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Stone in the Neck with Stones, Moans and Groans

Mayilvaganan Sabaretnam[1*], D. Vnssvams Mahalakshmi[1], P. R. K. Bhargav[2], Aromal Chekavar[2] and Neha Nigam[3]

[1]Department of Endocrine Surgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Rae Bareilly Road, Lucknow- 226014, India.
[2]Consultant Endocrine Surgeon, India.
[3]Department of Pathology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Rae Bareilly Road, Lucknow- 226014, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author MS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors DVM and PRKB managed the analyses of the study. Author NN managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Parathyroid carcinoma is a rare cause of Primary Hyperparathyroidism and this endocrine tumor may be aggressive or indolent. This disease is an enigma and there are challenges in diagnosis, management and adjuvant treatment and the endocrine surgeon should have a high index of suspicion based on clinical findings and investigationsin the form of very high parathyroid hormone levels, hard tumour, large tumour, severe hypercalcemia, compressive symptoms and ultrasound or imaging features suggestive of parathyroid carcinoma which is the key to preoperative diagnosis and appropriate and intraoperative managent and we report a classical case of parathyroid carcinoma with Hyperparthyroidism induced hypercalcemic crisis and classical pathological findings.

Keywords: Parathyroid carcinoma; endocrine tumor; normocalcemic; hyperparthyroidism.

**Corresponding author: E-mail: drretnam@gmail.com;*

1. INTRODUCTION

Parathyroid carcinoma is a rare cause of Primary Hyperparathyroidism and this endocrine tumor may be aggressive or indolent.This disease is an enigma and there are challenges in diagnosis, management and adjuvant treatment and the knife happy surgeon should have a high index of suspicion based on clinical findings and investigations which is the key to preoperative diagnosis and appropriate and intraoperative managent.. However most cases are diagnosed intra operatively or are a histological surprise postoperatively and pathologists also have difficulty in reporting especially in atypical adenomas [1-5]. Since the disease is rare there are limited large scale studies leading to controversies regarding management, staging and follow up.Parathyroid carcinoma may occur sporadically or may be part of a familial syndrome. The Genetic syndromes associated with Parathyroid Carcinoma include MEN1, MEN2a, Hyperparathyroidism Jaw Tumour Syndrome, and isolated Familial Hyperparathyroidism. The origin of PC has been a matter of debate, however there is recent evidence that indicate that PC may originate denovo rather than progression from adenoma to carcinoma sequence [6,7]. We report one such interesting case with classical features of parathyoid carcinoma as pictoral update.

2. CASE REPORT

A 56-year-old lady was presented in the emergency department with complaints of tachycardia, tachypnoea, hypercalcemic crisis, vomiting, and dehydration.She had previous history of passing stones, abdominal pain and also was on psychiatric treatment. She was not responding to the medical managementin the form of hydration, bisphosphonates and calcimemitics and had corrected calcium values of 21mg/dlalong with elevated parathormone levels (PTH) and low phosphorus levels. On examination, a hard mass was palpable on the right side of the neck and was not moving with deglutition. MIBI scan done in an another hospital was suggestive of a parathyroid tumor in the right side of the neck and Dexa scan was suggestive of severe osteoporosis. Since it was a semi-emergency she was taken for bilateral neck exploration under the cervical block and the right inferior parathyroid, which was greyish white and hard was removedwith the ispilateral thyroid lobe. The other parathyroid glands were normal and no gross lymphadenopathy (Figs. 1,2). The patient becomes normocalcemic 12 hours after surgery and also the Intraoperative PTH levels decreased to 60% of pre op value suggesting cure.On gross examination,the right inferior parathyroid gland was hard, lobulated, greyish-white, and measured 3x2 cm. Microscopic examination revealed a tumor disposed of in nodular pattern and is separated by thick fibrous bands. Tumor cells are largely monomorphic, display mild anisonucleosis, round to oval nuclei, fine chromatin, macronucleoli and moderate cytoplasm. Increased mitotic activity with few atypical mitotic figures is seen. Tumor cells are infiltrating into adjacent skeletal muscles and lymphovascular emboli are also seen. Immunohistochemistry for parafibromin was applied for differentiating the carcinoma from parathyroid adenoma and the final diagnosis given was parathyroid carcinoma (Figs. 3,4,5 and 6).

