

Parathyroid Carcinoma: A Case Series of Six Patients

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Abstract

Background: Parathyroid carcinoma is an extremely rare malignancy, accounting for < 0.005% of all cancers and <1% of parathyroid tumors. This study aims to research all the patients who were diagnosed with parathyroid carcinoma in the past 10 years in Sultan Qaboos University Hospital SQUH. The primary aim is to study the demographics of the patients, their risk factors, the histo-pathological characteristics, and the treatments administered and their effectiveness.

Methodology: This case series study retrospectively reviewed all patients diagnosed with parathyroid carcinoma at Sultan Qaboos University Hospital (SQUH) from 2012 to 2021. The study included all patients with a confirmed histopathological diagnosis of parathyroid carcinoma. Descriptive statistics were utilized to present the findings.

Results: Our study included six patients with histopathologically confirmed parathyroid carcinoma. The mean age of the patients was 36.67 years, with a male predominance of 66.7%. Five patients presented with symptomatic hypercalcemia. The mean serum calcium (Ca) and parathyroid hormone (PTH) levels at presentation were 3.6 mmol/L (range: 2.77–4.35) and 147 pg/mL (44.9–300), respectively. Imaging identified a mass in all patients, with no evidence of calcification or degenerative changes. Four patients underwent parathyroidectomy and hemithyroidectomy, while the remaining two had a simple parathyroidectomy. During follow-up, four patients developed postoperative hypocalcemia, and one patient experienced recurrence nine years after the initial treatment.

Conclusion: Our study indicates that parathyroid carcinoma can present in relatively young patients. Preoperative diagnosis remains challenging, but significantly elevated PTH levels, more than five times the baseline, suggest a higher risk of parathyroid cancer. Recurrence can occur many years after initial treatment, underscoring the necessity for long-term follow-up and surveillance in these patients.

Keywords: Parathyroid, Parathyroidectomy, Cancer, Malignancy, Parathyroid Cancer, Parathyroid Malignancy, Hypercalcemia, Primary Hyperparathyroidism.

Introduction

The first case of parathyroid carcinoma to appear in the literature was in 1909 by DeQuervain, in which the diagnosis was attributed to the macroscopic characteristics of the lesion.¹ Parathyroid carcinoma is an extremely rare malignancy, accounting for <0.005% of all cancers and <1% of parathyroid tumors.^{2,3,4,5} It is most found to be sporadic, but cases have also been reported associating parathyroid carcinoma with familial primary hyperparathyroidism as hyperparathyroidism-jaw syndrome and multiple endocrine neoplasia type one.⁶ Parathyroid carcinoma can be suspected preoperatively from the size of the tumor, which usually exceeds 4 cm, as well as a high

level of PTH.⁷ However histopathological features confirm the diagnosis.⁷ The main goal of treatment is en bloc resection of the tumour with negative margins; excising the ipsilateral thyroid lobe may be necessary to perform this however, it has not been proven to improve survival in patients with parathyroid carcinoma.^{8,9}

The aim of this study is to research all the patients who were diagnosed with parathyroid carcinoma in the past 10 years in SQUH. The primary objective is to study the demographics of the patients, their risk factors, the histopathological characteristic, and the treatments administered and their effectiveness. The secondary objective is to compare the findings of our study to the current literature. This will be the first case series to be done in Oman.

Methods

This case series study retrospectively reviewed all patients diagnosed with parathyroid carcinoma at Sultan Qaboos University Hospital (SQUH) from 2012 to 2021. Patient data was extracted from TrackCare, the information system being used in SQUH. All patients with the diagnosis of parathyroid carcinoma were included in the study. Data were collected in Microsoft Excel and analysed using SPSS version 25. During the research process, patients were not identified via names, rather, they had a generated specially generated identification code for confidentiality purposes. Ethical approval was obtained from the Medical and Research Ethics Committee (MREC) at the College of Medicine and Health Sciences (COMHS) at Sultan Qaboos University.

Results

Our study included 6 patients with histopathologically confirmed parathyroid carcinoma. Four patients (66.7%) were male representing the majority of patients. Mean age of our patients was 36.67 (20 - 70 years). Five out of the six patients had symptomatic hypercalcemia (Muscle weakness, anorexia, nausea, vomiting, and abdominal pain), the 3 youngest patients had recurrent nephrolithiasis and 2 of them developed pathological fractures. All our patients had elevated Ca and parathyroid levels at presentation, the mean Ca level was 3.6(2.77-4.35) and the mean PTH level was 147(44.9-300) (*Table 1*).

