

Parathyroid Carcinoma: A Rare Case Report

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ABSTRACT

Parathyroid carcinoma accounts for 0.5-5% of primary hyperparathyroidism and are usually difficult to diagnose clinically. Parathyroid lesions are rare and its carcinoma is much rarer. Here we discuss about a 51 years female suspected case of chronic pancreatitis with solitary thyroid nodule was hospitalised. On investigation, Serum amylase, alkaline phosphatase and parathyroid hormone levels were found raised. USG of neck showed another nodule near thyroid with suspected parathyroid origin. MIBI Scan showed increased tracer concentration in right superior parathyroid. The patient underwent parathyroidectomy on clinical basis of primary hyperparathyroidism. Grossly the gland was enlarged measuring 5 x 4 x 3 cm, with weight 8 gms. On histology, vascular invasion is an important absolute criteria for diagnosis of parathyroid carcinoma. Histopathology is the gold standard for diagnosis of Parathyroid carcinoma.

Keywords: Parathyroid Carcinoma, Primary Hyperparathyroidism.

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INTRODUCTION

Parathyroid carcinoma is a rare cancer accounting for 0.4–5.2% of cases of primary hyperparathyroidism. The first known case, described by De Quervain in 1909, was a non-functional tumor whose malignancy was only revealed by the lesion's macroscopic features. In 1938 Armstrong reported another case of metastatic parathyroid carcinoma associated with primary hyperparathyroidism. Most common age group affected is 45-55 years, with a slight predominance of cases in women.¹ We report a case of parathyroid carcinoma because of its rarity and deal with the histological diagnostic dilemmas and pitfalls.

CASE PRESENTATION

51 year female admitted with h/o thyroid swelling since 6months. Pain in upper abdomen with nausea and occasional vomiting since 15days. No h/o haematemesis, melaena or jaundice. On examination, mild pallor was present, there was no pedal oedema and no palpable neck nodes. Pulse 92/min, regular, BP-124/76mmof Hg. Firm nontender nodule adjoining Rt. Lobe of thyroid of size 6cmx4cm, which did not move with deglutition [Fig 1]. No palpable nodule in Lt. lobe thyroid. Per abdomen examination revealed tenderness with mild muscle guarding at epigastrium and umbilical region. Liver was not enlarged, spleen was non palpable, external hernial orifices was normal, and no ascites was seen. So final clinical diagnosis was Solitary Nodule Rt. Lobe of Thyroid with acute flare up of Chronic Pancreatitis.

Lab investigations showed Hb: 10.2 gm% ,Serum Urea: 80mg%,Serum Cr: 2.8mg%,Serum Amylase: 801mg%(25-86u/l), LFT: Bilirubin: 0.4mg%, AST 40IU/L (12-38),ALT 21IU/L (7-41), ALPhos 1157 IU/L (<360), Blood Sugar: Fasting-95mg%, 1hr PPBS-159mg%, Serum Calcium: 10.6mg% (8.4-10.6), Serum iPTH: 663.9pg/ml(14-72). Plain x-ray abdomen showed multiple radio opaque calculi in the KUB area on both sides [Fig 2].USG of neck showed Rt Lobe thyroid- isoechoic mass of 16x15x7mm. Another mixed echogenic mass adjoining Rt Lobe of thyroid of 67x45x26mm. No enlarged neck nodes were seen [Fig 3]. USG abdomen showed within Pancreas- well defined cystic lesion of size 47x26mm with echogenic material within and calcification at margin [Fig 4]. CT scan abdomen showed pancreatic cyst with calcification. MIBI –scan showed increased tracer concentration in Right superior parathyroid [Fig 5]. So pre-operative diagnosis was Primary Hyperparathyroidism possibly a Parathyroid Tumour. Rt. Superior Parathyroidectomy with Rt. Thyroid Lobectomy was done. Per operatively Rt. superior parathyroid tumor of 6x4.2x3mm was densely adherent to posterolateral aspect of Rt. Lobe thyroid. Rt lobe thyroid was enlarged containing a nodule of 2cm diameter. Cut surface was fleshy and there were no enlarged neck nodes. Grossly- Length 50 mm, width 40 mm, thickness 20 mm and weight 8gms with no fatty tissue attached [fig 6]. On histopathology we see a thick capsule with underlying tissue arranged in packets, trabeculae and sheets. They are polygonal in

shape with amphophilic to clear eosinophilic cytoplasm, uniform to pleomorphic looking nuclei, inconspicuous to prominent macronucleoli at places separated by thick hyaline stromal bands



Fig 1: Firm non tender nodule measuring 6cmx4cm.

