ONCOLOGÍA

ISSN: 2661-6653

DOI: https://doi.org/10.33821/780
Article / Artículo

Parathyroid carcinoma with multiple brown tumors and pathological fracture: A case report

Carcinoma de paratiroides con tumores pardos múltiples y fractura patológica: reporte de caso

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Received: 17/08/2025
Accepted: 28/01/2026
Published: 01/04/2026

ABSTRACT

Introduction: Parathyroid carcinoma is a rare endocrine neoplasia that accounts for less than 1% of cases of primary hyperparathyroidism and usually presents with severe hypercalcemia and bone involvement. **Clinical case:** A 27-year-old male patient was referred for persistent pain in his right knee, exacerbated by minor trauma. Radiographic studies identified a pathological fracture and multiple osteolytic lesions. Biochemical analyses showed severe hypercalcemia (16.9 mg/dL), acute renal failure, and electrolyte disturbances. A bone biopsy reported a brown tumor, and a parathyroid scan revealed an ectopic mediastinal adenoma. The parathyroid adenoma was resected, and immunohistochemical analysis showed vascular permeation with a positive CD31 staining, confirming parathyroid carcinoma. The patient underwent complementary hemithyroidectomy, orthopedic treatment with tumor dissection, cementation, and internal fixation, along with zoledronic acid. The patient is currently being monitored without clinical or biochemical recurrence. **Conclusion:** This case highlights the importance of considering parathyroid carcinoma in young patients with severe hypercalcemia and multiple bone lesions. Immunohistochemistry is essential to confirm malignancy and determine surgical treatment. Comprehensive multidisciplinary management reduces complications, controls hypercalcemia, and improves prognosis.

Keywords: Parathyroid carcinoma, brown tumors, pathological fracture, hyperparathyroidism, clinical case.

RESUMEN

Introducción: El carcinoma de paratiroides es una neoplasia endocrina poco frecuente que representa menos del 1 % de los casos de hiperparatiroidismo primario y suele manifestarse con hipercalcemia severa y afectación ósea. **Caso clínico:** Paciente masculino de 27 años, remitido por dolor persistente en rodilla derecha reagudizado por traumatismo leve. Estudios radiográficos identificaron fractura patológica y múltiples lesiones osteolíticas. Los análisis bioquímicos mostraron hipercalcemia severa (16,9 mg/dL), falla renal aguda y alteraciones electrolíticas. La biopsia ósea reportó tumor pardo, y la gammagrafía paratiroidea reveló un adenoma ectópico mediastínico. Se realizó resección de adenoma paratiroideo y el estudio inmunohistoquímico evidenció permeación vascular mediante positividad para CD31, que confirmó carcinoma de paratiroides. El paciente recibió hemitiroidectomía complementaria, tratamiento ortopédico con vaciamiento tumoral, cementación y osteosíntesis, junto con ácido zoledrónico. Actualmente, continúa en seguimiento sin recidiva clínica ni bioquímica. **Conclusión:** Este caso destaca la importancia de considerar carcinoma de paratiroides en pacientes jóvenes con hipercalcemia severa y lesiones óseas múltiples. La inmunohistoquímica resulta esencial para confirmar la malignidad y definir el tratamiento quirúrgico. El manejo integral multidisciplinario permite reducir complicaciones, controlar la hipercalcemia y mejorar el pronóstico.

Palabras clave: carcinoma de paratiroides, tumores pardos, fractura patológica, hiperparatiroidismo, caso clínico.

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How to cite: Zhindón Astudillo, M, Criollo Vargas, E, Arteaga Ludeña, L, Zambrano Franco E. Parathyroid carcinoma with multiple brown tumors and pathological fracture: A case report. Oncología (Ecuador). 2026;36(1): 1-6. https://doi.org/10.33821/780

1. Introduction

The parathyroid glands consist of four glands that regulate serum calcium levels through parathyroid hormone (PTH), which is produced by the chief cells. PTH acts on bones, kidneys, and the intestine, promoting calcium release, reabsorption, and absorption, respectively, as well as stimulating vitamin D production. Its secretion is regulated by serum calcium and vitamin D levels through a negative feedback mechanism. Oxyphil cells, which are present in smaller numbers, have no clearly defined endocrine function. Hyperparathyroidism increases serum calcium levels and may be primary, secondary, or tertiary, whereas hypoparathyroidism reduces calcium levels and is usually caused by surgery. Both disorders severely affect mineral and neuromuscular balance [1].

