Pharmacogn J. 2022; 14(6): 863-866
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Research Article

Parathyroid Carcinoma Mimicking Multiple Myeloma: A Tale of Refractory Hypercalcemia

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ABSTRACT

Primary hyperparathyroidism yields various symptoms, including hypercalcemia, pathological fracture, and renal impairment. Parathyroid carcinoma is the rarest cause of primary hyperparathyroidism, accounting for <1% of the cases. We reported a case of a 46-year-old male with closed fractures at the humerus and femur. Further findings revealed severe refractory hypercalcemia, renal impairment, anemia, and bone lytic lesion (CRAB). No palpable cervical mass was identified. Surprisingly, the serum protein electrophoresis was normal, and urinary Bence-Jones protein was negative along with normal bone marrow aspiration. Hence, multiple myeloma was unlikely. The intact parathyroid hormone level was very high, along with a suspicious nodule on the left thyroid lobe (TIRADS 4). Total thyroidectomy and total parathyroidectomy were performed. The post-surgical pathological examination confirmed the diagnosis of parathyroid carcinoma. After the surgery, the patient was in stable condition with normal intact parathyroid hormone and serum calcium levels. In this case, primary hyperparathyroidism was caused by parathyroid carcinoma with "CRAB" symptoms, mimicking multiple myeloma. Primary hyperparathyroidism should be considered in the patient with refractory hypercalcemia.

Key words: Primary hyperparathyroidism, Hypercalcemia, Parathyroid tumor, Multiple myeloma, Case report.

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History

- Submission Date: 18-09-2022;
- Review completed: 27-10-2022;
- Accepted Date: 14-11-2022.

DOI : 10.5530/pj.2022.14.180

Article Available online

http://www.phcogj.com/v14/i6

INTRODUCTION

Primary hyperparathyroidism (PHPT) yields numerous symptoms related to high parathyroid hormones (PTH), such as hypercalcemia, kidney stone, and bone disease. Parathyroid carcinoma (PC) is the rarest cause of PHPT which accounts for less than 1% of the cases.[1] While anemia is not common in PHPT, we reported a rare case of PC with "CRAB" symptoms mimicking multiple myeloma.

PATIENT AND OBSERVATION

Patient information

A 46-year-old male came to the ER with closed fractures of the right humerus and left femur. The patient complained of weakness in the extremities and fell from a motorcycle one week before. The patient experienced pain in the respective extremities for two months. History of previous and familial disease was denied.

Clinical findings

The general condition was weak with normal vital signs. The Wong-Baker Pain Scale was 8. The head and neck examination revealed anemic conjunctiva without any palpable mass on the neck. Assessment of chest and abdomen was normal. There were deformities in the right humerus and left femur.

Diagnostic assessment

The laboratory examination showed normocytic-normochromic anemia (Hb 7.2 g/dL), increased serum creatinine (2.23 mg/dL), BUN (23 mg/dL), serum calcium (15.3 mg/dL), alkaline phosphatase (491 U/L), and normal serum phosphate (3.1 mg/dL). While imaging examination revealed complete fractures at 1/3 midshaft right humerus and 1/3 proximal left femur. In addition, multiple diffuse small lytic lesions were identified at the pelvic bone, bilateral femur, and left tibia-fibular bone.

Timeline of the current episode

Based on these "CRAB" findings, the initial suspicion was multiple myeloma. The patient was planned for serum protein electrophoresis, urinary Bence-Jones protein analysis, and bone marrow aspiration. Surprisingly, the serum protein electrophoresis was normal, urinary Bence-Jones protein was negative along with normal bone marrow aspiration. Hence multiple myeloma was ruled out.

