Original Article

Parathyroid Neoplasms: The Army Hospital (Research & Referral) Experience

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Abstract

Background: Neoplasms of the parathyroid are common but parathyroid carcinoma is exceptionally rare. In contrast to most other malignant endocrine tumours that are usually less hormonally active, malignant parathyroid tumours are hyper functional. Malignant parathyroid tumours pose a diagnostic dilemma for the pathologist.

Objective: To study the clinicopathological profile of a case series of parathyroid neoplasms and determine features which facilitate a malignant diagnosis.

Methods: A retrospective analysis of seven cases of surgically treated parathyroid tumours over a three-year period at a single centre was done. Clinical, haematological, biochemical, and radiological data was accrued from medical records. The histopathology slides were reviewed along with the clinicopathological profile in an attempt to delineate markers of malignancy.

Results: Patients ranged from 30 to 58 years of age. Males and females were approximately equal. Weakness and bone pain were the commonest presenting symptoms. Over 50% had significant hypercalcaemia and all had elevated serum parathormone. Clinically apparent mass was seen in only one. All tumours were successfully localised using CT scan and MRI. Thick fibrous capsule and broad septal fibrosis was seen in both the carcinomas; these were thin in the adenomas. Mitotic counts of 1-3 per high power field (HPF), capsular invasion and nodal metastasis were noted in the malignant tumours.

Conclusion: Elevated serum calcium and parathormone values point to a parathyroid neoplasm. Current imaging modalities are successful in localising the tumour preoperatively. Markedly elevated serum calcium, broad fibrous bands, mitotic counts and capsular invasion are indicators of malignancy.

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Key Words: Parathyroid; Adenoma; Carcinoma

Introduction

Neoplasms of the parathyroid are common, but parathyroid carcinoma is exceptionally rare [1]. In contrast to other malignant endocrine tumours that are hormonally less active, malignant parathyroid tumours are hyper functional and are characterised by high levels of serum parathormone. The hyperparathyroidism is severe with high serum calcium levels, bone disease and renal stones. The clinical picture varies with the stage at presentation and is characterised by the consequences of prolonged elevation of serum parathormone, serum calcium and local recurrences in the neck. Metastases to lungs, bone and liver are a late feature. With the increasing use of automated screening techniques along with sophisticated imaging modalities, the detection of parathyroid disease is increasing. The endocrinologist is faced with complex presentations and cryptic manifestations of a rare disease. In the absence of metastasis, parathyroid carcinoma may be suspected, but cannot be confirmed prior to operation, complicating the treatment algorithm. In this case series apart from documenting the clinical profile, an attempt has been made to evaluate criteria useful in differentiating adenomas from carcinomas by clinicopathological co-relation.

Materials and Method

Consecutive patients with parathyroid tumours presenting at the Army Hospital (Research & Referral) from Dec 1999 to Dec 2002 were evaluated. Clinical, haematological, biochemical, and radiological data was accrued from medical records. The clinical presentation, serum calcium, phosphate and parathormone levels, radiological findings, operative findings, histopathology findings and course of the disease were noted. The per-operative tumour size, adherence to surrounding structures, lymph node involvement and extension to thyroid were also assessed. The histopathology slides were reviewed to identify morphologic criteria like fibrous capsule, broad fibrous trabeculae, cellular architecture, cell type, presence of mitosis and invasion. Based on these criteria, they were categorised into adenomas or carcinomas. An attempt was made to identify the most reliable biochemical, surgical or histological indicator of aggressive disease.

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Results

A total of seven cases of parathyroid disease were diagnosed and treated from Dec 1999 to Dec 2002. Our patients ranged from 30-58 years of age. Females and males were four and three respectively. Out of seven, four had significant hypercalcaemia ranging from 13.8 to 19.6 mg /dl. Serum parathormone was raised in all seven cases. The predominant clinical features were generalised weakness and joint pains, resulting in inability to walk. A palpable neck mass was present only in one case.

Imaging located the tumousr in all cases. Renal calculi were noted in four, with associated medullary sponge kidney in one and a simple cyst of the liver in another. Generalised osteopenia associated with fracture was seen in two cases (Table 1). Osteitis fibrosa cystica was confirmed on bone marrow biopsy in one. All seven cases underwent excision of tumour mass with or without nodal dissection. The gross size of the lesion varied from 0.8 to 2.5 cms. There were five adenomas and two carcinomas. The carcinomas showed a thick fibrous capsule with broad septal fibrosis in both cases. The fibrous bands in adenomas were thin and wavy (Fig 1). The pattern was trabecular in three adenomas and in two carcinomas, making it the commonest pattern encountered in our study, but excluding it as a reliable feature to differentiate between adenomas and carcinomas. We encountered predominantly clear cell adenomas but the carcinomas were both clear cell (one case) and mixed chief and oxyphil cell type (one case). Mitotic count was 1-3 per high power field in the carcinomas while it was negligible in the adenomas. Cellular pleomorphism was seen in both adenomas and carcinomas. Capsular invasion was noted in one but was not so distinct in the second case (Fig 2). This case however, showed tumour deposits in the neck nodes along with caseating granulomas suggestive of concurrent tubercular infection.