Parathyroid carcinoma (PC) is a very rare endocrine malignancy, accounting for less than 1% of cases of primary hyperparathyroidism and presenting with an extremely low annual incidence. It can occur at any age, including in the pediatric population. The mean age at diagnosis reported in most clinical series ranges from 51 to 57 years, with no clear sex predilection. Its etiology is often unknown, although it has been associated with genetic syndromes such as hyperparathyroidism–jaw tumor (HPT-JT) syndrome and mutations in the CDC73 gene, among others [2,3].

Clinically, PC presents symptoms of severe hyperparathyroidism and may include a palpable neck mass and serious metabolic complications. Definitive diagnosis requires histological confirmation of tumor invasion, which makes preoperative identification challenging. Early surgical intervention is the treatment of choice to improve prognosis. Due to the rarity of this disease, case reports are valuable to expand clinical and therapeutic knowledge [4].

This case report presents a clinical experience in Ecuador, it describes the diagnosis, treatment, and outcome of a patient with parathyroid carcinoma. It aims at contributing to the understanding and management of this rare disease in the local context.

2. Case report

A 27-year-old male patient with no relevant past medical or surgical history was referred from a hospital within the Ecuadorian public health network due to persistent pain in the right knee of approximately one year's duration, which worsened following a traumatic event. After the trauma, radiographic studies of the affected limb revealed an osteolytic lesion at the distal condyle of the right femur associated with a pathological fracture. Based on the radiological characteristics of the lesion, osteosarcoma was initially considered as presumptive diagnosis.

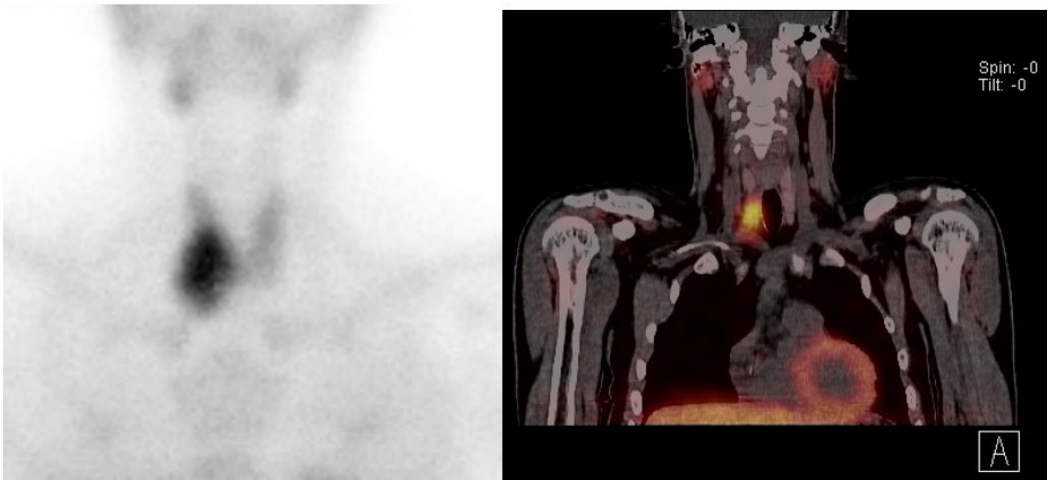
Upon hospital admission, the patient was conscious, hemodynamically stable, and reported mild pain localized to the affected limb. Physical examination revealed grade 3 edema according to the Godet scale and pain on deep palpation of the right knee. Initial biochemical studies showed significant metabolic abnormalities, including serum calcium of 16.9 mg/dL; ionized calcium, 7.94 mg/dL; creatinine, 1.22 mg/dL; PTH level, 1604 pg/mL; and electrolyte disturbances such as potassium imbalance, hypomagnesemia, and hypophosphatemia, as well as indirect hyperbilirubinemia. Given the clinical and biochemical context, a whole-body computed tomography scan was performed, which revealed multiple osteolytic lesions involving the left maxilla, distal condyle of the right femur with pathological fracture, pelvis, scapulae, sternum, several thoracic vertebrae, and bilateral costal arches, suggestive of disseminated bone disease.

