Parathyroid carcinoma in Oman: a 10-year single-center experience and literature review

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ABSTRACT

Background: Parathyroid carcinoma is an exceptionally rare endocrine malignancy with poorly understood pathogenesis due to limited global data. It is often associated with unfavorable outcomes, largely attributable to delayed diagnosis and severe hypercalcemia.

Aims and Objectives: To present the clinical, biochemical, radiological, and pathological features of parathyroid carcinoma.

Settings: This study was a retrospective chart review conducted at the Endocrine Surgery Unit of the Royal Hospital, Muscat, Oman.

Methods: The medical records of all patients with histopathologically confirmed parathyroid carcinoma between January 2012 and December 2023 were examined.

Results: Four patients (three males, one female) with a mean age of 49 years were identified. Three patients were presented with symptomatic hypercalcemia, and one was diagnosed incidentally. Preoperative parathyroid hormone (PTH) levels were elevated in all patients, with one exceeding 80 times the upper limit of normal. All patients underwent surgical resection. Postoperative outcomes were favorable with no disease recurrence observed over at least 2 years of follow-up.

Conclusion: Parathyroid carcinoma remains a diagnostic challenge due to its rarity and overlapping features with benign disease. A high index of clinical suspicion, supported by significantly elevated PTH and calcium levels, is essential. This report emphasized towards the importance of prompt diagnosis and complete surgical excision in optimizing patient outcomes in the Arab population.

Keywords: Parathyroid, cancer, endocrine, parathyroid hormone (PTH), surgery.

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Background

Parathyroid carcinoma (PC) is among the rarest endocrine malignancies, accounting for less than 1% of primary hyperparathyroidism cases. It typically presents with more severe hypercalcemia than benign parathyroid disorders [1] and poses considerable diagnostic and therapeutic challenges. The clinical symptoms and complications of PC largely stem from excessive PTH secretion rather than tumor burden [1,2].

Common presenting features include symptomatic hypercalcemia, nephrolithiasis, bone pain, or a palpable neck mass. Rarely, patients might present with vocal cord paralysis due to recurrent laryngeal nerve invasion. Distant metastases, particularly to the lungs and thyroid gland, might occur. Unlike parathyroid adenomas or hyperplasia, parathyroid carcinoma carries a poorer prognosis, primarily due to intractable hypercalcemia. Reported 5-10-year survival rates range from 78% to 85% and 49%-70%, respectively [3].

Most cases are sporadic; however, some are associated with familial syndromes. The risk of malignancy might increase in chronically stimulated parathyroid glands, suggesting a potential link between hyperplasia and malignant transformation [4]. Preoperative diagnosis is challenging due to overlapping biochemical and radiologic features with benign disease [4]. Fine needle aspiration is generally avoided due to the risk of tumor seeding and limited diagnostic utility [1].

A markedly elevated PTH level, often 5-10 times the normal limit or more, in conjunction with severe hypercalcemia, might raise clinical suspicion [1]. Imaging techniques such as neck ultrasonography and Sestamibi scanning assist in lesion localization but are not definitive for malignancy [5].

Surgical resection remains the cornerstone of treatment, typically requiring en bloc excision. Complete resection with negative margins significantly improves outcomes. Adjunct medical therapies might be necessary for refractory hypercalcemia, particularly in metastatic disease. Given the diagnostic ambiguity and rarity of this condition, case series and institutional reviews are essential to enhance understanding and guide clinical decision-making.

This study presented a retrospective analysis of four parathyroid carcinoma cases managed at a tertiary center in Oman, contributing regional insight into this uncommon malignancy.

Methods

This study was a retrospective chart review conducted at the Endocrine Surgery Unit of the Royal Hospital, Muscat, Oman. The medical records of all patients with histopathologically confirmed parathyroid carcinoma between January 2012 and December 2023 were examined.

Patients were identified through the hospital's pathology registry. Only patients with a definitive histopathological diagnosis of parathyroid carcinoma were included. Exclusion criteria included patients with benign parathyroid disease or cases with incomplete documentation. All patients were managed surgically, and follow-up data were obtained from outpatient clinic visits and laboratory records.

Data collected included demographic characteristics, clinical presentation, comorbidities, laboratory parameters (serum calcium and PTH levels), imaging findings (ultrasonography and Sestamibi scan), surgical procedures performed, intraoperative findings, histopathological features, postoperative complications, and follow-up outcomes.

