

## Pathological bone fractures in a patient with parathyroid carcinoma — A Case Report

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### Abstract

Parathyroid carcinoma is a rare malignant neoplasm of the parathyroid glands which results in enlargement and excessive production of parathyroid hormone (PTH) responsible for pathologically raising calcium levels in the blood resulting in bone pain/fractures, renal stones and other signs of hypercalcaemia.

A 37 year old woman presented with sudden, spontaneous bone pain and fracture of the right femoral shaft. This unusual presentation was explained by extremely high PTH levels and hypercalcaemia in the blood and a hard, solitary mass palpable in the neck. During surgical excision of this mass, finding of several adhesions, possible capsular invasion and lymph node enlargement led to a diagnosis of parathyroid carcinoma.

The neoplasm proliferates via adenoma-carcinoma sequence so early diagnosis and prompt surgical excision with post-operative care may provide palliation and keep recurrences in check. Pancreas and pituitary evaluation is also necessary as this presentation may be a part of Wermer (MEN-1) syndrome.

**Keywords:** Parathyroid, Carcinoma, Fractures, Neoplasia, Brown's tumour.

### Introduction

Parathyroid cancer forms in one or more of the parathyroid glands and is one of the rarest of all human cancers. Its estimated incidence is 0.015 per 100,000 people and estimated prevalence is 0.005% in the United States.<sup>1,2</sup>

Parathyroid carcinoma is the rarest cause (<1%) of primary hyperparathyroidism, the most common one being parathyroid adenoma (85-95%) followed by parathyroid hyperplasia (5-10%). Patients present with marked hypercalcaemia and hyperparathyroidism. Raised

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levels of calcium and parathyroid hormone (PTH) are the primary cause for the morbidity and mortality associated with parathyroid cancer and not the infiltration of tissues by malignant cells. Parathyroid cancer typically grows slowly and has a rather low malignant potential. It is more likely to invade local structures (thyroid, strap muscles, esophagus, trachea, recurrent laryngeal nerve) than to metastasize to the lymph nodes.

Patients of parathyroid carcinoma usually have palpable neck masses as opposed to parathyroid adenomas which are normally not palpable. The clinical features may include: fragile bones that fracture easily (osteoporosis), kidney stones, polyuria, abdominal pain, easy fatigability, depression, arthralgia, nausea, vomiting, loss of appetite, and frequent complaints of illness with no apparent cause.<sup>3</sup> Patients of parathyroid carcinoma have a much higher occurrence of bone disease than patients of parathyroid adenoma.<sup>4</sup>

If the patient has any of the following clinical findings, parathyroid carcinoma should be suspected:<sup>1,4</sup>

- ◆ Severe hypercalcaemia: > 14 mg/dl.
- ◆ Serum PTH level: > twice that of normal.
- ◆ Cervical mass palpated in a hypercalcaemic patient.
- ◆ Hypercalcaemia with unilateral vocal cord paralysis.
- ◆ Simultaneous renal and skeletal disease in a patient with primary hyperparathyroidism.

Surgically, parathyroid cancers may be differentiated from adenomas by their hard feel and lobulation; adenomas are usually soft, round/ oval in shape and reddish-brown in colour.<sup>5</sup> In most cases, parathyroid cancers have a maximum diameter of 3.0-3.5 cm compared with approximately 1.5 cm for adenomas.<sup>1</sup> In about 50% of the patients, the carcinoma is surrounded by a dense, fibrous capsule that penetrates surrounding tissues. Histopathologically, it is difficult to differentiate benign from malignant parathyroid tumours.<sup>1,5,6</sup>

Intraoperatively, when parathyroid carcinoma is

suspected based on severity or invasion of surrounding tissues by a firm parathyroid tumour, aggressive excision is performed, including the thyroid and surrounding tissues as necessary.<sup>7</sup>

Tumour recurrence occurs in nearly 40-60% of patients, usually within 2 to 5 years after the initial resection.<sup>8,9</sup>

Certain conditions appear to increase the risk of parathyroid cancer, including: multiple endocrine neoplasia type 1, autosomal dominant familial isolated hyperparathyroidism and hyperparathyroidism-jaw tumour syndrome. Parathyroid cancer has also been associated with external radiation exposure but most reports describe an association between radiation and the more common parathyroid adenoma.<sup>4</sup>

### Case Presentation

A 37 year old, rather emaciated, female presented at the emergency of services hospital, Lahore in July 2016 with a history of a road traffic accident and pain in the left thigh. She got a radiograph done which showed no fractures at that time. She was discharged on analgesics, and advised for restricting movements of left lower limb. However, mild pain persisted and 2 months later she presented again with suddenly developed severe pain, swelling and deformity of the same thigh and inability to move the left lower limb. Radiograph showed complete spiral fracture of the upper



**Figure-1:** X-ray showing diffuse fibrosis and periosteal thinning characteristic of osteitis fibrosacystica. (Brown's tumour).



