CASE REPORT

# A Rare Case of Parathyroid Carcinoma

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## ABSTRACT

Hyperparathyroidism has typical presentation due to osteopenic bones and raised serum calcium level. Adenoma of the parathyroid is the commonest cause of primary parathyroidism. Parathyroid Carcinoma is an extremely rare tumor and is associated with delayed diagnosis that decreases the possibility of achieving a histological margin-negative resection, as this is the patient's only hope for cure and prolonged disease-free survival. We present a case of rare parathyroid carcinoma in a lady who has been operated twice for parathyroid adenoma but later presented with histopathologically proven carcinoma.

**Keywords:** Parathormone, Parathyroid carcinoma, Calcium.

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## INTRODUCTION

Primary hyperparathyroidism (PHPT) is an endocrine disease characterized by excessive parathyroid hormone (PTH) secretion and hypercalcemia. Approximately 85% of the patients have a single parathyroid adenoma (PA), 10% hyperplasia and 3% double adenoma. In contrast, atypical PA and parathyroid carcinoma (PC) are extremely rare tumors, in fact one of the rarest of all human cancers with an incidence of 0.015 per 100,000 population and a prevalence of 0.005% in the United States.[1] In the following case report, we discuss an interesting case of a recurrent parathyroid adenoma which was reported to be a parathyroid carcinoma at the time of last admission.

## CASE REPORT

A 47 year old female presented with a swelling in front of the neck on left side for 4 months, body ache for 4 months, generalised weakness for 4 months , vomiting on and off for 4 months. She gives a history of fracture of right shaft of the femur following minimal trauma 2 days prior to admission.

She had a history of similar complaints in the past for which she was operated twice in 2013 and in 2019. She gave a history hip dislocation 4 years back for which she underwent a hip replacement. The patient was admitted to the endocrinology ward one month back for management of a hypercalcaemic crisis and after she was optimized, she was transferred to the surgery ward. She doesn't have any other comorbidities.

Previous records of patient were carefully studied, and patient was operated in 2019 for similar complaints and prior to surgery, her FNAC was suggestive of parathyroid adenoma and a sestamibi scan done showed features of left inferior parathyroid adenoma. Post surgery, her PTH was 62 pg/nL. Patient was not on regular follow up.

On examination (Figure 1) she had a 3x 2 cm lump present in anterior aspect of neck on left side which does not move on deglutition or protrusion of tongue. A 6 cm transverse scar is present over the lower part of neck extending over the swelling.

On palpation, there is no rise in temperature and no tenderness and a 3x2 cm lump on the left side of neck 1-cm above the medial end of the clavicle inferiorly, just at the medial border of lower 1/3rd of sternocleidomastoid laterally,1-cm from midline medially and 6–8 cm from mandibular ramus superiorly. The surface of swelling appears bosselated , firm to hard in consistency , all borders are well defined and swelling is mobile in all directions with skin over swelling pinchable. She has a shaft of femur fracture on the right lower limb for which skin traction was given.

Biochemically patient had a hemoglobin of 7 gm/dL, serum calcium of 11.3 and PTH level of 821 pg/mL. USG showed a few

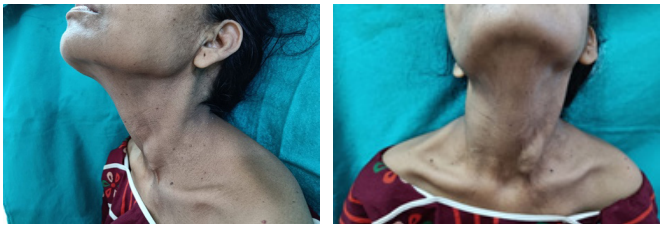

**Figure 1:** Lobulated lump along left sternocleidomastoid muscle.

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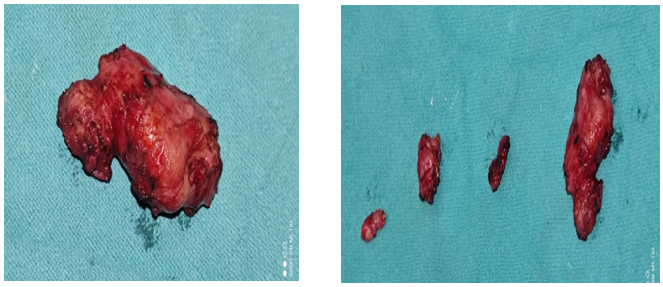

(a) (b)

**Figure 2(a):** Excised parathyroid tumour from left side, **(b)** 3 excised Lymph nodes

relatively defined hypoechoic lesion, the largest measuring 2.5 cm x 1.2 cm in left cervical region anterosuperior to left thyroid with internal calcification with a final impression suggestive parathyroid carcinoma with enlarged lymph nodes. USG KUB showed evidence of nephrolithiasis . FNAC showed features suggestive of parathyroid neoplasia.

During surgery a 3x2 cm solid mass was found along with three lymph nodes adjacent to the parathyroid (Figure 2). Postoperative course was uneventful and persistence of PTH was observed (252 pg/nL) and serum calcium was 13.1. Histopathology revealed features suggestive of parathyroid carcinoma and all three cervical lymph nodes excised were found to have metastatic deposits. Patient was advised a sestamibi scan postoperatively and is on regular follow up with no evidence of local or regional metastasis.