[Fig 7]. Focal areas of calcification and melanin deposition seen [Fig 8,9]. Capsular and vascular invasion present [Fig 10,11]. Focal atypia was seen at certain areas.



Fig 2: Xray abdomen-multiple b/l radioopaque Calculi in the KUB area.

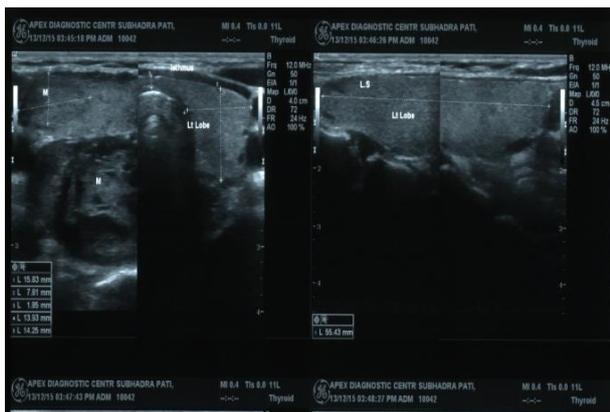


Fig 3: USG neck showing Rt Lobe thyroid-isoechoic mass of 16x15x7mm Another mixed echogenic mass adjoining Rt Lobe thyroid of 67x45x26mm. No enlarged neck nodes.



Fig 4: USG Abdomen showed Well defined cystic lesion in pancreas of size 47x26mm with echogenic material within and calcification at margin.

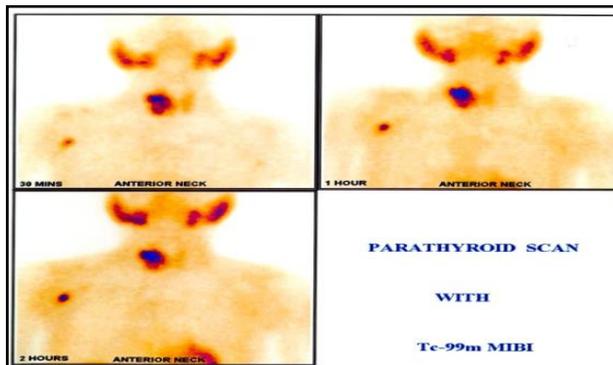


Fig 5: MIBI Scan showed increased tracer concentration in Rt superior parathyroid.



Fig 6: Gross- after formalin fixation, size 5x4x2, wt 8 gms.

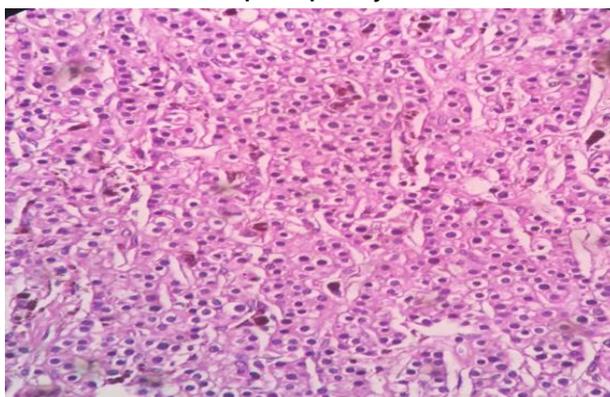


Fig 7: HP 400X-showing arrangement of tumor cells in trabeculae and Packets.

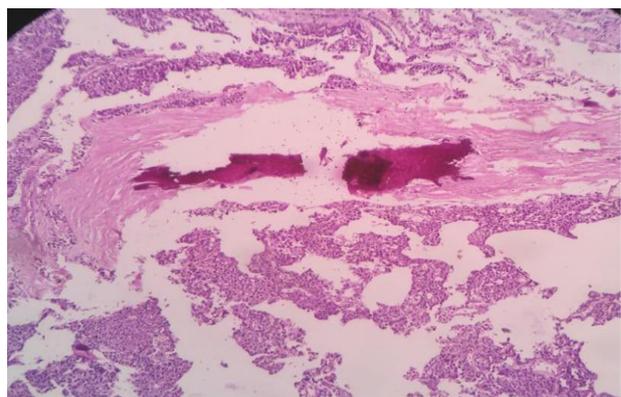


Fig 8: Photomicrograph 40X Showing Area of calcification.