**Figure-2:** Right inferior parathyroid mass excised measuring 5cm x 3cm x 2cm showing deficiency of capsule and hence possible local spread.

shaft of left femur and it was thought that she might have had an undisplaced fracture which was missed in first presentation. The fracture was repaired with an intramedullary nail. She was discharged and advised physiotherapy to maintain left hip, knee and ankle joints mobility intact. In November 2016, she presented again, now with pain in the right thigh reported to have been suddenly caused during her physiotherapy exercise. Detailed history also revealed complaints of constipation and depression. Neck examination showed that a solitary, hard mass palpable in the Para median position, right of the midline of the neck which was thought to be a parathyroid neoplasm of the right lower parathyroid gland causing primary hyperparathyroidism; Brown's tumour was suspected in bone due to enhanced osteoclast activity caused by hyperparathyroidism (osteitis fibrosacystica); X-ray showed cystic bone spaces with brown fibrous tissue, thinning of the subperiosteum and egg-shell type appearance among other signs of post-menopausal osteoporosis which are not commonly seen at such a young age. (Figure-1) Parathyroid scanning was done employing dual phase <sup>99m</sup>Techetium-methoxyisobutylisonitrilesintigraphy. Further lab evaluation revealed elevated serum PTH level of 135.6pg/ml (Reference range: 10-65pg/ml) and serum calcium of 14.4mg/dl (Reference range: 8.5-10.3mg/dl) while serum phosphorous was normal at 3.4mg/dl (Reference range: 2.7-4.5mg/dl). She

also had mildly deranged renal function tests and high alkaline phosphatase of 689U/L (Reference range: 35-104U/L)

The patient was scheduled for surgical excision of the abnormal mass after receiving informed consent. During surgery, resection of the mass was rather difficult due to adhesions formation with adjacent structures and parathyroid capsule also seemed to have been breached (Figure-2). As suspicion of parathyroid carcinoma grew stronger, lymph nodes of the neck were also examined and were found to be enlarged. The surgical procedure was proceeded with removal of the right lobe of the thyroid gland as well. The parathyroid mass measured 5cm x 3cm x 2cm and weighed 22grams. Recurrent laryngeal nerve and blood supply of the thyroid gland was identified and their integrity was successfully preserved. Postoperatively, patient's calcium levels started to decline toward normal and there was no sign of hoarseness. Patient was consulted with oncology and endocrinology departments and also scheduled for repair of the right femoral fracture.

## Discussion

The first known case of parathyroid carcinoma, described by De Quervain in 1909, was a non-functional tumour whose malignancy was revealed only by its macroscopic features. Parathyroid carcinomas are mostly hyperfunctional unlike other endocrine tumours that become less hormonally active when malignant.<sup>1</sup> The diagnosis of parathyroid carcinoma is difficult to make preoperatively especially when the tumour is nonfunctional. A palpable/ visible neck mass associated with markedly raised serum calcium (>14 mg/dl) and high serum PTH (more than twice that of normal) are important findings that strongly suggest parathyroid malignancy. An analysis of parathyroid carcinoma includes the histologic diagnosis on the basis of capsular, vascular, or perineural invasion or metastasis.<sup>10</sup>

Initially very few patients have metastases either to regional lymph nodes (<5%) or distant sites (<2%).<sup>1</sup> In the National Cancer Database series of 286 patients, only 16 (5.6%) had lymph node metastases at the initial surgery.<sup>2</sup> In this patient local lymph nodes were seen to be enlarged during the initial surgery.

Nonsurgical treatments such as radiotherapy and chemotherapy have given poor results in the management of parathyroid carcinoma. If carcinoma is suspected, en bloc resection should be the initial surgery with special care taken to prevent capsular damage and tumour spillage. The neoplasm proliferates via adenoma-

carcinoma sequence so early diagnosis and prompt surgical excision with post-operative care may provide palliation and keep recurrences in check. Pancreas and pituitary evaluation is also necessary as this presentation may be a part of Wermer (MEN-1) syndrome. Tumour recurrence is likely, and it is advisable that patients undergo long-term clinical follow-up along with regular measurements of serum calcium and PTH.<sup>10</sup>

**Consent:** Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

**Competing Interests:** The authors declare that they have no competing interests.

**Disclaimer:** This report has never been published or presented in any conference in the past.

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