

# Minimally Symptomatic Severe Hypercalcaemia in a Patient with Parathyroid Carcinoma

Aisha Sheikh, Najmul Islam

Department of Medicine, Aga Khan University Hospital, Karachi.

### Abstract

The case of a 38 years old man with generalized pains fatigue, anorexia, constipation, polyuria serum calcium level of 20.6mg/dl in paired renal function parathyroid hormone is presented. Sestamibi scan showed a functioning left inferior parathyroid tumor, which was successfully removed. Before surgery he was managed with rehydration, diuretics and pamidronate infusion.

Five months post surgery the serum calcium levels are normal and renal function has improved.

### Introduction

Serum Calcium level above 14mg/dl is considered as severe hypercalcaemia and the patients are usually acutely ill necessitating urgent hospitalization and treatment.<sup>1</sup> Clinical manifestations affect the neuromuscular, gastrointestinal, renal, skeletal, and cardiovascular systems. The most common causes of hypercalcaemia are primary hyperparathyroidism and malignancy.<sup>1</sup> Hypercalcaemic crisis is a life-threatening emergency. Aggressive intravenous rehydration is the mainstay of management in severe hypercalcaemia, and antiresorptive agents, such as calcitonin and bisphosphonates, frequently can alleviate the clinical manifestations of hypercalcaemic disorders.<sup>1,2</sup> We report a case that had serum calcium of more than 20mg/dl and he walked into the endocrine clinic.

### Case Report

A 38 years old man who had one year history of generalized pains more marked in shoulders and legs, fatigability, anorexia, constipation and polyuria was seen at a medical care facility and was found to have a serum calcium of 17.6mg/dl (normal range: 8.6-10.5mg/dl) with an intact Parathyroid Hormone (PTH) of 1205pg/ml (normal range: 7-53mg/dl). Suspecting Parathyroid adenoma a Sestamibi scan was done which showed a functioning left inferior parathyroid tumor. He had a pepper pot skull on radiograph. He was treated with bisphosphonates with which his symptoms improved and there was a reported fall in serum calcium to 10.4mg/dl. He was advised surgery but he was lost to follow up.

Six months later he presented to our endocrine clin-

ic with history of pain in extremities, weakness, fatigability, anorexia, constipation and vomiting of one week duration and had a report of his serum calcium which was 20.6mg/dl. He was alert and oriented and his clinical examination was unremarkable except that there was a small nodule (<1cm) palpable on the left side of the neck. He was admitted and was treated with normal saline infusions followed by pamidronate infusion and intravenous frusemide. He had a serum creatinine of 3.3mg/dl which was thought to be due to renal impairment secondary to hypercalcaemia. His intact PTH was 2240pg/ml. He was screened for multiple endocrine neoplasia which turned out to be negative. His 25-hydroxyvitamin D level was 9.4mg/dl (normal range: 9.0-37.6mg/dl). With treatment his serum calcium fell to 11.3 g/dl and then he underwent surgical removal in which left inferior parathyroidectomy and left thyroid lobectomy was done. Immediately after surgery his PTH level came down to 138pg/ml.

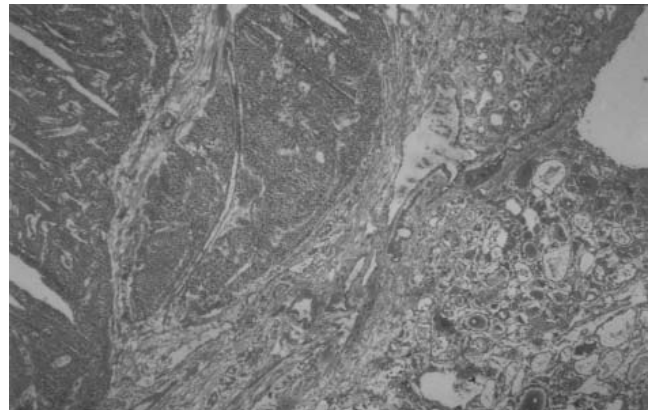


Figure. Parathyroid Carcinoma infiltrating the thyroid gland

The histopathology revealed cellular neoplastic lesion composed of pleomorphic cells arranged in trabeculae and clusters incompletely separated by thick fibrous bands. The cells were pleomorphic having clear cytoplasm with indistinct cell boundaries. Nuclei showed pleomorphism and hyperchromasia with inconspicuous nucleoli. Increased mitotic activity was noted. Cellular invasion was identified. Neoplastic cells were seen abutting the thyroid acini (Figure). These findings were consistent with parathyroid carcinoma.