3. DISCUSSION

Although the distinction between Parathyroid Carcinoma and benign PHPT can be difficult especially in the developing countries where patients with benign PHPT present with severe disease, it is a good practice to consider Parathyroid Carcinoma as a differential diagnosis in cases of severe hypercalcemia and also palpable parathyroid tumors which would enable early diagnosis resulting in more complete resection and good prognosis on follow up [8,9]. On gross examination Parathyroid Carcinoma is hard, lobulated mass which is tan to greyish white in colour with or without adherence to the surrounding structures. The adenoma is usually soft, red or brownish in colour and shows no sign of local infiltration. However in a large number of cases it may be difficult to differentiate between adenoma and carcinoma intraoperatively and the final diagnosis made only after histopathology. Grossly the tumours are large (>3cm) and majority weigh between 2 and 10gms.So the diagnosis of Parathyroid Carcinoma is a challenge for the pathologist and still remains a dilemma. Frozen Section done intraoperatively is not reliable in differentiating benign adenoma from Parathyroid Carcinoma [1,4,5].

Immunohistochemistry staining may assist in the differentiation of Parathyroid Carcinoma from adenoma. The most commonly used marker is Parafibromin, which is encoded by the *HRPT2* gene. When this*HRPT2* gene is mutated, a loss of parafibromin expression and loss of staining is seen, making it a highly specific test for PC. Additional markers for the diagnosis of

malignancy in parathyroid tumors include increased expression of galectin-3 and Protein Gene Product (PGP) 9.5 and the loss of the adenomatous polyposis coli (APC) gene product [10,11]. However, use of these markers requires additional studies.

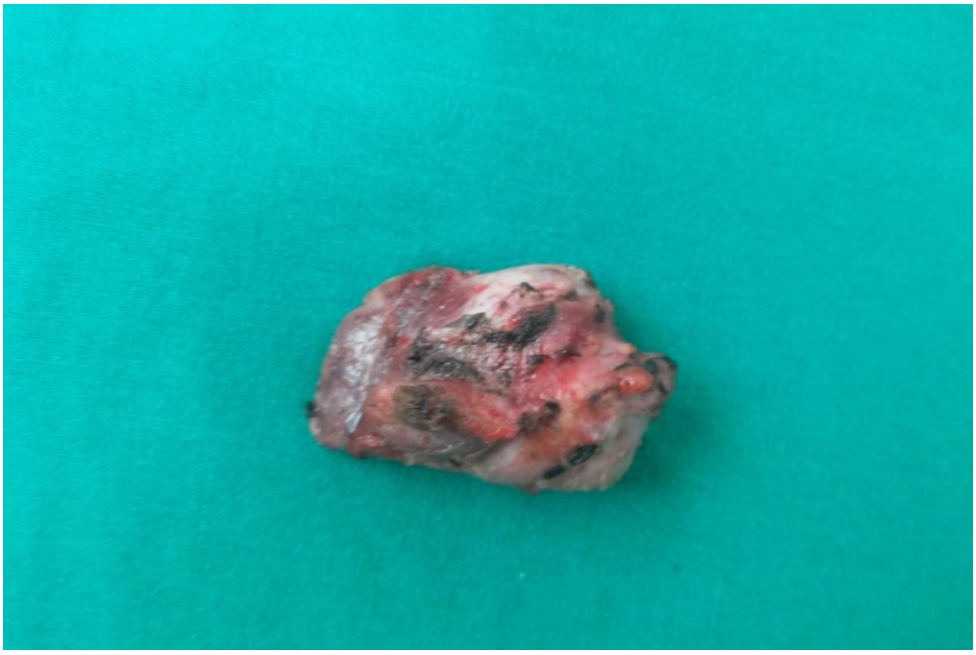

Fig. 1. Gross specimen of parathyroid carcinoma showing greyish white stony hard tumor, measured 3x2 cm

