

Can Diabetes Associated With Hyperparathyroidism Be an Additional Indication for Parathyroidectomy? A Case Report

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P rimary hyperparathyroidism is not uncommon. It has varied presentations ranging from asymptomatic disease to the classic "stones, groans, moans".

This is a case report of a 49 year-old woman, who presented with sensory obtundation, abdominal pain, associated with vomiting and denovo detected diabetes mellitus. She had a past history of bilateral nephrolithiasis, and was found to have hypercalcemia (serum corrected calcium 12.8 mg/dL) with elevated serum intact parathormone (183 pg/mL, normal range 13-54 pg/mL). The 99m-Tc MIBI scintigraphy localized the source of parathormone to the right inferior parathyroid gland. Being dehydrated, she was treated with saline diuresis, salmon calcitonin and intravenous pamidronate. Her blood sugar was reported to be 421 mg/dL, and the glycemia was controlled with insulin therapy. A 2 X 2 cm sized right inferior parathyroid adenoma was later removed. The glycemic status improved dramatically after parathyroidectomy and the patient was euglycemic on low doses of glimepiride. This case study suggests that primary hyperparathyroidism might also contribute to hyperglycemia in subjects with diabetes mellitus.

Key Words: Primary hyperparathyroidism, Coma,

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Introduction

Primary hyperparathyroidism is not an uncommon disease, more so in the elderly. Patients with primary hyperparathyroidism have alterations in carbohydrate metabolism characterized by insulin resistance, hyperinsulinemia, and glucose intolerance. The clinical significance of these findings in the management of patients with diabetes mellitus (DM) after parathyroidectomy for hyperparathyroidism has been controversial. We present a case with improved glycemic control after treatment of primary hyperparathyroidism.

Case presentation

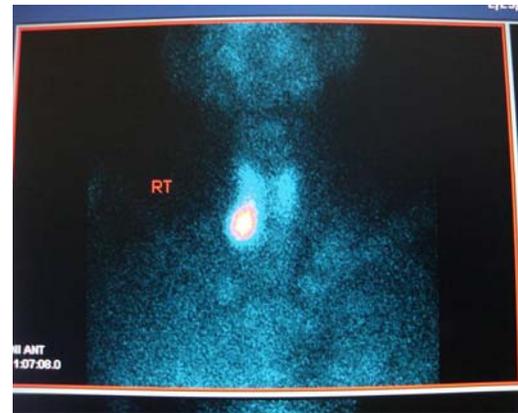
A 49 yr old woman presented to the emergency department with complaints of abdominal pain, vomiting, inability to sit up (from a lying position), to stand (from sitting position) since the last 10 days, and a progressively worsening altered sensorium for the past 4 days. She had no history of head-

ache, seizures, fever, rash, trauma or any focal deficit prior to, or during the illness. She had been suffering from constipation for the last 2 years and was taking laxatives. Apart from the laxatives, there was no history of prolonged drug intake. There was no history of emotional lability, depression or fractures in the past. She had had four episodes of abdominal pain over the last one year, for which she had undergone upper GI endoscopy, with unremarkable results. Two years previously, she had been diagnosed with bilateral renal stone disease, for which she underwent endoscopic shock wave lithotripsy. The patient had attained menopause ten years ago. She was not a known diabetic or hypertensive and there was no history suggestive of thyrotoxicosis or breast malignancy. Examination revealed that she was drowsy, confused, with GCS of E₃M₅V₄, with a pulse rate of 96/min and BP of 150/90 mm of Hg. She was having moderate to severe dehydration with diffuse abdominal tenderness. There was no palpable neck mass, no thyromegaly and rest of the systemic examination was unremarkable. Neurological examination did not reveal any focal neurological deficit.

Investigations revealed the presence of high blood glucose, 23.4 mmol/L (421 mg/dL), without any acidosis or ketosis. There was prerenal azotemia. The liver functions were normal; her corrected serum calcium was 3.3 mmol/L (12.8 mg/dL) and serum inorganic phosphorous was 1.5 mmol/L (4.60 mg/dL); 24 hr urinary excretion of calcium was 18.1 mmol/day (694 mg/day) with 32.5 mmol/day (1008 mg) of phosphorus and 952 mg of creatinine. Serum 25 hydroxy-vitamin D was 30.2 nmol/L (normal 20-100 nmol/L) and serum intact parathormone was 183 ng/L (normal 13-54 ng/L). Her urine Bence Jones proteins were negative, and she was biochemically euthyroid. X-rays of the chest, pelvis, spine, and hand showed faintly visible bones; no skeletal lytic lesions were visible on radiographs, and CT scan of the head was normal. An ultrasonography of the abdomen was normal, but one of the necks revealed a 2 x

2.4 cm mass behind the lower pole of right lobe of thyroid. The 99m-Tc MIBI scintigraphy (Fig.1a) showed abnormal uptake at the lower pole of the right lobe of the thyroid, which persisted in the delayed images, acquired after 90min interval (Fig.1b) and was seen in all the views of that region, suggestive of parathyroid adenoma. USG guided FNAC of the mass showed cuboidal to round cells, with vesicular nuclei suggestive of parathyroid adenoma.