Table 1: Shows the demographic, clinical presentation, and the labs of PTC patients.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	24	70	20	40	39	27
Gender	M	M	M	F	M	F
Presentation	Pathological fracture nephrolithiasis	Weakness /abdominal pain	Pathological fracture nephrolithiasis	Incidental	Weakness /abdominal pain	Weakness /abdominal pain nephrolithiasis
Serum Ca (mmol/L)	4	3.1	3.3	4.35	4.04	2.77
PTH (pg/mL)	128	73	264	73	44	300
Alkaline phosphatase (U/L)	470	101	1135	1117	122	220

Five patients underwent preoperative neck ultrasound; a mass was identified in all cases, but none showed calcification or degenerative changes. Two of the scans showed increased vascularity of the mass. Two patients had CT scan of the neck with contrast but, with no additional findings. Two patients underwent fine needle aspiration demonstrating small uniform-shaped nuclear with no atypia and abundant colloid noticed in the first sample and marked ulceration and nuclear membrane irregularity in the second (table 2).

Table 2: Distribution of radiological studies done preoperatively to PTC Patients.

Imaging	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
US neck	Yes	No	Yes	Yes	Yes	Yes
CT neck	No	Yes	No	Yes	No	No
NM parathyroid	No	No	Yes	No	No	No
Skeletal survey	Yes	Yes	Yes	Yes	No	Yes

Four patients underwent parathyroidectomy with hemithyroidectomy while the remaining 2 undergoing simple parathyroidectomy (**Table 3**) (**Figure 1**). With a follow up period of 2 years for each patient recurrence was not observed in any of the patients but with more extensive follow up recurrence was observed in 1 patient (patient 4) at 9 years post initial diagnosis. Radiation therapy was used with one patient (Patient 4) as palliative therapy. Following the recurrence the malignancy was related to the patient mortality that same year. Four of the six patients developed hypocalcaemia post operatively.

Table 3: Histopathological features of resected parathyroid glands.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Surgery	Left inferior parathyroidectomy with hemithyroidectomy	Left inferior parathyroidectomy & hemithyroidectomy	Right inferior parathyroidectomy	Right inferior parathyroidectomy	Left inferior parathyroidectomy & hemithyroidectomy	Subtotal parathyroidectomy with right hemithyroidectomy
Tumor size (cm x cm)	2 x 1.9	4.5 x 1.5	4.5 x 2	6 x 3	3 x 2.5	3 x 1.6
Tumor weight (g)	-	17	4.8	30	24	-
Capsular Invasion	Yes	Yes	Yes	Yes	Yes	Yes
Lympho-vascular invasion	Yes	Yes	Yes	Yes	No	No
Thick fibrous capsule	Yes	No	Yes	Yes	Yes	No
Lymph nodes	No	No	No	No	No	No

