CASE REPORT

# Parathyroid Carcinoma with Hungry Bone Syndrome Complication After Parathyroidectomy: a Case Report

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**ABSTRACT**

*Parathyroid carcinoma is one of the causes of primary hyperparathyroidism, and the most effective treatment is parathyroidectomy. It is important to acknowledge the occurrence of Hungry Bone Syndrome following parathyroidectomy, as it could lead to higher death rates and longer hospital stays. In this report, we provide a case of a 27-year-old male who presented with repeated occurrences of bone fractures. The physical examination revealed a mass in the right thyroid region and deformities in the humerus and femoral regions. The laboratory analysis revealed increased calcium levels and significantly raised parathyroid hormone levels. The imaging findings revealed widespread bone lytic lesions and a mass in the right parathyroid region. The patient was diagnosed with primary hyperparathyroidism and underwent a parathyroidectomy, and the pathology results revealed the presence of a parathyroid carcinoma. On the fourth day following parathyroidectomy, the patient reported symptoms of tingling and muscle cramping. We noticed a decline in the calcium levels, which raised the possibility of Hungry Bone Syndrome. We implemented calcium correction and rigorous monitoring to prevent potentially lethal occurrences.*

**Keywords**: *Hungry bone syndrome, parathyroid carcinoma*

## INTRODUCTION

Parathyroid carcinoma is the least common cause of primary hyperparathyroidism, representing approximately 1 to 2% of cases.[1] Individuals diagnosed with parathyroid carcinoma typically experience a greater number of symptoms, including renal and skeletal complications, neck masses, and notable elevations in calcium and parathyroid hormone (PTH) concentrations.[2]

Surgery is the most effective and reliable treatment for parathyroid carcinoma, achieving a success rate of 95%.[3,4] Hypocalcemia commonly occurs briefly and transiently following parathyroidectomy, but there is a possibility of developing Hungry Bone Syndrome (HBS), which can lead to prolonged and potentially life-threatening hypocalcemia.[5] Patients with parathyroid carcinoma who have extremely high levels of parathyroid hormone (PTH) and skeletal abnormalities are at an increased risk of developing hungry bone syndrome (HBS) after undergoing parathyroidectomy.

The rarity of parathyroid carcinoma and the potentially life-threatening HBS syndrome led us to select this case. To avoid negative outcomes, it is critical to promptly identify and effectively manage this condition.

## CASE ILLUSTRATION

A 27-year-old male patient experienced repeated occurrences of bone fractures. The patient had confirmed hematuria one month before hospital admission, and further examination revealed the presence of renal calculi. During the last two years, the patient has encountered a sequence of falls, leading to fractures in the right femur, as well as fractures in the left femur and right humerus. There is a lack of symptoms such as increased urine (polyuria), increased thirst (polydipsia), problems with bowel movements (constipation), abdominal discomfort, feelings of illness (nausea), vomiting, or changes in mental state. There is a lack of visual impairments and neurological issues. There is no evidence of any medical records within the family that show the existence of neck tumors, fractures, or kidney stones.

The physical examination revealed a firm and immobile mass measuring 3x3 cm in the right thyroid region. There were no detectable swollen lymph nodes in the neck. The abdominal bowel sounds were normal. Upon inspection of the limbs, abnormalities were observed in the right upper arm and right thigh regions.

