Case Report

Malignancy of parathyroid: An uncommon clinical entity

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ABSTRACT
Parathyroid carcinoma is a very rare cause of hyperparathyroidism. The diagnosis is usually established on histopathological grounds of capsular and vascular invasion, but a potential clue to the diagnosis is also offered by the severity of clinical profile, abrupt onset of symptoms, and a high degree of hypercalcemia and raised serum parathyroid hormone (PTH). We report a case of an elderly female with a prolonged history of generalized weakness and bone pain along with bilateral renal calculi, classical bony lesions, and a high serum calcium and PTH level who underwent a right inferior parathyroidectomy considering a parathyroid adenoma as our diagnosis. However, the biopsy report was consistent with a parathyroid carcinoma, and so, she was further subjected to an ipsilateral hemithyroidectomy as a completion procedure. So, we would like to emphasize that its preferable to have a high index of suspicion for parathyroid carcinoma when these clues are present, than to miss the opportunity for surgical cure in the first go by failing to consider it in the differential diagnosis.

Key words: Carcinoma, parathyroid, rare endocrine malignancy

INTRODUCTION
Parathyroid carcinoma is a slow-growing, invasive neoplasm of parenchymal cells. It accounts for 1% of all cases of primary hyperparathyroidism. Parathyroid carcinoma is the least common endocrine malignancy and accounted for only 0.005% of cases reported to the National Cancer Database (NCDB) between 1985 and 1995. Due to its rarity, a preoperative diagnosis is uncommon. Patients usually present with a severe form of hyperparathyroidism at diagnosis, such as bone disease (brown tumors, subperiosteal bone resorption, lytic bone lesions, pathological fractures, salt and pepper appearance of skull), renal disease (nephrolithiasis, nephrocalcinosis), or hypercalcemic crisis, in contrast to the relatively asymptomatic presentation of benign parathyroid disease. An aid to the diagnosis is offered by the severity of clinical spectrum and a high degree of elevation of serum calcium > 14–15 mg% and serum PTH, 3–10 times of normal.

An average of 50% patients of carcinoma parathyroid may have a palpable neck mass which is almost never the presentation in parathyroid adenoma.

CASE REPORT
Our patient was an 80-year-old female with a history of generalized weakness, pain in the back and knees for 4 years, and bilateral flank pain for 1 year. She was seeing a dentist for a tooth extraction when she was advised to undergo an x-ray for a suspicious swelling on the lingual aspect of right mandible which revealed an osteolytic lesion of the vertical ramus of right mandible [Figure 1]. Same day an ultrasound abdomen done for her flank pain showed bilateral tiny renal stones. Patient had no urinary complaints. Other routine investigations at that time were essentially normal other than raised S. Creatinine.
For further confirmation of the lytic lesion of the right mandible a computerized tomography CT head and neck was done which demonstrated an expansile osteolytic lesion in the right posterior body, right mandibular ramus, and coronoid process (reported as brown tumor of mandible) and a well-defined lesion postero-inferior to the right lobe of thyroid showing few specks of calcification (parathyroid lesion). At this point in view of her lytic mandibular lesion, bilateral renal calculi and a suspected parathyroid lesion the probability of hyperparathyroidism was entertained and patient was evaluated further. Her laboratory values were: S. Ca+ 14.30 mg%, S. Creatinine 1.78 mg%, S. BUN 47 mg%, S. Alk Phos 557 IU/L, and Intact PTH 1881 pg/ml. A “salt and pepper” appearance seen on x-ray of the skull [Figure 1] and lytic lesions in the left frontal region and left supracetabular region on respective x-rays further strengthened the diagnosis. Preoperative vitamin D levels were not obtained nor was a bone mineral density done. There was no history of pancreatitis, fractures, depression/psychiatric features, and constipation. Physical examination was essentially normal and there was no palpable neck mass. Based on these findings, a diagnosis of primary hyperparathyroidism due to parathyroid adenoma was made; however, she did not undergo a sestamibi scan.

Patient was taken up for right inferior parathyroidectomy under GA. A mini incision of 2.5 cm was made over the right side of neck, two fingerbreadth above the sternal notch. The adenoma was found posterior to the inferior border of the right lobe of thyroid with minimal adhesions to the thyroid. The size of the adenoma was 1.5 × 1 × 0.4 cm and it weighed 2 g. No lymph nodal excision was done. Excised gland was sent for histopathological examination.