The collected data were stored in an Excel sheet. Continuous variables, such as serum calcium and parathyroid hormone (PTH) levels, were expressed as mean with their normal ranges in interquartile range, depending on data distribution. Categorical variables, including clinical presentation, imaging findings, surgical procedures, and postoperative complications, were summarized as frequencies. The results were presented in tables and scans as figures for clarity, ensuring a comprehensive evaluation of clinical and pathological factors associated with parathyroid carcinoma outcomes.

Results

A total of four patients were identified over the 10-year study period, comprising three males and one female, with a mean age at diagnosis of 44.5 years (range: 27-74 years). Clinical presentation was primarily due to hypercalcemia-related symptoms in three patients, including bone pain, joint discomfort, hematuria, and urolithiasis. One patient was diagnosed incidentally during evaluation for unrelated urological complaints. None of the patients had a family history of parathyroid disease or genetic syndromes associated with parathyroid neoplasia, such as MEN types 1 and 2A (Table 1).

Preoperative corrected calcium levels ranged from 2.84 to 4.00 mmol/l (normal: 2.1-2.6 mmol/l), while preoperative PTH levels ranged from 23.9 to 590.4 pmol/l (normal: 1.6-6.9 pmol/l), representing elevations up to 85 times the upper limit of normal (Table 2).

Table 1. *Demographics of individuals with parathyroid carcinoma included in the study.*

Variables	Patient 1	Patient 2	Patient 3	Patient 4
Gender	Male	Female	Male	Male
Age at diagnosis	74	47	30	27
Year of diagnosis	2016	2021	2022	2022
Presentation	Incidental	Urolithiasis	Joint pain and hematuria	Bone pain in a patient with ESRD
Family history	No	No	No	No
Co-morbidities	DM	DM, HTN	HTN	ESRD, HTN

DM=Diabetes mellitus; HTN=Hypertension; ESRD=End stage renal disease.

Table 2. *Calcium and PTH levels of individuals with parathyroid carcinoma included in the study.*

Variables	Patient 1	Patient 2	Patient 3	Patient 4
Corrected Calcium*	3.18	3.61	4	2.84
Pre-Operative PTH*	150	23.9	92.3	590.4
PTH above normal	21 times	3.4 times	13 times	85 times
Post-Operative PTH	1.5	2.7	0.8	62.6
Post-operative Calcium	2.37	2.4	2.26	2.06

*Normal PTH: (1.6-6.9 pmol/l), Normal Corrected Calcium: (2.1-2.6 mmol/l)

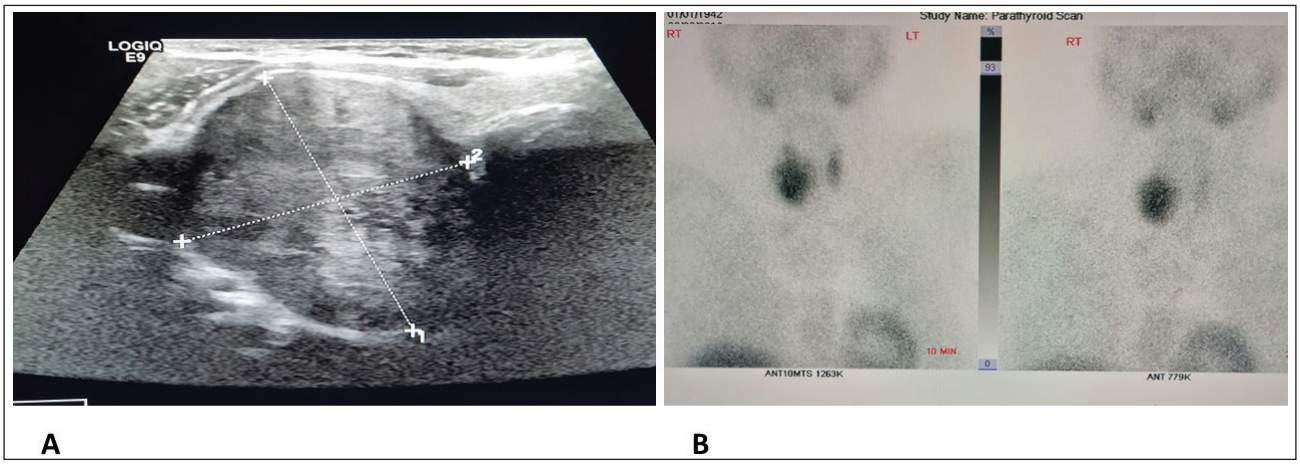

Figure 1. *(A) Ultrasonography and (B) Sestamibi scan of the parathyroid of one of the patients, which was the largest parathyroid mass in this case series.*