During the treatment course, hypercalcemia was resistant to correction (Figure 1). The intact parathyroid hormone was tested and showed a very high concentration (4.063 pg/mL), suggesting primary hyperparathyroidism. The neck and thyroid ultrasound imaging discovered a regular, solid, iso- to heteroechoic lesion (1.57 x 2.10 x 2.66 cm) with macrocalcification and intra- and peri-vascularization at the left thyroid lobe, suggesting a moderately suspicious nodule on the left thyroid lobe (TIRADS 4). A fine-needle aspiration biopsy with USG guiding revealed nodular colloid goiter with atypical cells. The abdominal X-ray and USG also revealed bilateral nephrolithiasis potentially due to hypercalciuria (urine calcium 1.086 mg/24 hours).

Diagnosis

The pre-surgical diagnosis was a parathyroid tumor with suspicion of malignancy.

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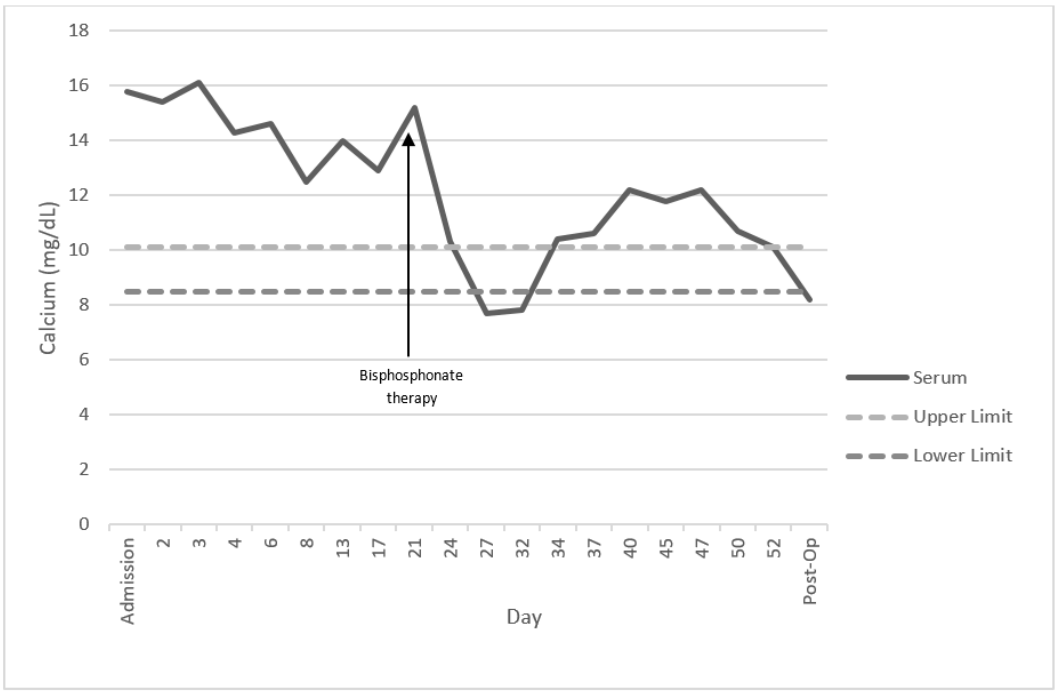

Figure 1: Serum calcium levels during treatment.