Our patient's serum calcium levels remained in normal range in the immediate postoperative period on supplemental calcium and calcitriol. Five months after surgery his serum calcium levels are within normal range on follow ups. His serum creatinine level has also come down to 2.0mg/dl but has not normalized.

## Discussion

The most common cause of hypercalcaemia is primary hyperparathyroidism, followed by malignancy. Together they account for more than 90% of cases<sup>2</sup>; however, malignancy accounts for the majority of cases of severe hypercalcaemia and hypercalcaemic crises.<sup>1</sup> A case of hypercalcaemic crisis (serum calcium 5.9mmol or 23.6mg/dl) due to parathyroid hormone related protein (PTHrP) secreting pancreatic neuroendocrine tumor in pregnancy has been reported by Abraham et al.<sup>3</sup>

Hypercalcaemia in the setting of raised intact parathyroid hormone is pathognomonic for primary hyperparathyroidism. Benign primary hyperparathyroidism rarely produces severe hypercalcaemia and/or hypercalcaemic crises, unless renal insufficiency and/or dehydration is superimposed on the underlying hyperparathyroidism<sup>1</sup>. In contrast parathyroid carcinoma is associated with severe hypercalcaemia i.e. more than 14mg/dl level.<sup>1,4</sup> Severe hypercalcaemia produces gastro-intestinal symptoms-anorexia, nausea, vomiting and constipation, neuro-psychiatric symptoms-fatigue, lethargy, poor concentration, depression, obtundation, coma and occasionally causes cardiovascular complications-bradyarrhythmias, heart block and cardiac arrest.<sup>1,5</sup> Our patient was minimally symptomatic with serum calcium of 20.6mg/dl which might be due to the chronic nature of his illness.

Parathyroid carcinoma is an uncommon cause of PTH-dependent hypercalcaemia<sup>4,6</sup> and it accounts for less than 1% of patients with primary hyperparathyroidism.<sup>7</sup> Different case series have reported serum calcium in the range of 9.9-18.4mg/dl<sup>8,9</sup> and 11.4-15.6mg/dl<sup>9</sup> in patients with parathyroid carcinomas. Spinelli C et al reported three cases of parathyroid carcinoma, one of them had serum calcium of 20.2mg/dl.<sup>10</sup> Our patient had serum calcium of 20.6mg/dl which is the highest reported with parathyroid carcinomas.

The initial treatment of severe hypercalcaemia is the same regardless of the etiology. Therapy is aimed at increasing renal excretion of calcium and decreasing bone resorption. Patients with hypercalcaemic crisis are volume depleted and initial therapy should be intravenous hydration with

isotonic saline as was done in our patient. Following aggressive rehydration intravenous loop diuretics are used to inhibit calcium resorption in the distal tubule. Bisphosphonates, which directly inhibit osteoclast activity, are the most effective of the pharmacological agents. Pamidronate has often been used in such cases as was used in our patient. Calcitonin, glucocorticoids and rarely pliamycin and gallium nitrate have been used for hypercalcaemic crisis with variable success. In patients with renal failure, dialysis with a low or zero calcium dialysate should be initiated.<sup>1,5</sup>

The single most effective therapy for parathyroid carcinoma is complete resection of the primary lesion at the time of initial operation when extensive local invasion and distant metastases are less likely.<sup>5</sup> Surgical treatment results in prompt correction of serum calcium and parathyroid hormone with gradual resolution of the metabolic consequences of severe hypercalcaemia. The prognosis of parathyroid carcinoma is quite variable. Five-year survival rates vary from 40-86%.<sup>5</sup> Persistent hypercalcaemia following initial surgery is a poor prognostic indicator as 60% of patients die within 3 years.<sup>11</sup>

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