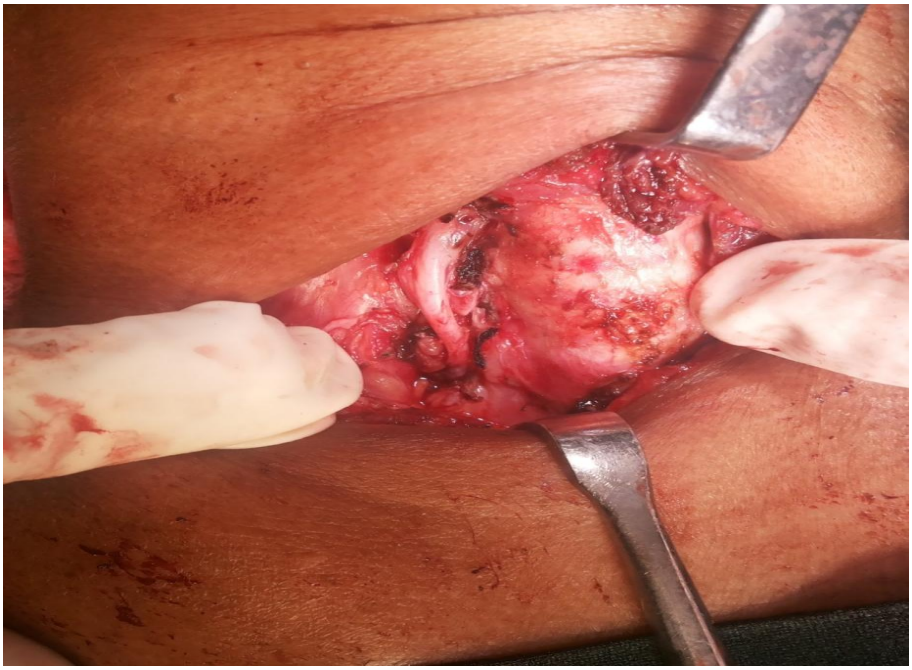

Fig. 2. Intraoperative Picture after en-bloc resection of Parathyroid Carcinoma with intact recurrent laryngeal nerve

Surgery is the mainstay of treatment and the only curative treatment in the management of Parathyroid Carcinoma. The recognition of this disease during the initial neck exploration followed by en bloc resection offers the best chance of cure.En bloc resection includes removal of the tumour along with removal of the ipsilateral thyroid lobe, removal of contiguous lymph nodes and any suspicious or adherent components of the ipsilateral central neck compartment. During surgery it is important to prevent the rupture of parathyroid capsule to prevent tumour seedling which may increase the likelihood of recurrence of disease. The recurrent laryngeal nerve is preserved if not involved by tumour. If the tumour involves a functioning recurrent laryngeal nerve then effort must be made to preserve the nerve unless it is circumferentially involved.Most studies recommend ipsilateral central compartment lymph nodal clearance as part of the enbloc resection. Modified neck dissection is done only if the lateral compartment lymph nodes are involved [8,9,11].

