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CASE REPORT

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Diagnostic dilemma in a rare case of nonfunctional parathyroid carcinoma at a referral facility in Northern Tanzania

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Key Clinical Message

Rare cancer originating from parathyroid parenchymal cells. Preoperative diagnosis is often difficult. Presents with normal serum levels of calcium and parathyroid hormone. Treated by en bloc resection. Benefits of adjuvant therapy are unclear.

Abstract

Parathyroid carcinoma is an uncommon endocrine tumor. Its typical presentation is that of primary hyperparathyroidism with elevated serum calcium and parathormone levels. Nonfunctioning carcinoma of the parathyroid gland with normal serum calcium levels is extremely rare. This paper describes a case of nonfunctioning parathyroid carcinoma and brief literature review thereof.

KEYWORDS

histopathology, hyperparathyroidism, nonfunctional parathyroid carcinoma, Tanzania

1 | INTRODUCTION

Parathyroid carcinoma (PTC) is an uncommon endocrine tumor which comprises about 0.1%–5% of all cases of primary hyperparathyroidism (PHPT).[1] On the basis of serum levels of parathyroid hormone (PTH) and calcium, PTC tumors are categorized into two subtypes; functioning and nonfunctioning PTC; the vast majority being functioning PTC and produce elevated levels of functional PTH. Patients that present with hyperparathyroidism have high chances of having disease clinically detected early due to signs and symptoms of profound hypercalcemia. These include but not limited to kidney stones, nausea, abdominal pain, musculoskeletal aches, confusion, generalized body malaise, pancreatitis, headaches, osteoporosis, and depression.[2–4]

Patients with PTC who show normal or slight elevated serum levels of calcium and PTH are diagnosed as nonfunctioning PTC. The nonfunctional PTC is even rarer. As these patients do not experience of hypercalcemia, the diagnosis is usually delayed and thus, made because of locally advanced disease, such as a palpable neck mass, dysphagia, vocal cord paralysis, or hoarseness.[2] To date, only a few cases have been documented in the English literature. Herein, a case of nonfunctioning PTC is described and a brief review of the literate provided.

2 | CASE REPORT

A 42-year-old male presented to our institution's ear, nose, and throat clinic with a 6-month history of gradual onset and recent rapidly progressing left neck mass accompanied with hoarseness and tension pain. He denied history of fever, difficulty in swallowing and hearing loss. Physical examination revealed a 6×8×12 cm mass **(**Figure 1A**),** slightly mobile and non-tender with limitation of the neck rotation. Ultrasonography revealed a well-circumscribed heterogeneous and highly vascularized mass. The thyroid glands appeared of normal in size and consistency. A contrast CT imaging **(**Figure 2**)** showed a heterogeneous enhancing mass in the left supraclavicular region measuring 8×12 cm abutting the major vessels, and was associated with borderline neck lymphadenopathy.

Laboratory investigations demonstrated normal ranges of serum calcium and phosphorus levels. In addition, thyrotropin hormone, free thyroxine, and free triiodothyronine were within normal limits. Similarly, the serum PTH level was within normal range. Differential diagnoses of paraganglioma, parathyroid adenoma, and PTC were suggested. With multiple uncertain diagnoses and the rapidly worsening condition of the patient, an emergency left neck en bloc tumor resection was performed after obtained an informed consent which included a thorough counseling on the benefits and potential complications of the surgery such as the likelihood of postoperative cervical plexus neurological deficits.

Intraoperatively, the tumor appeared to arise from the ipsilateral substernal region extending superiorly into the tracheoesophageal groove, and laterally to invade the cervical plexus, the carotid sheath, sternocleidomastoid muscle, and the accessory nerve. Tumor resection-free margins could not be established. Subsequent neck dissection of left level II through V was carried out.

The specimen, **(**Figure 1B**)** was submitted for histopathology evaluation. Histopathology analysis of the mass reported infiltrating sheets of atypical cells with spherical nuclei, prominent nucleoli, inconspicuous cytoplasm, intervening fibrous bands, and ample necrosis **(**Figure 3A,B**).** The morphology was consistent with PTC as confirmed by positive immunostaining **(**Figure 3C**)** with PTH. Postoperative care was uneventful except for mild pain during sleeping as well as minimal discharge from the wound site. He was discharged on Day 7 after surgery. About 8 weeks postoperative, the he presented back with a slurred speech, left side mild trismus, cranial nerve IV, VII, IX, X, and XII palsy. At this point, the patient was not willing to undertake oncological treatment, opting for nonmedical remedies at home. He is lost to follow-up currently.