A bone biopsy of the right femoral lesion was performed, and the histopathological report revealed the presence of a brown tumor associated with hyperparathyroidism. Based on these findings, parathyroid scintigraphy was requested, which demonstrated an ectopic adenoma located in the right anterosuperior mediastinum (Figure 1).

The patient underwent exploratory cervicotomy with resection of a parathyroid adenoma, following an intraoperative PTH monitoring protocol using the Miami criteria. The following PTH values were obtained: 1529 pg/mL post-incision, 297 pg/mL at 5 minutes, 231 pg/mL at 10 minutes, and at 15 minutes [value]. Intraoperative frozen section analysis was performed and reported as negative for malignancy; macroscopic features were consistent with benign pathology. However, subsequent immunohistochemical analysis demonstrated positivity for CD31, thus confirming tumor vascular invasion and allowing reclassification of the case as low-grade parathyroid carcinoma. Consequently, right hemithyroidectomy was indicated as part of the oncologic surgical management.

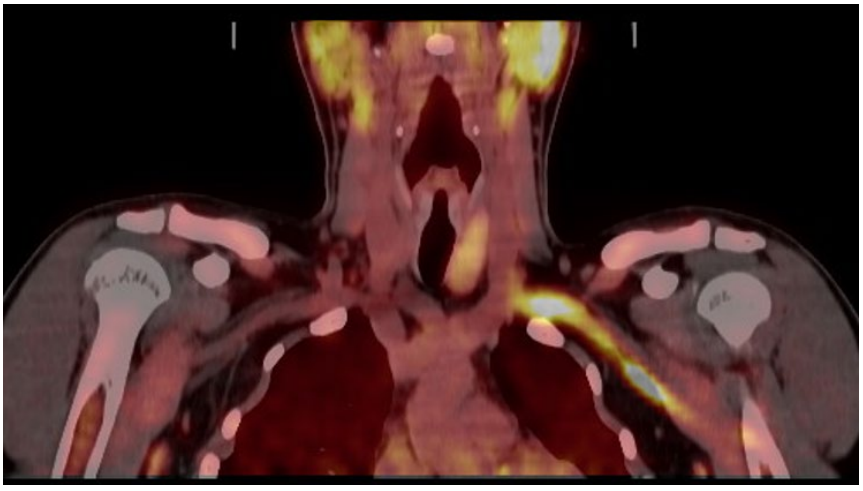
Subsequently, due to the pathological lesion of the right femur, an orthopedic procedure was performed. It included tumor curettage, bone cementation, and prophylactic osteosynthesis of the affected limb. As part of the metabolic management, the patient received an infusion of zoledronic acid. At present, the patient remains under multidisciplinary outpatient follow-up and is receiving replacement therapy with calcitriol, calcium carbonate, and cholecalciferol. Serum parathyroid hormone levels have remained within normal limits (PTH 58 pg/mL) with no clinical or biochemical evidence of disease recurrence according to the most recent PET/CT report (Figure 2).

Figure 1. Parathyroid scintigraphy: Hyperfunctioning ectopic parathyroid adenoma located in the right anterosuperior mediastinum.



Source: SOLCA - Guayaquil

Figure 2. 18F-choline PET/CT: Thyroidectomy. The left thyroid lobe shows a homogeneous appearance, with no evidence of hypermetabolic foci suggestive of active functional lesions.



Source: SOLCA - Guayaquil

3. Discussion

Parathyroid carcinoma (PC) is a rare endocrine malignancy (<1% of primary hyperparathyroidism cases) characterized by severe hypercalcemia (≥17 mg/dL), markedly elevated PTH levels (>1600 pg/mL), and significant skeletal involvement, including pathological fractures and lytic lesions such as those observed in this patient [5,6].

Definitive diagnosis is established through histopathological examination of the complete surgical specimen following parathyroidectomy. Although certain features—such as cytological atypia or trabecular growth patterns—may suggest malignancy, the diagnosis requires clear evidence of invasion into surrounding tissues or the presence of metastases. According to the 2022 World Health Organization (WHO) classification, parathyroid neoplasms are considered malignant when angioinvasion, lymphatic invasion, perineural invasion, local invasion, or documented metastases are present [7]. Vascular invasion identified by CD31 is a known predictor of poor prognosis and is associated with increased mortality and recurrence rates. Atypical parathyroid tumors share some histological features with PC but lack definitive invasive characteristics. Immunohistochemistry, particularly markers such as parafibromin, galectin-3, and a Ki67 index >5%, supports the diagnostic process [8]. In cases where an initial simple resection is performed and malignancy is confirmed postoperatively, surgical re-exploration with hemithyroidectomy is mandatory to ensure tumor-free surgical margins [6,9].