Table 3. *Surgical management and postoperative complications among individuals with parathyroid carcinoma included in the study.*

Variables	Patient 1	Patient 2	Patient 3	Patient 4
USS size	5.3 × 4 × 3.6 cm	Not detected by USS: 2.8 cm in Histopathology	2.45 × 1.9 × 3.9 cm	2.9 × 1.8 cm
Lateralization	RI	RI	LI	LI
Surgery done	PT + HT	PT + HT	PT + Limited esophageal wedge resection with primary closure and SCM muscle flap reinforcement	PT + HT
Admission days	4	2	4	14
Thyroid involvement	No	No	No	No
Histopathology stage	En bloc resection	En bloc resection	PT then HT	PT then HT
Complication	Hematoma (D0 postoperatively) Did not need exploration. Transient voice change.	-	Hematoma (D0 postoperatively) Did not need exploration. Transient hypocalcemia	Transient hypocalcemia

R: Right, L: Left, I: Inferior, S: Superior, PT: Parathyroidectomy, HT: hemithyroidectomy.

Ultrasonography identified parathyroid lesions in three patients, while Sestamibi scans confirmed the location of the diseased gland in all cases. Lesion sizes ranged from 2.45 cm to 5.3 cm in maximum dimension (Figure 1).

All patients underwent surgical excision. In two cases, a hemithyroidectomy was performed concurrently due to the proximity of the lesion to the thyroid intra-operatively. In one case, the hemithyroidectomy procedure was conducted in a separate surgery after confirming the malignant nature of the disease and discussion in Multidisciplinary Team. One patient required partial esophageal resection with reconstruction due to local adherence of the tumor. Histopathological analysis confirmed parathyroid carcinoma in all cases, with findings of capsular and vascular invasion in three patients. No evidence of thyroid microscopic involvement was noted in any patient.

Postoperative complications were minimal. Two patients developed neck hematomas that were resolved without the need for surgical intervention. One patient experienced transient hypocalcemia. Hospital stays ranged from 2 to 14 days. Postoperative PTH and calcium levels normalized or significantly declined in all patients. One patient with end-stage renal disease had persistent mild PTH elevation attributed to underlying secondary hyperparathyroidism. Follow-up ranged from 23 to 102 months. None of the patients developed disease recurrence or distant metastasis during this period (Table 3).

Discussion

Parathyroid carcinoma remains one of the rarest endocrine malignancies, accounting for less than 1% of parathyroid tumors globally. This case series, derived from a single tertiary center in Oman, aligns with global trends in terms of age, gender distribution, clinical presentation, and diagnostic challenges. The mean age at diagnosis (44.5 years) and the predominance of male patients are in line with published literature, although some reports suggested an equality between genders [6].

Hypercalcemia-related symptoms were the principal presenting complaints in this cohort, which is consistent

with existing studies that emphasize the metabolic effects of excessive PTH secretion as the main driver of morbidity. Typical manifestations include nephrolithiasis, bone pain, fatigue, and neurocognitive disturbances. In the presented series, PTH levels exceeding 10-fold the upper limit of normal were observed in most patients, an important biochemical clue that should heighten clinical suspicion for malignancy, which is supported by other studies [1,6]. One case with very high (85-fold) PTH might represent a delay in referring the patient from the nephrology department, as the patient was known to have secondary hyperparathyroidism. However, it cannot be confirmed that such aggressive values indicate ethnic or genetic factors because of the lack of similar studies.

Imaging studies, while helpful in localizing parathyroid lesions, were not sufficient to differentiate carcinoma from benign adenomas. Ultrasound and Sestamibi scans successfully identified the affected glands in most patients but did not offer definitive preoperative diagnoses. This underlines the continued reliance on postoperative histopathology for confirmation, particularly the presence of capsular and vascular invasion. The high PTH levels and relatively large lesion sizes (average > 3.7 cm) in this case series are typical of carcinoma (a size of < 3 cm is suggestive of malignancy in many studies [6]) and can serve as important intraoperative cues.