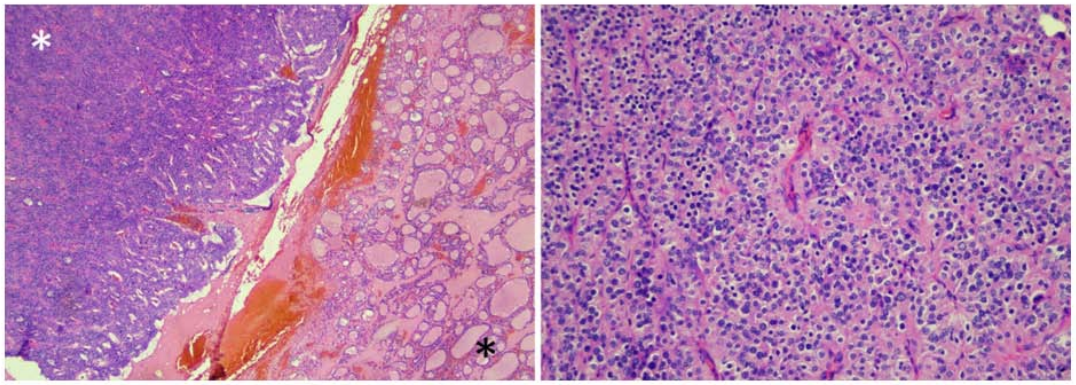

Figure 2: Post-surgical pathological findings: A. White asterix: parathyroid carcinoma, black asterix : normal thyroid tissue (200x) and B. anaplastic cells of parathyroid carcinoma (400x).

Therapeutic interventions

The patient underwent total thyroidectomy and total parathyroidectomy. The post-surgical pathological examination revealed homogenous anaplastic cells with round-hyperchromatic nuclei and prominent nucleoli. These cells formed a solid and trabecular structure with high mitotic activity (13/10 HPF), confirming the diagnosis of parathyroid carcinoma (Figure 2).

Follow-up and outcome of interventions

The iPTH (26.74 pg/mL) and serum calcium level (8.2 mg/dL) were normal after the surgery. The patient was stable and received calcium supplementation (3x1000 mg) and calcitriol (2 x 0.5 mcg).

DISCUSSION

Hypercalcemia is defined as serum calcium concentration above 10.5 mg/dL. About 90% of hypercalcemia is caused by hyperparathyroidism and malignancy. The concentration of intact PTH is the primary key in determining the etiology of refractory hypercalcemia. Conditions such as cancer, bone lysis, and granulomatous diseases often cause hypercalcemia with a low level of intact PTH. On the contrary, hyperparathyroidism (primary and tertiary) causes refractory hypercalcemia with elevated intact PTH and normal to increased 24-hours urine calcium.[2-4]

Primary hyperparathyroidism (PHPT) is a parathyroid gland abnormality causing inappropriately high and unsuppressed PTH.

The symptoms of PHPT are related to PTH hyperactivity, such as hypercalcemia, bone diseases (fracture and pain), and kidney stone formation. In contrast to tertiary hyperparathyroidism, PHPT has a normal serum phosphate level.[1]

In our case, the patient experienced all "CRAB" symptoms, increasing the suspicion of multiple myeloma. However, the serum protein electrophoresis, urinary Bence-Jones, and bone marrow aspiration (the critical diagnostic modality of myeloma) were normal.[5] Primary hyperparathyroidism and multiple myeloma have similar calcium and bone-related symptoms such as hypercalcemia, renal impairment, and bone diseases. However, anemia is one distinguishable feature of multiple myeloma.

Anemia is not a common feature of PHPT. Only 5.3% of PHPT patients had anemia. Interestingly, the PTH level was four times higher in those with anemia, suggesting PTH influences erythropoiesis.[6] Growing theory hypothesized that a very high concentration of PTH reduces erythropoietin receptors on erythroid progenitor cells, resulting in normocytic-normochromic anemia.[7] In this patient, the iPTH was 4.063 pg/mL, 60-folds higher than local standard value.

Parathyroid carcinoma (PC) is the rarest cause of PHPT which accounts for <1% of the cases. Characteristics of PC include hypercalcemia (>14 mg/dL), kidney involvement (calcification, nephrolithiasis, impaired function), and bone diseases (diffuse osteopenia, osteitis fibrosa cystica, "salt and pepper" calvaria). Palpable mass in the neck was observed in 37,5-76% of the cases.[8-10] Most of the PC are functional, which produces markedly high PTH concentration, which might explain the cause of anemia in this patient.