3 | DISCUSSION

PTC is a rare tumor and accounts for less than 1% of the cases of PHPT. PTC tumors are initially characterized by indolent, and later progressive and severe clinical manifestations.[1] The nonfunctioning variant accounts for less than 10% of all parathyroid tumors. While benign parathyroid diseases are four times predominant in the female population, PTC occurs equally in both sexes where the age of diagnosis is a decade earlier in the mid-40s compared to mid-50s in the benign variant.[1–4]

Etiology of PTC remains unclear, and there is no proof that it develops from parathyroid lesions that had already been present.[5] Instead, the recently discovered aberrant microRNA expression profile and methylation signature in PTCs show that benign lesions and cancers of the parathyroid gland are two different things. PTC can be sporadic or be a component of a hereditary disease.[6] Sporadic PTC has been associated with radiation exposure[7] and,

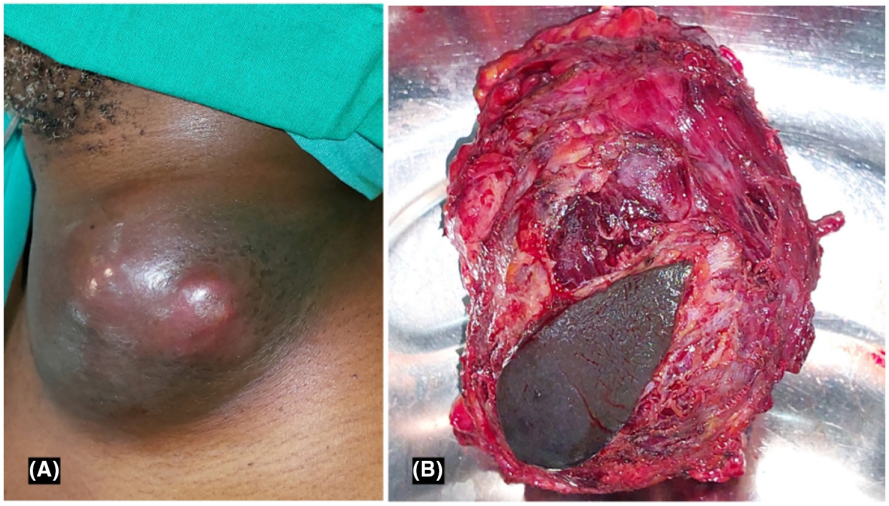

FIGURE 1 Preoperative image of the left neck tumor with infiltration of the overlying skin, (A). Gross appearance of the tumor specimen, (B).

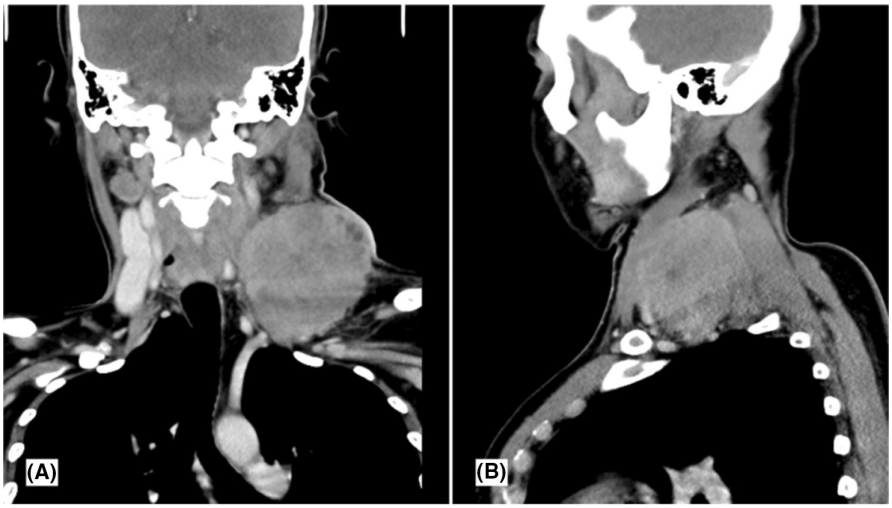

FIGURE 2 Coronal (A) and sagittal sections (B) of neck CT scan showing an enhancing mass occupying the left supraclavicular region extending to the posterior triangle with a displacement of the sternocleidomastoid muscle and the carotid sheath.