These molecular and histopathological alterations not only contribute to understanding tumor pathogenesis but also allow for individualized targeted therapies. Recent literature highlights the emerging role of molecular biomarkers, such as circulating tumor cells, as well as novel imaging modalities (including ^18FFDG PET/CT and 4D CT) for advanced staging and follow-up [10].

En bloc resection with negative margins remains the cornerstone of treatment, as simple local excision is associated with high recurrence rates ranging from 8% to 51%. In this case, complementary hemithyroidectomy was consistent with current evidence-based recommendations [11,12].

Refractory hypercalcemia significantly contributes to morbidity and mortality. The patient received zoledronic acid and calcium/vitamin D supplementation, in accordance with current clinical guidelines [13]. In advanced cases, agents such as Cinacalcet, Denosumab, and even targeted therapies have been evaluated in recent reports, showing favorable effects on calcium control and tumor stabilization [14,15].

In patients with advanced or metastatic disease, promising responses have been reported with tyrosine kinase inhibitors (TKIs) such as Sorafenib, Lenvatinib, Everolimus, and Sunitinib, as well as combinations with Denosumab and calcimimetics—particularly in patients harboring activating mutations in pathways such as PI3K/AKT/mTOR, KDM5C, and *CDC73* [16]. Although clinical trials remain limited, these therapies offer new perspectives, especially in multidisciplinary referral centers [15].

Five-year survival rates range from 60% to 93%, largely dependent on effective hypercalcemia control and complete surgical resection. The presence of bone metastases, as seen in this case, requires a multidisciplinary surgical approach, including orthopedic intervention, curettage, and cementation—to relieve symptoms and normalize calcium levels, findings that are consistent with previously reported series [17]. Strict long-term follow-up with monitoring of serum calcium, PTH levels, and functional and structural imaging is essential due to the high risk of late recurrence, ideally in experienced centers with adequate endocrinologic and orthopedic support [18].

4. Conclusion

Parathyroid carcinoma is an uncommon but potentially lifethreatening endocrine neoplasm characterized by severe hypercalcemia and serious skeletal complications. Its diagnosis requires specific histological criteria, such as vascular permeation and capsular invasion. En bloc surgical resection with negative margins remains the treatment of choice. In advanced cases, adjuvant and targeted medical therapies have been incorporated with encouraging results. A multidisciplinary approach is essential to control hypercalcemia, stabilize bone lesions, and reduce recurrence. Survival depends largely on metabolic control and complete tumor resection. Longterm followup is mandatory due to the high rate of late recurrence.

5. Abbreviations

PTH: Parathyroid hormone

PC: Parathyroid carcinoma

HPTJT: Hyperparathyroidism–Jaw Tumor syndrome

PET/CT: Positron emission tomography/computed tomography

WHO: World Health Organization

^18FFDG PET/CT: Fluorine18 fluorodeoxyglucose PET/CT

4D CT: Fourdimensional computed tomography

TKIs: Tyrosine kinase inhibitors

6. Administrative Information

6.1 Acknowledgements

The authors sincerely thank the patient for consenting to the publication of this clinical case for academic and scientific purposes. We also acknowledge the patient's trust and the contribution of this experience to the continuous education of healthcare professionals.

6.2 Author Contributions (CRediT taxonomy)

María Zhindón Astudillo: Conceptualization, original draft preparation, writing, review and editing.

Emilio Criollo Vargas: Supervision.

Luis Arteaga Ludeña, Erick Zambrano Franco: Writing, review and editing.

All authors read and approved the final version of the manuscript.

6.3 Funding

This study did not receive any external funding. The research was conducted using the authors' own resources.

6.4 Declarations

The authors declare no conflict of interest.

Written and verbally informed consent was obtained from the patient for publication of this case report.

The authors are responsible for the content and writing of this manuscript. This article does not constitute an official therapeutic recommendation but represents an academic contribution based on clinical experience and literature review.

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