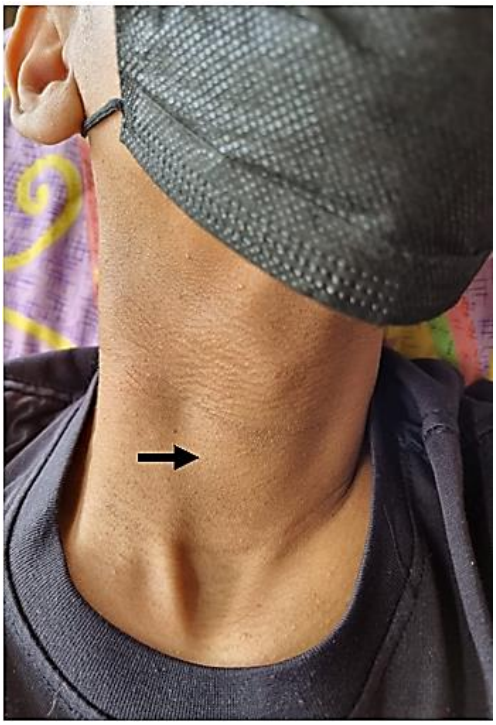

**Figure 1.** Mass in the right thyroid region (black arrow)

From the laboratory examination, the calcium level was found to be elevated at 8.58 mg/dL (normal range: 4.5 - 5.6 mg/dL). There was a significant increase in parathyroid hormone levels, measuring 1720 pg/mL (normal range: 15 - 65 pg/mL). Alkaline phosphatase levels were elevated at 2166 U/L (normal range: 46 - 116 U/L). Phosphate levels were decreased at 1.99 mg/dL (normal range: 2.5 - 4.9 mg/dL). Additionally, vitamin D levels were found to be decreased at 6.8 mg/dL (normal range: 30 - 100 mg/dL).

The right femoral X-ray revealed a malunion fracture with an accompanying plate

screw. The X-rays revealed malunion fractures and reduced bone density in the left femoral and right humerus. Radiographs of the thorax and pelvis revealed a reduction in bone density throughout all skeletal areas. The abdominal ultrasonography revealed the presence of multiple nephrolithiasis in both kidneys. An ultrasound of the neck revealed a heterogeneous hypoechoic mass with anechoic components, well-defined borders, irregular edges, and calcifications, measuring 3.65 x 2.08 x 4.41 cm. The mass originates from the right parathyroid gland and exerts pressure on the right thyroid gland. The ultrasound image was validated by a CT scan of the neck, which revealed a tumor in the right parathyroid gland and enlarged lymph nodes at levels IIA and IIB, with the largest measuring 1.82cm. The patient also had a Technetium-99m sestamibi parathyroid scan, which revealed evidence of a parathyroid adenoma located in the midpole lobe of the right thyroid. This finding was consistent with the Perrier Type D classification. Based on the available supporting investigations, it may be determined that this is a case of primary hyperparathyroidism with a possible diagnosis of parathyroid carcinoma.