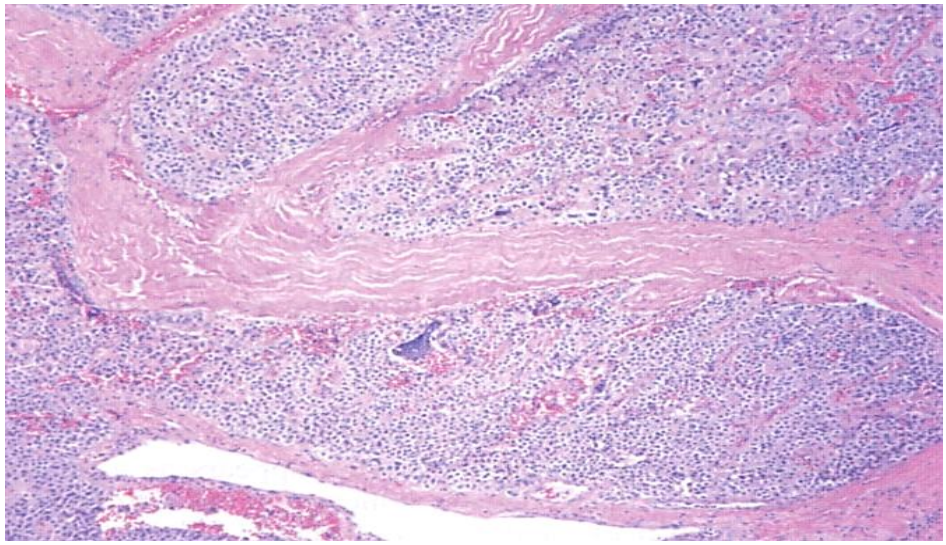

Fig. 3. Nodular growth pattern separated by thick fibrous bands in Parathyroid Carcinoma (H&E stain; 100x)

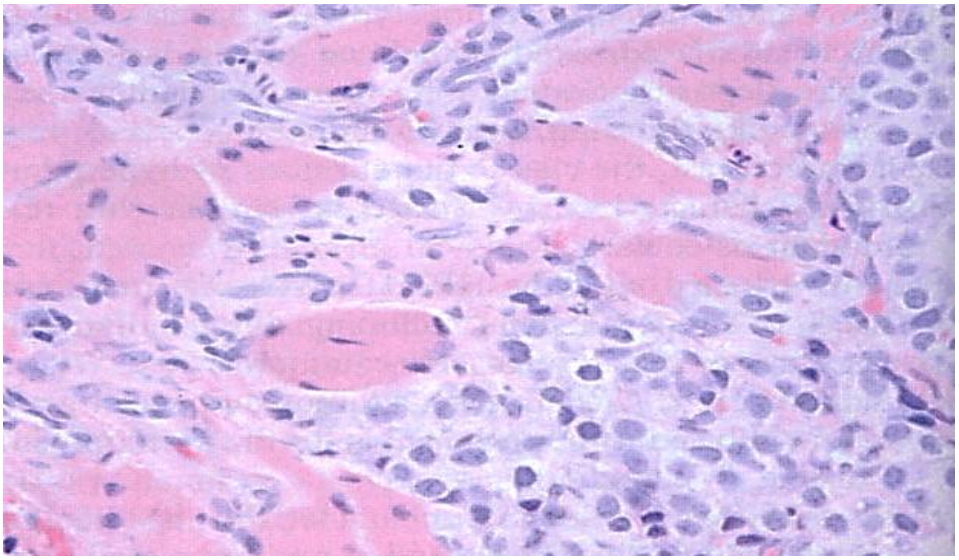

Fig. 4. Skeletal muscle invasion by parathyroid carcinoma (H&E stain; 400x)