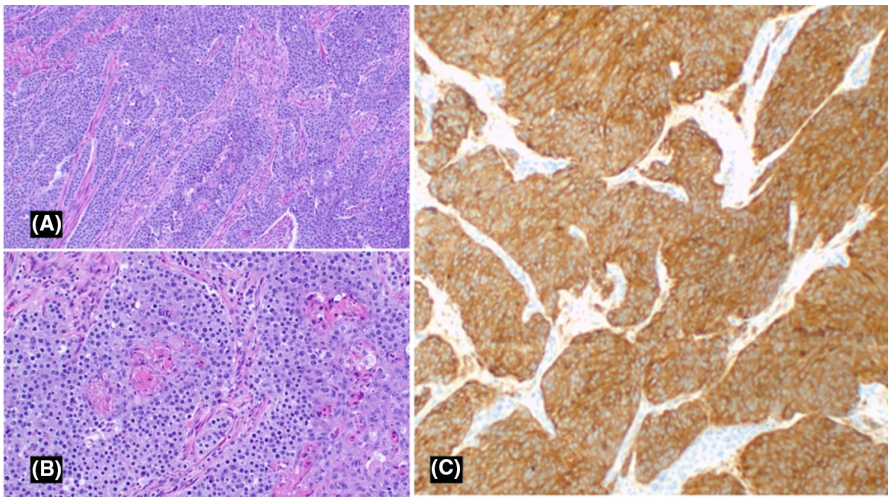

FIGURE 3 Hematoxylin & eosin stain photomicrographs of PTC tumor highlighting sheets of atypical cells with spherical nuclei, prominent nucleoli, inconspicuous cytoplasm, intervening fibrous bands, and ample necrosis, original 40× (A), and ×100 (B) magnifications, respectively; photomicroscopy of the tumor cells demonstrating positive immunostaining with PTH; 200× original magnification (C).

less frequently, secondary and tertiary HPT brought on by chronic renal failure. There has also been evidence linking PTC, whether synchronous or metachronous, to a history of PT gland hyperplasia, PA, or thyroid malignancy with concurrent parathyroid adenoma.[4,8] The parafibromin gene (CDC73/HRPT2) inactivating somatic mutations are the most frequent genetic abnormalities linked to PTC; other abnormalities include altered expression of the p53 and retinoblastoma proteins, as well as oncosuppressor genes on chromosome 13.[5] Up to one-fifth of cases from a recent large single-institution series indicated changes of the PI3K/AKT/mTOR oncogenic pathway, and roughly one-third of patients had cyclin D1 overexpression supported by its relative expression.[5]

About 10%–15% of the cases is related to hyperparathyroidism jaw tumor (HPT JT) syndrome.[5] An association with familial isolated hyperparathyroidism, multiple endocrine neoplasia types 1 and 2 have been reported.[6] Functional PTC normally presents with the effect of severe hypercalcemia, markedly raised PTH and manifestations in the renal and skeletal systems.[8] As evidenced in our patient, nonfunctioning PTCs may be asymptomatic or symptomatic with a neck mass being an isolated sign during physical examination.[2] CT and MRI are useful in detecting regional lymph nodes and distant metastasis.

Recommended treatment of choice is en bloc resection with ipsilateral hemithyroidectomy and central lymphadenectomy.[4,9] Benefits of adjuvant therapy (chemotherapy and radiotherapy) are unclear.[10] A good prognosis is dependent on the extent of resection of tumor-free margins. In our patient, we failed to extirpate the tumor in totality which implies that our surgery was not curative. This was partly due to considerably huge size and infiltrative nature of the tumor in relation to the vital neighboring organs including major blood vessels. Other prognostic indicators include necrosis, macronucleoli and more than 5 mitoses per 10 mm^2 which were also seen in our case. Similarly, older age at time of diagnosis, larger tumor size, and male gender have been established to carry negative prognostic factors as mirrored in the index case. Estimated 5-year and 10-year overall survival rates are estimated to be 78%–85% and 49%–70%, respectively.[11] While clinical assessment remains a challenge in the diagnosis of PTC,

histopathology analysis is a valuable tool to help to get a conclusive diagnosis.[12–15]

4 | CONCLUSION

In summary, nonfunctional PTC is an extremely rare malignant tumor. Due to limited symptoms of which a palpable neck mass is the most common, most patients with nonfunctional PTC tumors tend to present late with advanced disease stage and therefore, they have poorer outcomes than do those with functioning PTC and these tumors behave more aggressively.

AUTHOR CONTRIBUTIONS

Alex Mremi: Conceptualization; data curation; investigation; writing – original draft. **Michael Kayuza:** Data curation; writing – review and editing. **Patrick Amsi:** Data curation; investigation; writing – original draft. **Marco Magwizi:** Data curation; writing – review and editing. **Desderius Chussi:** Conceptualization; data curation; validation; writing – original draft.

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CONFLICT OF INTEREST STATEMENT

All authors have declared that no competing interests exist.

DATA AVAILABILITY STATEMENT

None.

ETHICAL APPROVAL

The patient provided written informed consent to allow for his deidentified medical information to be used in this publication. A waiver for ethical approval was obtained from the authors' institution review board committee.

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