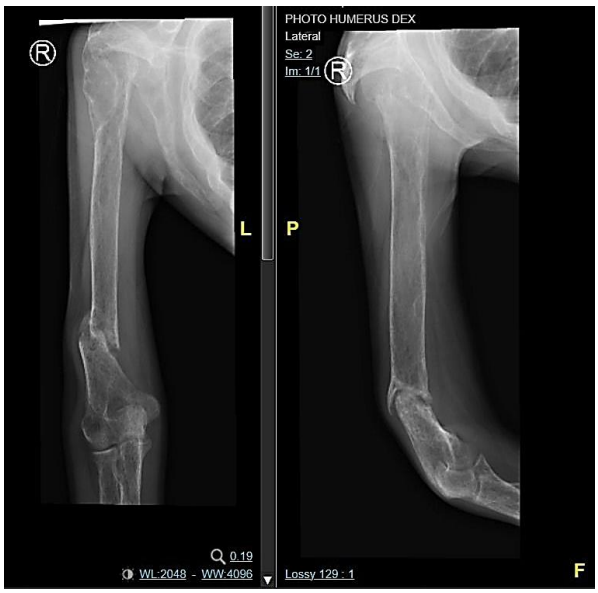


**Figure 2.** Right humerus X-Ray. There were fractures and lytic lesions of the bones.

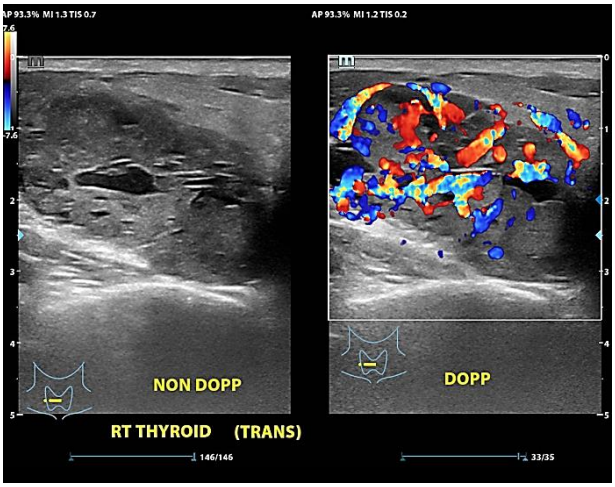


**Figure 3.** Right thyroid ultrasound. There was a mass pressing against the right thyroid, suspecting a parathyroid tumor.

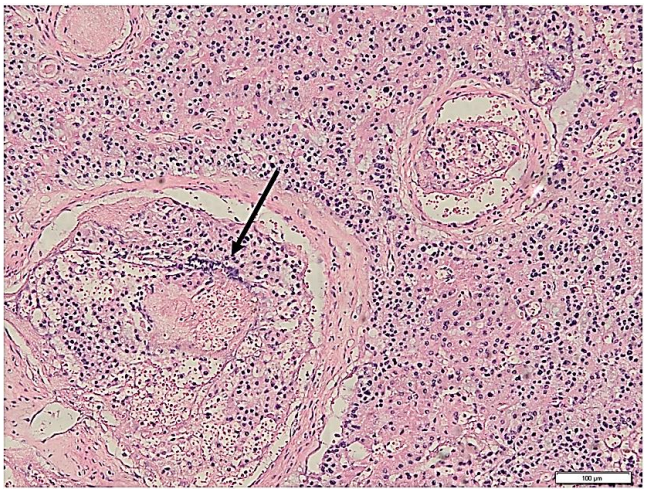

**Figure 4.** Histopathological analysis showing the tumor cells invaded the lymph vascular vessel (black arrow)

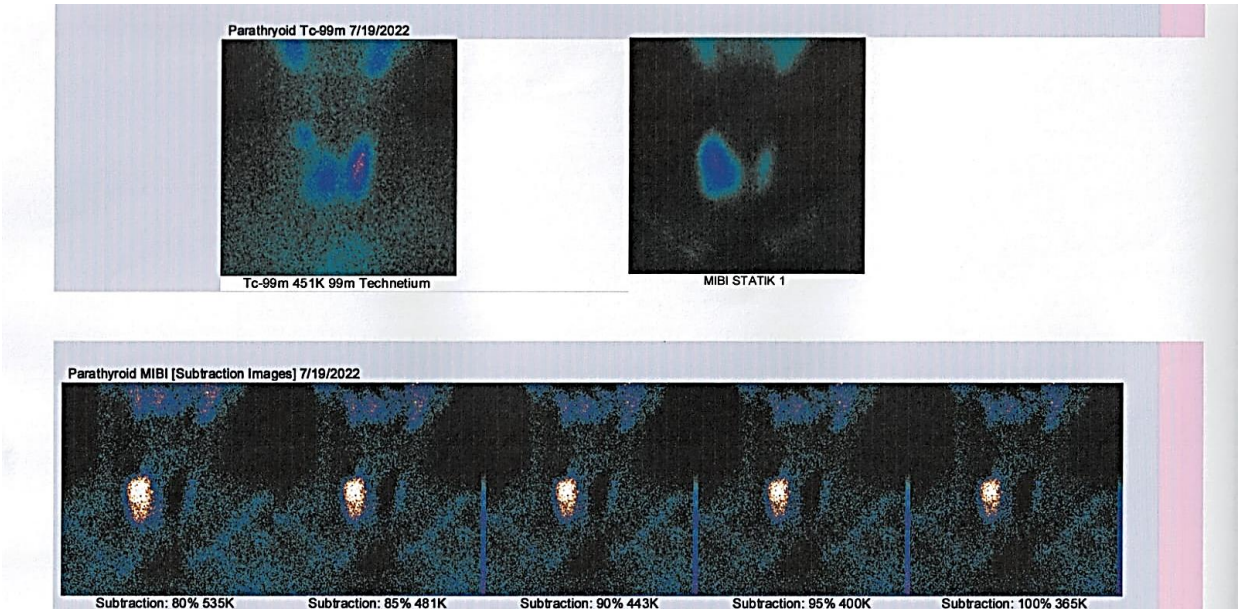


**Figure 4.** A Technetium-99m scan of Sestamibi showed parathyroid enlargement in the midpole of the right thyroid lobe.