Surgical resection remains the cornerstone of treatment. All patients underwent complete resection, and in three cases, hemithyroidectomy or en bloc resection was necessary due to tumor adherence or proximity to surrounding structures. One case requiring esophageal resection was a rare but well-documented scenario [6], reflecting the aggressive local behavior of some tumors, although in this case, pre-operative imaging was not suggestive, and no comment was made regarding this proximity. Importantly, there was no observed thyroid involvement or lymph node metastasis in the current study cohort, and none of the patients experienced local or distant recurrence during follow-up. No intraoperative frozen sections were conducted in the presented case series. Frozen section might be useful to confirm parathyroid tissue as opposed to a thyroid mass, but it is not usually sufficient to diagnose parathyroid carcinoma [7].

Postoperative complications were minimal and manageable. The most notable was transient hypocalcemia and minor hematomas, neither of which required re-intervention. One patient with End Stage Renal Disease was diagnosed with PC years after being diagnosed with his expected secondary hyperparathyroidism (HPT), which was investigated as it transformed into tertiary HPT. Postoperatively, this patient exhibited persistently elevated PTH, attributed to coexisting secondary hyperparathyroidism rather than tumor recurrence, which is indeed another rare presentation of PC in a tertiary renal disease patient [8,9].

In the current study, the patients were followed up for an average of 43.25 months (102, 23, 17, and 31 months, respectively). All patients were alive at the time of writing this paper and had no recurrence. Yearly follow-up with oncology and endocrine surgery departments is planned with imaging in the first 3 years and annual laboratory investigations [6].

This study emphasized the importance of maintaining a high index of suspicion in patients with severe hypercalcemia and markedly elevated PTH, especially when radiologic features are inconclusive. Early recognition and complete initial surgical excision are essential for favorable outcomes. Although the rarity of the disease limits the size of this case series, however, the current study findings are consistent with international data and highlight key diagnostic and management principles applicable across various populations.

Future research from multicenter registries in the region could provide deeper insights into the epidemiology and genetic basis of parathyroid carcinoma in Arab populations, potentially improving early detection strategies and therapeutic approaches.

This study had its limitations, the small sample and the retrospective design. Having no policy for conducting genetic and molecular studies also contributes to the inability to extend the field of research. However, this study contributes to the limited data available on parathyroid carcinoma in Arab populations and reinforces the importance of a multidisciplinary approach in diagnosis, surgical planning, and long-term follow-up. Continued case reporting and regional collaboration are essential to enhance understanding and management of this rare entity.

Conclusion

Parathyroid carcinoma is an uncommon but clinically significant malignancy that poses considerable diagnostic and therapeutic challenges. Its presentation often mimics benign primary hyperparathyroidism, making preoperative diagnosis difficult. However, the presence of markedly elevated PTH levels, severe hypercalcemia, and large lesion size should raise clinical suspicion. This study underscores the value of prompt surgical intervention with complete tumor excision to optimize long-term outcomes. All patients in this study cohort had favorable postoperative courses with no recurrence observed during follow-up. While biochemical and radiologic assessments are useful, histopathological confirmation remains the gold standard for diagnosis.

What is new?

Parathyroid carcinoma is an uncommon but clinically significant malignancy that poses considerable diagnostic and therapeutic challenges. Its presentation often mimics benign primary hyperparathyroidism, making preoperative diagnosis difficult.

However, the presence of markedly elevated PTH levels, severe hypercalcemia, and large lesion size should raise clinical suspicion. This case series underscores the value of prompt surgical intervention with complete tumor excision to optimize long-term outcomes. All patients in our cohort had favorable postoperative courses with no recurrence observed during follow-up. While biochemical and radiologic assessments are useful, histopathological confirmation remains the gold standard for diagnosis. This study contributes to the limited data available on parathyroid carcinoma in Arab populations and reinforces the importance of a multidisciplinary approach in diagnosis, surgical planning, and long-term follow-up. Continued case reporting and regional collaboration are essential to enhance understanding and management of this rare entity.

List of Abbreviations

DM	Diabetes Mellitus
ESRD	End Stage Renal Disease
HPT	Hyperparathyroidism
HT	Hemithyroidectomy
HTN	Hypertension
I	Inferior
L	Left
PC	Parathyroid carcinoma
PT	Parathyroidectomy
PTH	Parathyroid hormone
R	Right
S	Superior

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent to participate

Not applicable.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report or series or original article based on retrospective chart reviews.

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