The pre-surgical diagnosis of PC is very challenging due to similar clinical presentations with adenoma. About 52% of the PC diagnosis was made after the histopathological examination of the surgical specimen. The PC is characterized by large mass (>3 cm), irregular, and often infiltrated to adjacent tissues. Common microscopic findings are thick fibrous bands, high mitotic activity, invasion of the vascular or capsular, trabeculae, and lymphatics invasion.[11] Immunohistochemistry examination using Ki-67 and Cyclin D1 also improve the diagnostic accuracy of PC.[12]

While pathology is paramount, laboratory and imaging examinations are also important in diagnosing PC. Serum calcium above 14 mg/dL, PTH level of 3-15 folds of the standard upper limit, increased alkaline phosphatase, and hCG are suggestive features of PC compared to adenoma. Ultrasonography is the most widely used modality, which describes the PC as lobulated, hypoechoic, irregular mass. In addition, local infiltration, presence of vascularization, and thick capsules are predictive of malignancy.[13]

The patient underwent total thyroidectomy and total parathyroidectomy and was stable after the surgery. These surgical procedures increase the risk of hypocalcemia. Hence, the patient received calcium supplementation and calcitriol to prevent post-operative hypocalcemia.[14]

CONCLUSION

This case describes PC with "CRAB" symptoms mimicking multiple myeloma. Diagnosis of hyperparathyroidism should be considered among patients with refractory hypercalcemia and its related symptoms.

COMPETING INTERESTS

The authors declare no competing interest.

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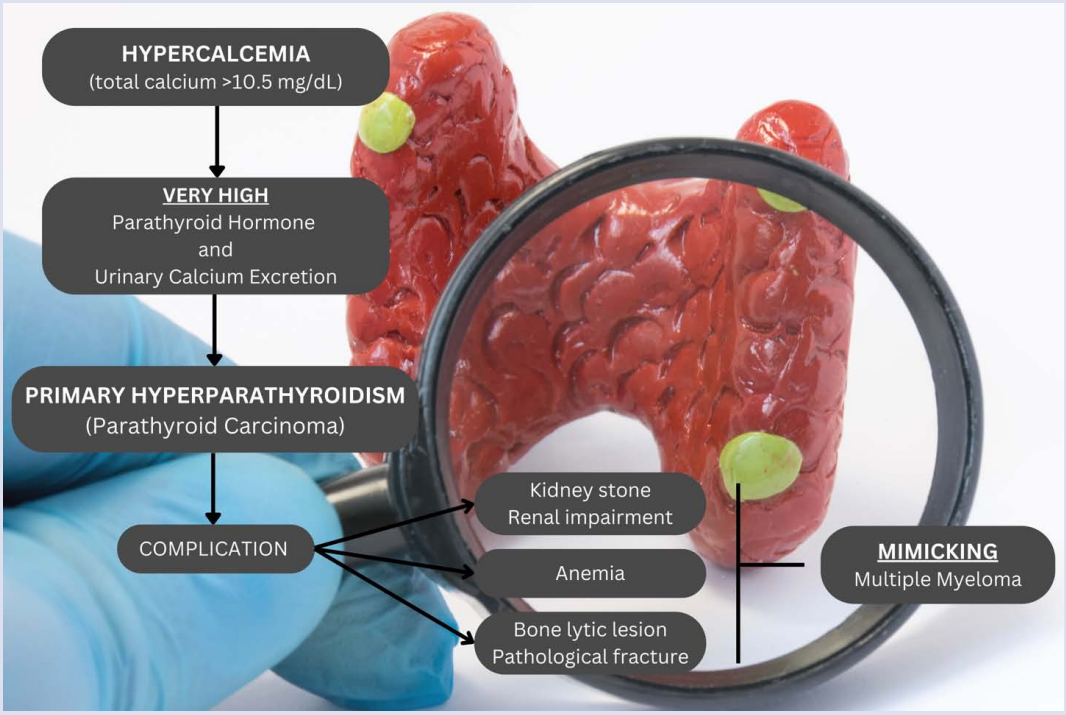
GRAPHICAL ABSTRACT



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