## DISCUSSION

Parathyroid carcinoma is a rare endocrine malignancy. It accounts for <1% of cases of sporadic primary hyperparathyroidism (PHPT) and is usually associated with more severe clinical manifestations than its much more common benign counterpart, parathyroid adenoma.[2] It occurs equally in men and women and around 5$^{th}$ decade. This contrasts with benign parathyroid lesions which are more prevalent in women. The diagnosis of malignancy is often made only when local recurrence or metastases occur, because the histology of parathyroid tumors can be equivocal or frankly misleading. Most patients with recurrent disease ultimately succumb to the effects of hypercalcemia rather than to direct tumor invasion or distant metastases.[2]

The etiology of parathyroid cancer is unknown. There is an increased risk of PC in families with endocrine diseases (such as familial hyperparathyroidism and multiple endocrine neoplasia type), prior neck radiation and end-stage renal disease. Several different mutations have been implicated and include the retinoblastoma, p53, breast carcinoma susceptibility (BRCA2) and cyclin Dl/parathyroid adenomatosis gene 1 (PRAD1) genes.[3]

Majority of parathyroid cancers are functioning tumors. Therefore, patients most often present with symptoms and signs of hypercalcemia, such as fatigue, malaise, weakness, weight loss and anorexia; psychiatric manifestations (*i.e.* depression) and digestive symptoms (e.g. nausea, vomiting, abdominal pain, peptic ulcer, pancreatitis and constipation), some of which were seen in our patient. More prominent are symptoms of renal and skeletal involvement, which are generally the symptoms with which the patient presents. In our case, the patient presented with a history of multiple pathological bone fractures and ultrasonography showed the presence of renal concretions.

The clinical criteria for suspicion of malignant parathyroid neo-plasm as said by Obara *et al.*, are: (1) age below 55 years (2) marked hypercalcemia and increased parathormone levels (more than10 times over the limit) (3) severe bone symptoms (fibrocystic osteitis in 40%–70% of cases) and kidney symptoms (nephrocalcinosis, nephrolithiasis in 30%–60% of cases) (4) recurrent laryngeal paralysis due to tumor invasion (5) palpable cervical swelling, that is rare in benign disease. Up to 50% of patients present with a palpable neck mass related to either advanced local or regional metastatic disease.[3] Patient in our case had a marked hypercalcemia, increased parathormone levels , severe bone symptoms and a palpable neck swelling

Laboratory criteria to distinguish parathyroid adenoma from carcinoma are nonspecific. The average serum calcium level in patients with parathyroid carcinoma is higher (15.9 mg/dL). The case report here was in severe hypercalcaemic crisis on presentation but was managed conservatively in the endocrinology ward.

Imaging studies (ultrasound, CT scan, MRI, Technetium–99 m sestamibi scan ) are not definitive in the differential diagnosis between adenoma and parathyroid carcinoma, so in cases where malignancy is suspected, higher-resolution anatomical studies are of considerable value. Fine needle aspiration cytology is not recommended

They are difficult to diagnose microscopically. Except for invasion of surrounding structures, lymph node metastases, or mitotic figures, there are no histological features that can distinguish between an adenoma and carcinoma. Newer methods such as immunohistochemistry and DNA analysis are being developed. No single marker thus far has shown to be perfectly sensitive and specific.[2]

In the absence of a standard gold test, a multidisciplinary approach offers the best chance for accurate diagnosis. Patient in our case had been operated twice previously with all previous pathological investigations showing a confirmed diagnosis of benign adenoma. (details and records of first surgery were not available). It was only during evaluation in third admission she was found to have parathyroid neoplasm with metastasis to lymph nodes

Most studies recommend en-bloc resection of the tumor together with the ipsilateral thyroid lobe, and excision of any adjacent structures involved at the initial surgery to offer the best opportunity for better local disease control and significantly improved long term-survival.[2] Every effort should be made not to rupture the capsule of the tumor and spill tumor cells in the field. Prophylactic or radical neck resection is usually performed only if enlarged or abnormal-appearing lymph nodes are found to be involved, as unnecessary prophylactic radical neck dissection may increase the risk of surgical complications.

Use of intra-op PTH test has been reported in parathyroid cancer. After surgery, close monitoring of calcium levels and adequate replacement is necessary to avoid severe hypocalcemia due to 'hungry bone syndrome'. Adjuvant therapy with RT or QT was not deemed effective.

In spite of all technological and technical advances, recurrence is very common in parathyroid carcinoma.[5] Patients who had a complete en-bloc tumor resection at the time of initial surgery have a lower recurrence rate–with survival rates as high as 90% at 5 years and 67% at 10 years.[6] Unfortunately, most patients are not diagnosed at the initial presentation and therefore don't undergo complete resection. On average, recurrence occurs 2–3 years after initial surgery but can be longer.[5] Like in our case an initial misdiagnosis resulted in incomplete resection was done and unfortunately patient had a recurrence in 3 years which is common in case of PC. The most common relapse pattern after the initial surgery is local recurrence and distant metastases (e.g., lung, bone and liver metastases). The treatment strategy consists of controlling hypercalcemia, localizing studies and surgical excision of resectable disease when feasible.

Patients may require multiple operations and is the best palliative option.[3] The aim of follow-up is early detection. It includes clinical examination with calcium levels and PTH monitored every 3 months for the first 3 years, 6/6 months till the 5$^{th}$ year and yearly lifelong after that.[3] When there is any suspicion, it should be confirmed afterward with imaging studies.

## CONCLUSION

PC is an extremely rare tumor and is associated with a delayed diagnosis that decreases the possibility of achieving a histological margin-negative resection, as this is the patient's only hope for cure and prolonged disease-free survival. This difficulty in differentiating between an adenoma, PC and atypical adenoma is detrimental to patient and effort should be taken to establish more reliable diagnostic tools. Regular follow-up of patients is very necessary for early detection of recurrence.

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