Discussion

The rarity of parathyroid carcinoma limits reports to small institutional series. Even Massachusetts General Hospital or the Mayo Clinic have reported one to two dozen cases in clinical reviews spanning four to five decades [1,2,3]. Age distribution in most series ranged between 14-88 years with a mean of 54 years. Our patients in the age group 30 – 58 years, reflected the demographic profile of our service population. The equal male: female ratio is comparable to most series. These tumours are difficult to diagnose clinically unless a high index of suspicion is maintained [3,4]. In most situations, symptoms are vague and often ignored both by the patient and the doctor. Patients in our series had been symptomatic from six months to five years. Bone pains, pathological fracture, or other evidence of bone diseases are seen in approximately 90%, followed by renal stones (50-80 % cases) as reported in most series. Symptoms of hypercalcaemia are vague and include fatigue, weakness or constipation. We encountered a neck mass in two patients and both had carcinoma. All the malignant cases in our series had extreme elevations of serum parathormone and serum calcium, were symptomatic with renal and bone symptoms with one having mental obtundation and chronic renal failure (CRF).

Non-functioning parathyroid carcinomas have been reported in literature, and a more aggressive course is attributed to them. All the patients in our series had hyper

Table 1

Symptoms	Number
Weakness	5/7
Bone Pains	5/7
Pathological fractures	2/7
Palpable neck mass	2/7
Nephrocalcinosis	3/7
CRF	1/7
Serum Calcium	10.8 - 14.1 mg/dl (N=9-11 mg/dl)
Parathormone	980-1962 pg/ml (N=10-55pg/ml)
CT localisation	6/6
MRI localisation	1/1

Duration of symptoms ranged from six months to five years

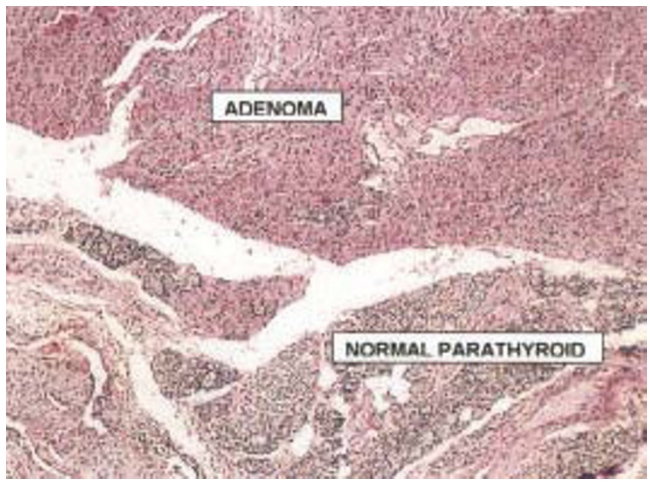

Fig. 1 : Microphotograph showing the border between adenoma and normal parathyroid gland

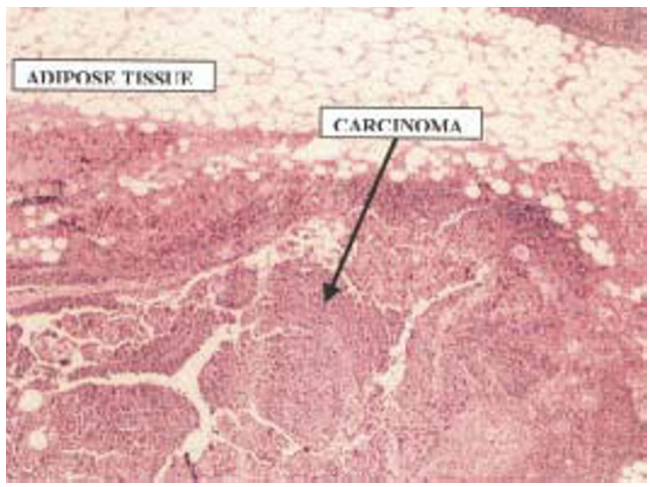

Fig.2 : Malignant cells infiltrating surrounding fat