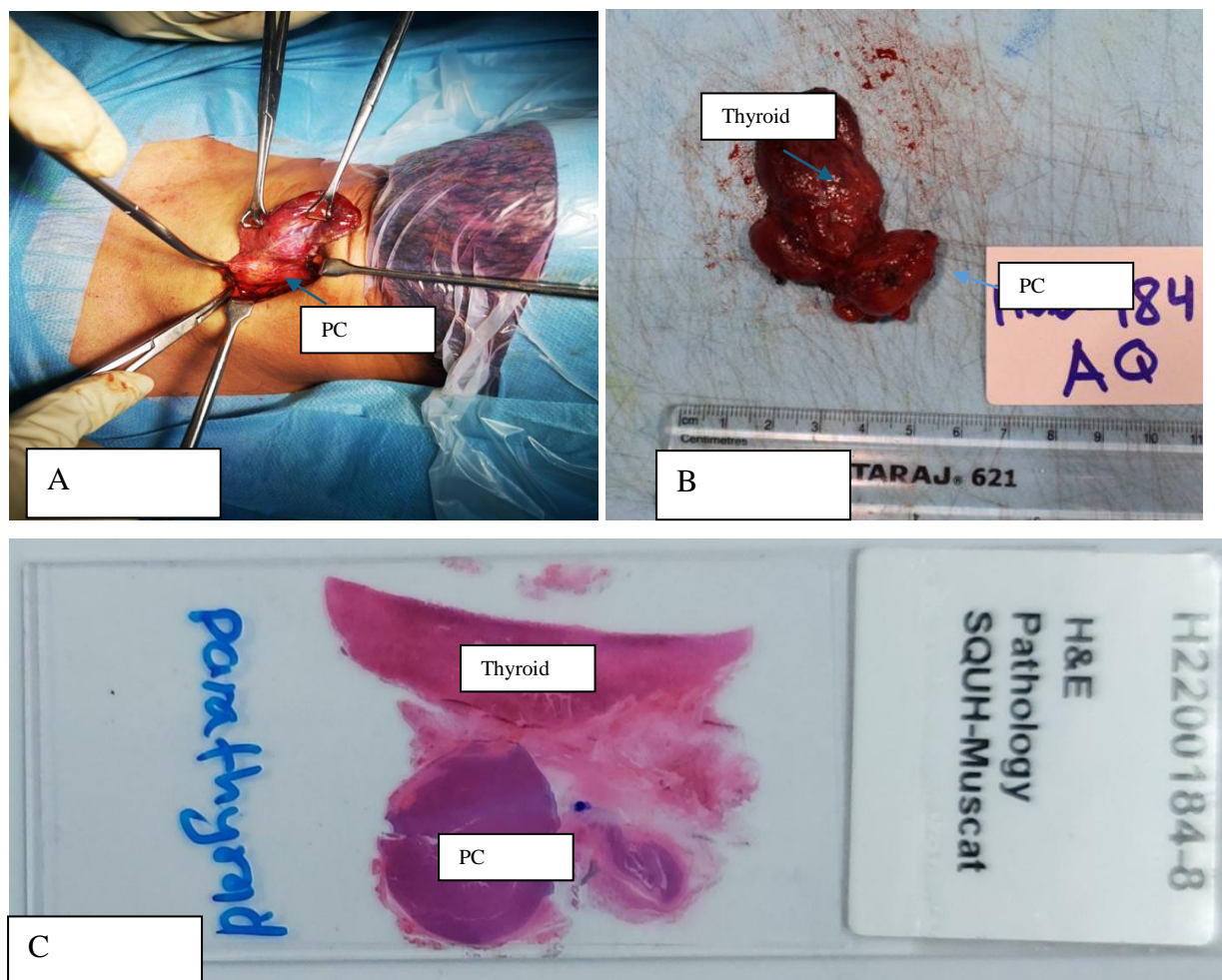


Figure 1: En bloc resection and Histopathological identification of the parathyroid carcinoma (PC).

Discussion

Parathyroid carcinoma is a rare entity representing less than 0.005% of all cancers and less than 1% of parathyroid tumors.^{3,4,5} Our cohort was younger (mean age: 36.7 years) than Western registries (mean age: 56 years), suggesting potential genetic or regional differences.² In our study we also had a male dominant 4:2 where the western register did not show a gender variant.² Parathyroid carcinoma seems to present with symptoms of hypercalcemia exclusively including bone pain, constipation, and muscle asthenia.¹ Some patients with recurrent renal stones and bone fractures may have long-standing hypercalcemia. Severe hyperparathyroidism, with signs and symptoms including hypercalcemia, bone pain, osteoporosis, fractures, and kidney stones or other kidney damage at young age should be highly suspicious for malignancy.¹¹

Preoperative diagnosis of parathyroid carcinoma is still a challenge hence a high level of suspicion should be present in patient presenting with severe hypercalcemia. There are no established criteria for the diagnosis of parathyroid carcinoma preoperatively; but our data support the use of elevated PTH higher than 5 folds of the baselines as an indicator of elevated risk of parathyroid cancer with positive predictive value of 81%.^{8,10} Even though elevated PTH and hypercalcemia can present rarely with benign parathyroid conditions.¹

Even though radiological studies including US neck or CT neck were used in all patients, the diagnosis of parathyroid carcinoma was only made post operatively in our study and that was consistent with other publications.

En bloc resection of the parathyroid with or without hemithyroidectomy showed to be the corner stone of management of parathyroid carcinoma.^{1,2,7} Adjuvant therapies including both radiation and chemotherapy were not shown to have improvement in mortality and morbidity.^{2,7} Radical neck dissection is not recommended for patient with suspicion of parathyroid cancer intraoperative.⁷

Even though preoperative PTH level, Ca level and tumour size had a diagnostic value they had not a prognostic rule.² Post operatively hungry bone syndrome was the most common complication both in our study and in available publications. No other complications were reported, and recurrence was observed in 1 patient 9 years post operatively which is consistent with previously reported 5 years recurrence rates of 33% to 82%.^{8,9}

Conclusion

Our study shows that parathyroid carcinoma can present in young patients. Preoperative diagnosis of parathyroid carcinoma remains challenging, but elevated PTH higher than 5 folds of the baselines indicates elevated risk of parathyroid cancer. One patient (16.7%) developed recurrence 9 years postoperatively, underscoring the need for lifelong surveillance.

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