Postoperatively on day 1, her serum PTH fell down to 12.45 pg/ml and serum calcium levels came down to 9.4 mg/dl.

To our surprise, the histopathologist reported it as a carcinoma of the parathyroid gland. The tumor was composed predominantly of chief cells arranged in multiple nodules separated by thick fibrous bands. There was capsular invasion by tumor cells along with lymphovascular invasion [Figure 2]. Tumor cells were uniform with minimal atypia and brisk mitotic activity (0–4/10 HPF).

Later an ipsilateral hemithyroidectomy was done on the basis of histopathology report as a completion procedure.

There was no preoperative or postoperative evidence suggestive of a distant spread of the malignancy.

At present, she is maintaining normocalcemia with oral calcium and calcitriol supplementation. She is on regular follow-up and is not receiving any chemo or radiotherapy.

**DISCUSSION**

Carcinoma of the parathyroid gland is a highly uncommon cause of primary hyperparathyroidism.

There are several presenting features of a patient with primary hyperparathyroidism which when present should suggest a malignant rather than a benign etiology.

The formation of renal “stones” and involvement of “bones” occur with greater frequency and severity in parathyroid carcinoma.[1-3]

Renal involvement in the form of nephrolithiasis, nephrocalcinia, and renal insufficiency is a common occurrence in patients of malignancy of parathyroid. Renal colic is a frequent presenting complaint of parathyroid carcinoma.

Bone pain and pathological fractures are quite often seen in a parathyroid carcinoma. Readily apparent radiological

**Figure 1:** Radiograph showing brown tumor of right mandible and “salt and pepper” appearance of skull

**Figure 2:** Picture showing microscopic appearance of parathyroid carcinoma
features of hyperparathyroid bone disease such as osteitis fibrosa cystica, subperiosteal bone resorption, “salt and pepper” skull, and osteopenia are commonly seen in parathyroid carcinoma (44%–91%). In contrast, benign primary hyperparathyroidism rarely have skeletal complaints and specific radiological signs are found in less than 5%.7

A palpable neck mass has been reported in 30%–70% patients with parathyroid carcinoma. This finding is a striking difference between benign and malignant parathyroid disease, as a palpable neck mass is quiet unusual in primary hyperparathyroidism.9 In addition, recurrent laryngeal nerve palsy in a patient with primary hyperparathyroidism who has not had a previous neck surgery is also very suggestive of parathyroid carcinoma. The serum calcium level of most patients with parathyroid carcinoma is higher compared to patients having benign lesions and are generally >14 mg/dl. The serum PTH levels are also elevated and are about 3–10 times above the limit of normal.1‑3 Levels of alkaline phosphatase are also higher in patients with parathyroid carcinoma than in a case of parathyroid adenoma.7

Intraoperatively, parathyroid carcinoma may be distinguished from adenomas by their firm, stony hard consistency and lobulation. Adenomas tend to be soft, round, or oval and of a reddish brown color.10

The histological criteria for diagnosis of parathyroid carcinoma were given by Schantz and Castleman4 in 1973, based upon an analysis of 70 cases of the same and are still valid today. These include:
1. sheets or lobules of tumor cells separated by tense fibrous bands;
2. capsular or vascular invasion; and
3. mitotic figures within tumor parenchymal cells.

Single best therapy of parathyroid carcinoma is complete resection of primary tumor at the time of initial operation when extensive local invasion and metastasis are less likely and hence lies the great importance of a preoperative suspicion and intraoperative recognition.

If a diagnosis is made in early postoperative period on the basis of histopathological examination, a re-exploration of the neck is warranted and a completion procedure be performed in which ipsilateral thyroid lobe and isthmus and structures adjacent to the tumor site should be excised.1,10

Samuel et al. rightly pointed out in their case report that parathyroid carcinoma is often undiagnosed preoperatively, suspected intraoperatively, and confirmed postoperatively.11

**CONCLUSION**

To conclude, we report a case of an uncommon endocrine malignancy with the emphasis on preoperative diagnosis to prevent undue morbidity of a second surgery.

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