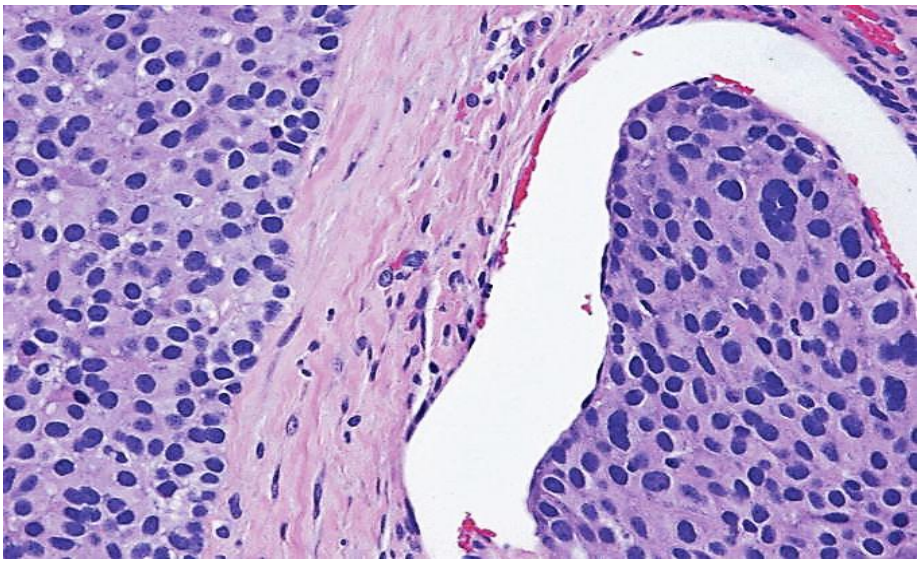

Fig. 5. Vascular invasion in Parathyroid Carcinoma(H&E stain; 400x)

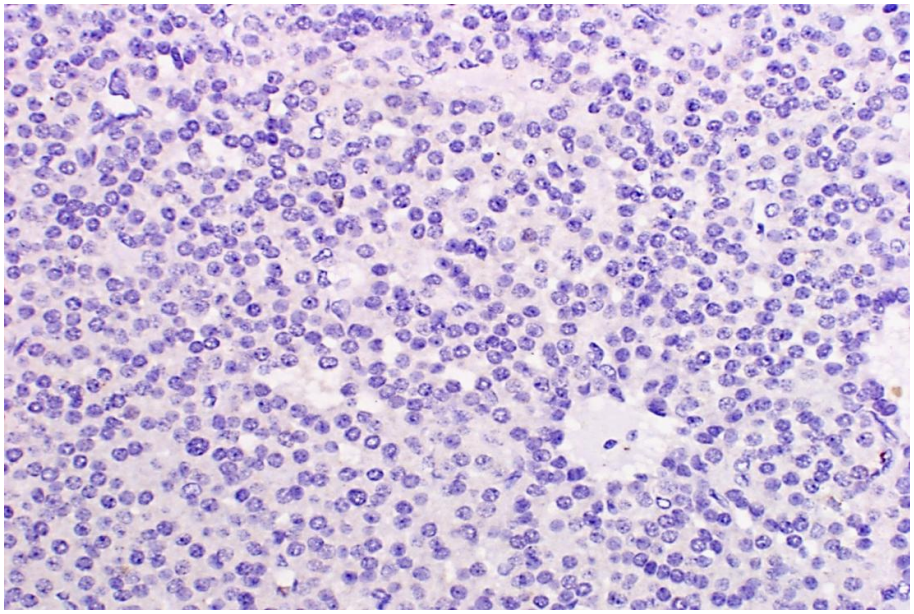

Fig. 6. Negative immunohistochemistry staining for parafibromin

The main issue of controversy is the appropriate surgical management in a patient with postoperative pathological diagnosis of Parathyroid Carcinoma who was not suspected to have Parathyroid Carcinoma preoperatively or intraoperatively. Does the patient warrant re-exploration and enbloc resection or can the patient be observed? There is no concrete evidence to support one way or the other. Some surgeons advocate close observation of serum calcium and PTH levels for evidence of recurrence and utilizing enbloc resection as a reserve in the event of recurrence [8,9,11].

4. CONCLUSION

Parathyroid carcinoma is a rare endocrine malignancy that often presents with severe hypercalcemia and diagnosis can be difficult.A high index of suspicion is essential to diagnose it preoperatively or intraoperatively. Surgery is the main modality of treatment.

CONSENT AND ETHICAL APPROVAL

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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