### Therapeutic Intervention

The patient had preoperative preparations for parathyroidectomy surgery, which included hydration with a 0.9% sodium chloride solution, administration of zoledronic acid, and a single dose of 5000 units of vitamin D. An oncology surgeon performed surgery on the patient, resulting in the extraction of a tumor measuring 6 x 4.5 x 3 cm. The histopathological analysis revealed the presence of hyperplastic oval round cells, forming the trabecular structure. The cell nucleus displayed pleomorphism, hyperchromatism, and the presence of mitosis. Additionally, the tumor cells had invaded the lymph vascular vessels, leading to the diagnosis of parathyroid carcinoma. Following the procedure, the patient was treated with a 1-gram intravenous bolus of calcium gluconate, followed by a 4-gram intravenous drip. We monitored calcium levels at 6-hour intervals for a total of 72 hours after the operation. The patient had measurements of parathyroid hormone levels both during and after the surgery. Additionally, the patient was prescribed a daily dose of 0.5 mg of calcitriol twice a day and a daily dose of 5000 units of vitamin D.

Continuing monitoring until the fourth day after the surgery, calcium levels returned to the normal range, and both the intraoperative and 4-hour postoperative parathyroid hormone (PTH) levels were within the normal range. However, on the fifth day after the surgery, patients experienced sensations of tingling and muscle cramping, but did not have seizures. The patient's vital signs were steady during the physical examination, nevertheless, Chvostek's Sign and Trousseau's Sign yielded favorable findings. The ECG study revealed no extended QTc or arrhythmia. The laboratory tests indicate a notable reduction in calcium levels, as depicted in the chart.