(A)



(B)

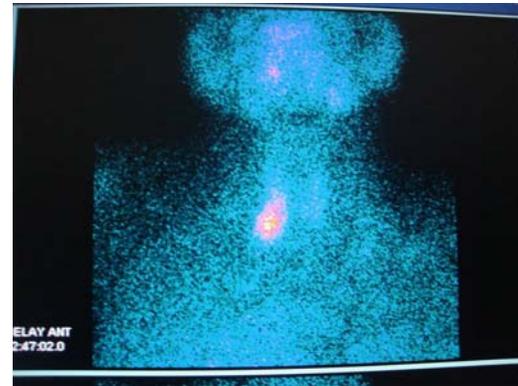


Figure 1(a): Initial Image, 99m-Tc MIBI scintigraphy (parathyroid, dual phase scintigraphy). Abnormal tracer uptake seen at lower pole of right lobe of the thyroid gland.

(b): Delayed Image - 90 min. Abnormal uptake persists, highly suggestive of parathyroid adenoma

She was rehydrated with 0.9% saline, following which saline diuresis was attempted with six liters of 0.9% saline and frusemide, after which she was started on salmon calcitonin, 100 IU (subcutaneously), 12 hourly, for 4 days. Once renal functions improved, intravenous pamidronate at a dose of 30 mg/day was given for two days.

Following treatment, her serum calcium normalized, hydration improved and her neurologic status improved. Glycemic control was achieved with premixed (30:70) insulin, 38 units/day in two doses and glimeperide 3 mg/day. Three months after her initial presentation with severe hyperglycemia, the patient underwent interval parathyroidectomy. In the intervening period, long after the initial stress had settled, unsuccessful attempts were made to taper insulin while continuing with Glimeperide 3 mg per day. However plasma glucose was seen to rise, whenever insulin doses were reduced, necessitating continuation of insulin till the date of surgery.

Right lower parathyroidectomy was done under general anesthesia. The parathyroid nodule was 2 X 2 cm in size and firm in consistency; other parathyroid glands were atrophic. Intraoperative PTH levels at 5, 10 and 15 minutes after tumor removal were 57 ng/mL, 8.1 ng/mL and 7 ng/mL respectively.

She developed hypocalcemia on the 1st postoperative day which was treated with intravenous calcium gluconate; on the 4th postoperative day, parenteral calcium was stopped and she was put on oral calcium carbonate (3000 mg/day) and calcitriol (0.25 µg/day), the latter being withdrawn after 10 days.

On follow up she was asymptomatic and on calcium supplements. Her serum calcium was 2.5mmol/L (9.7mg/dL) and phosphorous was 1 mmol/L (3 mg/dL). Insulin was successfully withdrawn and glycemic control (fasting blood sugar 108 mg/dL, HbA1c 7.1%) was achieved with glimeperide 3 mg/day.

Histopathology revealed a discrete capsule separating the adenoma and the normal

parathyroid tissue. The adenoma showed sheets of cuboidal to round cells with vesicular nuclei forming trabecular and microacinar structures. Absence of adipose tissue within the adenoma was noted in contrast with that seen in between cells in normal parathyroid glands.

Discussion

Severe hyperglycemia can worsen hypercalcemia by causing osmotic diuresis leading to dehydration and hypercalcemia, which, in turn, can worsen or induce hyperglycemia by causing insulin resistance¹. The incidence and prevalence of frank diabetes mellitus (DM) is significantly increased in patients suffering from hypercalcemia². In a retrospective analysis series of 441 patients operated for primary hyperparathyroidism (PHPT), the prevalence of diabetes mellitus was three times higher than in the unselected age-matched population³. At presentation with PHPT, oral glucose tolerance test commonly identifies new cases of DM and IGT. After successful parathyroidectomy, fasting and 2-hr post glucose fall significantly ($p < 0.05$, $p < 0.01$ respectively) and DM and IGT/IFG often ameliorate to IGT or normal glucose tolerance⁴ respectively. Elevated levels of cytosolic free calcium (Ca^{++}) are responsible for the insulin resistance. Elevated or sustained levels of Ca^{++} impair insulin-stimulated glucose uptake. Ca^{++} induced impairment appears to take place at the post binding steps of insulin action and probably interferes with the tyrosine kinase activity of insulin receptors and the intrinsic activity of glucose transporters⁵.

Despite the presence of several promising agents for medical management, the presence of DM may be an indication for parathyroidectomy⁶, which may result in either stabilization or improvement in glycemic control and reduce the need for use of antidiabetic agents.

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