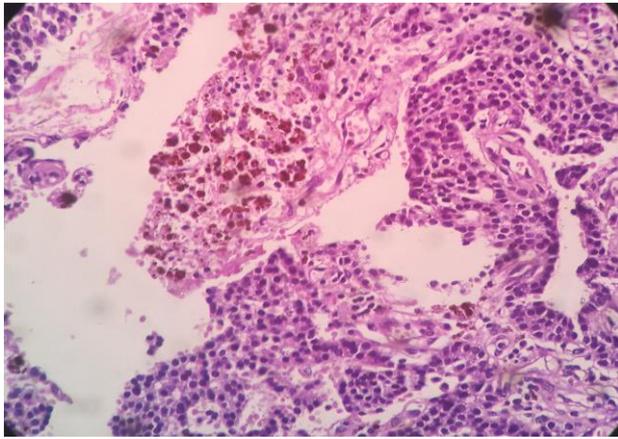


Fig 9: Photomicrograph LP 100X-Showing presence of Melanin pigments

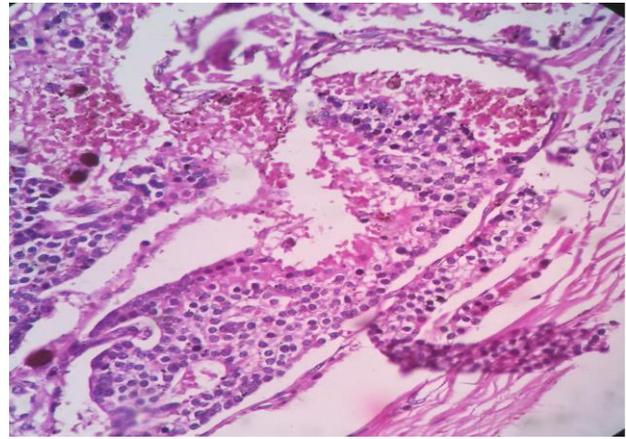


Fig 10: Photomicrograph LP 100X – Showing Presence of Vascular invasion

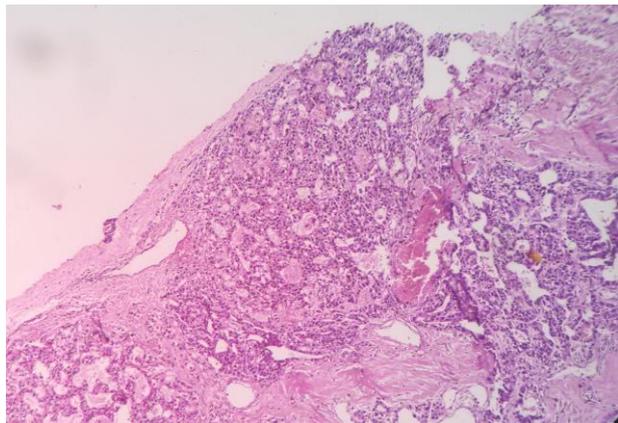


Fig 11: Photomicrograph LP 100x-Showing Presence of Capsular Invasion.

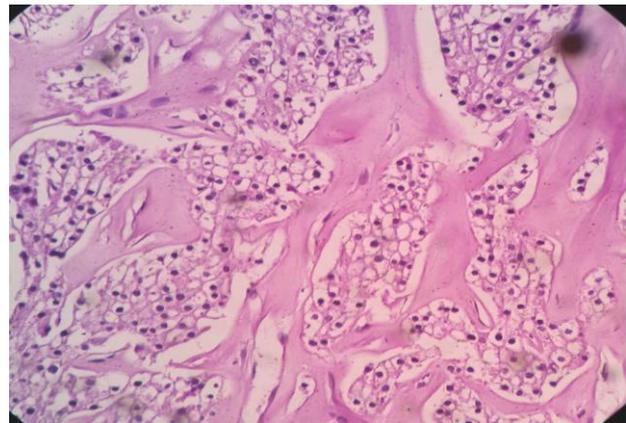


Fig 12: Photomicrograph HP 400X- Showing areas of Hyaline Stroma.