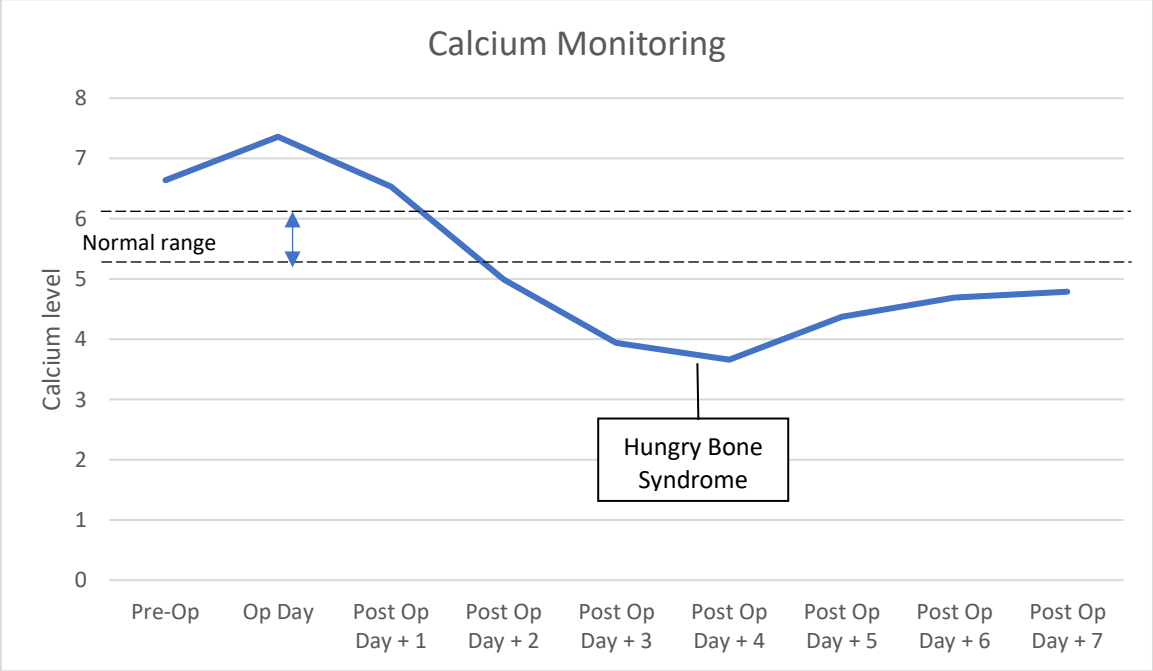


**Figure 6.** Calcium monitoring

The patient received a diagnosis of Hungry Bone Syndrome following the parathyroidectomy. To correct the low calcium levels, the patient received periodic intravenous administration of calcium gluconate, and the dose of calcitriol was increased to 4x0.5 mg. This treatment resulted in a positive therapeutic response. On the seventh day after surgery, the patient was discharged and prescribed home medications, including calcium carbonate 1x1000 mcg, calcitriol 2x0.5 mg, and vitamin D 1x5000 units. Three months later, there were no reports of hypocalcemia, and the laboratory examination showed normal calcium levels.

## DISCUSSION

Primary hyperparathyroidism is a condition characterized by the parathyroid glands overproducing parathyroid hormones. When the PTH Levels increase, the kidneys enhance the reabsorption of calcium, leading to an increased excretion of phosphorus in the urine. This results in the production of more 1,25-dihydroxy vitamin D and an accelerated breakdown of the bone tissue. This condition will result in elevated levels of calcium in the blood (hypercalcemia), low levels of phosphate in the blood (hypophosphatemia), reduced bone density, excessive calcium in the urine (hypercalciuria), and other long-term illnesses associated with high levels of calcium in the blood. The etiology of primary hyperparathyroidism includes parathyroid adenomas (75 - 80%), parathyroid hyperplasia (20%), and parathyroid carcinoma (<1 - 2%).[2]

Parathyroid carcinoma is the least common kind of primary hyperparathyroidism. The incidence rate is equal among both males and females, with an average age ranging from 44 to 54 years. Parathyroid carcinoma can arise due to genetic anomalies, either in the familial form, such as hyperparathyroidism-jaw tumor syndrome, or in the nonfamilial (sporadic) type. Parathyroid carcinoma is exceptionally uncommon in cases with multiple endocrine neoplasia.[2] No malignancy was detected in the patient's jaw area, and there was no reported family history of similar concerns.

The primary manifestations of parathyroid carcinoma typically include neck masses (34 - 52%), skeletal abnormalities (34 - 73%), and renal abnormalities (32 - 70%). Metastases can form in lymph nodes or spread to distant sites, such as the liver. The average calcium laboratory values range from 14.6 to 15.9 mg/dL, whereas the levels of parathyroid hormone are

typically 5 to 10 times higher than the upper limit of normal. Parathyroid carcinoma should be suspected in patients presenting with recurrent hypercalcemia, elevated PTH levels, a neck mass, or hoarseness.[6-8] Carcinomas are typically considered during surgery when there is evidence of local invasion into surrounding tissue.[2,6,7,9] The presence of pathological fractures, nephrolithiasis, neck masses, and significantly raised PTH levels in this patient support the suspicion of parathyroid carcinoma.

The imaging techniques used to locate the mass in the parathyroid glands include cervical ultrasound, sestamibi scan, or CT scan. An ultrasound examination is the most economically efficient procedure when conducted by a skilled operator. Combining sestamibi scan and ultrasound can improve the examination's precision and sensitivity.[9] An ultrasound examination and sestamibi scan revealed an expansion of the parathyroid glands in the midpole of the patient. Additionally, a cervical CT scan showed an enlargement of the lymph nodes.

