his lower extremities, hips and back; and pain in his teeth. His renal function had not improved significantly and his serum calcium again increased to 5.36 mmol/L. He also experienced an attack of AP, causing significant nausea, vomiting, and abdominal pain, active bowel sounds as well as elevated serum (1063 IU/L) and urinary (1354 IU/L) amylase concentrations. However, abdominal ultrasound still showed no abnormal finding. The patient was treated with fasting, water deprivation, continuous gastrointestinal decompression, gastric acid suppression, inhibition of pancreatic secretion, fluid replacement, nutritional support, anti-infectious agents and continuous renal replacement therapy used as a means of blood purification therapy for critically ill-patients with renal failure. After 3 days, he experienced significant reductions in abdominal pain and his serum (333 IU/L) and urinary (303 IU/L) amylase concentrations decreased.

Further examination showed normal thyroid function, serum protein electrophoresis and bone marrow biopsy as well as negative serum tumor markers and urinary Bence-Jones protein. X-rays showed skull bone changes, including, low bone mineral density (osteoporosis), fine-grid reconstruction and rough edges while X-rays of his pelvis, lumbar spine, bilateral femurs, knees, and ankles showed no abnormal bone findings. Computed tomography (CT) examination of his head showed a focus of local malacia in his left temporal lobe due to an intracranial hemorrhage 1 year earlier. His

serum parathyroid hormone (PTH) concentration was 1278.66 pmol/L, indicating hyperparathyroidism. Moreover, neck ultrasonography showed a hypoechoic lesion at the posteromedial region of his right thyroid lobe, suggesting a parathyroid tumor.

Surgical examination of his thyroid showed multiple nodules in his right thyroid lobe. He therefore underwent a right parathyroidectomy and a right subtotal thyroidectomy. Histopathological examination confirmed the diagnoses of nodular goiter and parathyroid adenoma (acidophilic cell type). Immediately post-operatively, his serum calcium concentration decreased to normal [Table 1]. By 4 months after the surgery, mild renal insufficiency (serum creatinine 125 $\mu\text{mol/L}$) remained. A repeat renal biopsy showed chronic changes in his primary renal lesion. Fortunately, there was no significant increase in serum creatinine after oral administration of creatinine-lowering drugs.

Discussion

Hypercalcemia, a potentially lethal endocrine disorder, may be caused by a broad range of conditions, but is secondary to malignancy or PHPT in up to 90% of patients, with malignancy being the most frequent cause. Malignancies typically associated with hypercalcemia include lung, breast, prostate, and colon cancer as well as adult T-cell malignancies and multiple myeloma. Our patient had hypercalcemia associated with elevated PTH. Further work-up, however, indicated that hypercalcemia in this patient was not due to multiple myeloma or leukemia.

PHPT is a common endocrine disorder resulting from the parathyroid gland adenomas (80-85%), hyperplasias (10-15%) and carcinomas (<1%).^[1] Most patients with

Table 1: Comparison of pre-and post-operation hematological parameters

Hematological parameters	Pre-operation	Post-operation
PTH (pmol/L)	1278.66	54.71
BUN (mmol/L)	27	8.90
Cr (μ mol/L)	389	277
UA (μ mol/L)	390	346
HS-CRP (mg/L)	55.05	8.34
K ⁺ (mmol/L)	3.42	3.91
Na ⁺ (mmol/L)	141.50	142
Cl ⁻ (mmol/L)	106.40	107.30
Ca ²⁺ (mmol/L)	4.56	2.42

PTH=Parathyroid hormone; BUN=Blood urea nitrogen; UA=Uric acid; HS-CRP=High-sensitivity C-reactive protein

PHPT have mild symptoms or are asymptomatic. Our patient, who had symptoms and complications of severe hypercalcemia, was diagnosed with PHPT. Although, we attempted to stabilize his calcium levels by the medical treatment, his hypercalcemia did not normalize until after parathyroid surgery. Histologic examination of his resected parathyroid tumor showed that it was a parathyroid adenoma.

AP caused by PHPT-induced hypercalcemia is very rare, occurring in 1%-8% of patients.^[2] Our patient presented with significant nausea, vomiting, and abdominal pain as well as increased serum and urine amylase concentrations. Calcium has been shown to activate trypsinogen in a dose dependent manner, and increased intracellular trypsinogen activation is an early step in the pathogenesis of hypercalcemia induced pancreatitis.^[3,4]

About 1 year before admission, our patient had SAH, which was confirmed by head CT and magnetic resonance imaging examinations. A repeat head CT performed about 1 month before admission demonstrated no abnormal findings. Marked increases in PTH and PTH receptor over time have been reported after SAH.^[5] Up-regulation of PTH and PTH receptor may have stimulated parathyroid hyperplasia, causing a parathyroid adenoma.

Although hyperparathyroidism may be associated with

multiple organ failure secondary to sepsis,^[6] there have been few reports of multiple organ dysfunction due to PHPT. In our patient, PHPT-induced hypercalcemia may have been responsible for his gastrointestinal symptoms, fatigue, polydipsia, renal dysfunction, nephrolithiasis, renal hypertension, bone and joint pain, osteoporosis, AP, and cerebral vascular accident.

In conclusion, our findings suggest that PHPT should be considered in the differential diagnosis of patients with severe hypercalcemia. Patients can present with the nonspecific symptoms reflecting multi-organ involvement. These patients require immediate medical management of their hypercalcemia, followed by emergency surgery. Furthermore, parathyroidectomy is the preferred therapy for PHPT.^[7] Despite these treatments; however, a hypercalcemic crisis still carries a significant risk of mortality, especially in patients with extremely high serum calcium levels, and chronic lesions may occur.

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