DISCUSSION

Parathyroid carcinoma accounts for < 1% of cases of primary hyperparathyroidism.² It is less common in secondary or tertiary forms.³ Its occurrence in secondary hyperparathyroidism is due to the chronic stimulation of hyperplastic glands that results in malignant transformation of these glands.⁴ An estimated incidence of 5.73 per 10 million persons has been reported.⁴

Majority of case reports show equal gender distribution F:M=1:1 while some case reports shows a female preponderance as in cases of carcinoma arising from an adenoma or hyperplastic glands.⁵

The main signs and symptoms of parathyroid carcinoma include pathological fractures, joint and bone pain, fatigue, polyuria and polydipsia, kidney stones, muscular asthenia, nausea, vomiting, loss of appetite and weight loss which is attributed mainly due to elevated levels of PTH and calcium. These signs and symptoms are not cancer specific as they are also seen in patients who do not have parathyroid carcinoma.

The etiology is unknown in most cases although several genetic defects have been reported. Mutations of the HRPT2 gene (1q 25-31) cause hyperparathyroidism jaw tumor syndrome, and about 15% of these patients develop parathyroid cancer.⁶ The gene codes for a tumor suppressor protein called parafibromin.

A visible or palpable lump in the front of the neck which on palpation appears to be hard and solid varying from a few millimeters to some centimeters in size, strongly adhering to the thyroid and infiltrating the adjacent structures, are clinical features suspicious of parathyroid carcinoma but a higher serum calcium (>14 mg/dL) and PTH (especially when twice the normal

value) which are unlikely to be seen in cases of benign hyperparathyroidism are considered as indicators of carcinoma.

Although ultrasound can reveal some signs of malignancy, such as echostructure and irregular margins which is nonspecific, other diagnostic modalities like invasion Computed tomography (CT), magnetic resonance imaging (MRI), bone scintigraphy with ^{99m}Tc-sestaMIBI and bone scintigraphy help in arriving at the diagnosis. However, the definitive and an accurate diagnosis are always provided by the pathologist.

The histopathological distinction between benign and malignant parathyroid tumors is always difficult; however the diagnosis of malignancy can be reached on consideration of constellation of features as proposed by Shantz and Castleman⁷ in the year 1973. Under the microscope, capsular invasion (without extension to soft tissues), vascular invasion, stromal calcifications, fibrous trabeculae, diffuse monotonous small cells with high N:C ratio, enlarged macronuclei and strong mitotic activity(>5/10hpf) are considered to be signs of malignancy. However, none of these are pathognomonic as several features have occasionally been found in parathyroid adenomas.⁸

The features that clinched our diagnosis of parathyroid carcinoma were a characteristic histomorphology, presence of capsular and vascular invasion with focal areas of calcification and melanin deposition were seen. Focal atypia and areas of hyaline stroma [Fig 12] seen at certain areas. There was no mitosis, no broad fibrous bands and no adherence or metastasis to adjacent organs. Immunohistochemistry is helpful to confirm parathyroid nature of non-functioning or ectopic parathyroid carcinomas. Diffuse strong immunostaining for PGP9.5 has utility in diagnosing parathyroid

malignancy with a sensitivity of 78% and 100 % specificity.⁹ and Galectin 3 expression has positivity of 92 % and help in distinction from parathyroid adenoma.¹⁰ IHC was not done in our case as histopathology diagnosis was confirmatory.

Parathyroid carcinoma is an indolent tumor with local recurrences occurring in one third patients within three years of surgery¹¹ while metastasis is seen in another one third patients, sites of predilection being neck, mediastinum, lung, liver and bones.

Surgery is the gold standard for the treatment of parathyroid carcinoma. *En bloc* dissection of the tumor with the thyroid lobe, the ipsilateral parathyroid and any other affected tissue is the most suitable treatment. Apart from surgery it is also essential to obtain biochemical remission: normalization of blood calcium and PTH levels, arrest of bone calcium depletion and regression of vascular, renal and neurological disorders. Continued high postoperative calcium and PTH levels are indicators of disease's persistence (metastasis or residual disease). Routine follow-up by monitoring the levels of calcium and PTH levels is essential as they serve as markers of disease's recurrence. Some authors consider post op radiotherapy to have some effect on preventing recurrences, used as a complementary treatment when resection margins are involved¹² while chemotherapy is agreed by all to be ineffective.

CONCLUSION

Due to variable diagnostic criteria the real incidence of parathyroid carcinoma is difficult to establish.^{13,14} Parathyroid carcinomas, although rare, must be considered in the differential diagnosis of a nodular thyroid mass. They are often under-diagnosed pre-operatively, resulting in diagnostic dilemmas. For this reason, the tumor's malignancy must be confirmed only after prolonged follow-up, taking into consideration histological (capsular and vascular invasion) and clinical features (invasive appearance, recurrences, distal metastasis)^{15,16} for better management and survival of these patients.

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