Trabecular patterns, mitotic features, fibrosis bands, and signs of vascular or capsular invasion are common histological features of parathyroid carcinoma. A definite diagnosis is established when lymph node metastases or distant metastases are present.[10,11] Our patient's histopathological findings reveal lymph vascular invasion, corroborated by the CT scan's observation of enlarged lymph nodes. These results validate the diagnosis of parathyroid carcinoma.

Surgery remains the most effective treatment for primary hyperparathyroidism, including cases of parathyroid carcinoma. The surgical success rate is 95%.[3] Postoperative hypocalcemia is usually mild and transient, occurring on days 2 or 3 postoperatively. Some patients can develop prolonged hypocalcemia after parathyroidectomy with normal PTH results, this phenomenon is called Hungry Bone Syndrome (HBS). Although there is no consensus definition of HBS, some literature states that it occurs when there is severe hypocalcemia on day four or more postoperatively.[12] This phenomenon can arise because of the discontinuation of bone resorption followed by bone formation and subsequent remineralization after parathyroidectomy. Hypocalcemia may present with moderate symptoms such as muscle cramps or tingling, more severe symptoms like tetany or seizures, or life-threatening signs such as cardiac arrhythmias.

The prevalence of HBS in primary hyperparathyroidism following parathyroidectomy varies between 8.6% and 59%. The occurrence of the condition is higher when bone abnormalities are detected in radiology, as compared to when there are no bone abnormalities (25 - 90% vs. < 6%). Elevated pretreatment levels of PTH and alkaline phosphatase (ALP) can serve as indicator for the development of HBS following parathyroidectomy.[13] Low vitamin D levels as a predictor of HBS remain controversial.[5]

The primary approach in HBS treatment is to replenish calcium levels in the bones. Following intravenous calcium administration, oral calcium supplementation and the active form of vitamin D (calcitriol) should be initiated right away. The recommended daily dosage for calcium supplementation might range from 6 to 12 grams. Phosphate supplementation is not generally indicated for correcting hypophosphatemia due to the potential to worsen hypocalcemia, unless there is notable weakness and heart failure.[14]

There are several methods to prevent HBS after parathyroidectomy, including the preoperative use of cholecalciferol, calcitriol, and bisphosphonates.[14] Researchers suggest cholecalciferol to enhance blood levels of vitamin D, but the evidence for its use in preventing HBS is debatable.[14,15] Calcitriol has been found to be effective in enhancing calcium levels, but, research investigations have not demonstrated favorable outcomes in terms of preventing HBS. Administration of bisphosphonates, such as clodronate, alendronate, pamidronate, zoledronate, or ibandronate, has demonstrated efficacy in

preventing HBS. However, their effectiveness is limited in individuals with severe and long-lasting bone abnormalities.[14]

The patient exhibited persistent hypocalcemia on days 3 and 4 after surgery, while having normal levels of PTH, which provides evidence for HBS. Patients had modest symptoms associated with hypocalcemia but did not show any abnormalities in the electrocardiogram (ECG) attributable to arrhythmia. Treatment for hypocalcemia involved administering calcium gluconate intravenously and calcium carbonate orally at a dosage of 1000 mg. Additionally, calcitriol and cholecalciferol were given. We closely monitored calcium levels and electrocardiogram (ECG) readings during the treatment. The radiography reports indicated that our patient has been experiencing significant bone anomalies for an extended period. Despite the administration of cholecalciferol, calcitriol, and bisphosphonates as preventive measures, our patient still suffers from HBS. The therapeutic intervention yielded favorable outcomes, leading to the patient's discharge with a notable improvement in calcium levels.

## CONCLUSION

Parathyroid carcinoma should be considered a potential cause of primary hyperparathyroidism, particularly in patients who have bone lesions, nephrolithiasis, and significantly elevated levels of parathyroid hormone. Parathyroidectomy is the primary treatment option for parathyroid carcinoma. It is important to evaluate the occurrence of Hungry Bone Syndrome following parathyroidectomy in patients with parathyroid carcinoma, since they have a higher likelihood of developing this complication due to severe and prolonged hypocalcemia.

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