

Parathyroid cancer presenting with Brown tumours mimicking bone metastasis

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ABSTRACT

Bone metastasis is the most common diagnosis considered for lytic lesions in the bone. Parathyroid cancer presenting as overt bone disease with diffuse lytic lesions secondary to untreated hyperparathyroidism (HPT) is a rare entity nowadays. We report the case of a 50-year-old Chinese lady who presented with diffuse bone lesions consistent with Brown tumours, vertebral body collapse and hypercalcaemia mimicking bone metastasis and was later diagnosed with parathyroid cancer.

Keywords: Adenocarcinoma, Brown tumour, hyperparathyroidism, parathyroid neoplasm

INTRODUCTION

Parathyroid cancer is a rare endocrine malignancy. In most series this entity accounts for less than 1% of patients with primary hyperparathyroidism. ¹The largest study to date was based on the United States National Cancer Data Base that included 286 cases of parathyroid carcinoma. ¹Primary hyperparathyroidism (HPT) is usually diagnosed as asymptomatic hypercalcaemia or presents with symptoms of hypercalcaemia. The initial presentation as metabolic bone disease is

more common in parathyroid cancer than benign parathyroid disease. Overt bone disease secondary to untreated HPT presenting with radiographic changes of Brown tumours and fractures have become a rare entity. ² Classical skeletal lesions appear as sub-periosteal cortical erosions, diffuse osteoporosis and cystic lesions. However, these occur in less than 5% of patients with HPT. ³ Brown tumours are uncommon sequelae and vertebral brown tumours are considered very rare in primary HPT with only five cases reported in the literature. ⁴ Severe bone involvement can mimic metastatic bone disease and constitute a real challenge for the clinician. We report the case of a 50-year-old Chinese lady with

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parathyroid cancer and HPT mimicking metastatic bone disease.

CASE REPORT

A 50-year-old Chinese lady was initially referred to the Urology Clinic with a right stag-horn calculus and chronic backache. Her backache has been there for the previous six months and she was taking regular analgesics for pain relief. A computed tomography (CT) of the kidney, ureter and bladder showed multiple lytic lesions of the sixth thoracic spine with collapse of the vertebral body and other lytic lesions of the fourth, fifth lumbar vertebral bodies and pelvic bones (Figure 1a). She was admitted for further investigations with a probable diagnosis of metastatic bone disease. She gave no other history of note except for the backache. The patient was also on treatment for depression for the last six years and there was a strong family history of lung cancer. General examination

was essentially unremarkable, except for tenderness over the fifth, sixth and seventh thoracic spines. There was no neurological deficit.

Routine blood investigations revealed normal serum creatinine of 75 $\mu\text{mol/l}$ (range 44-80), hypercalcaemia of 3.18 mmol/L (2.23-2.58) and elevated serum alkaline phosphatase of 624 U/L (38-126). Serum albumin was 35 gm/L (35-48) and phosphate was 0.58 mmol/L (0.78-1.53). A magnetic resonance imaging revealed multiple cystic and sclerotic lesions in the pelvic bones, thoracic and lumbar vertebrae with collapse of the sixth thoracic vertebra causing cord compression (Figure 1b). A myeloma screen was negative and fine needle aspirate of the sixth vertebral lesion was negative for malignancy. The iPTH (intact Parathyroid Hormone) was markedly elevated at 108.3 pmol/l (1.3-7.6). An ultrasound scan of the neck showed a 3.3

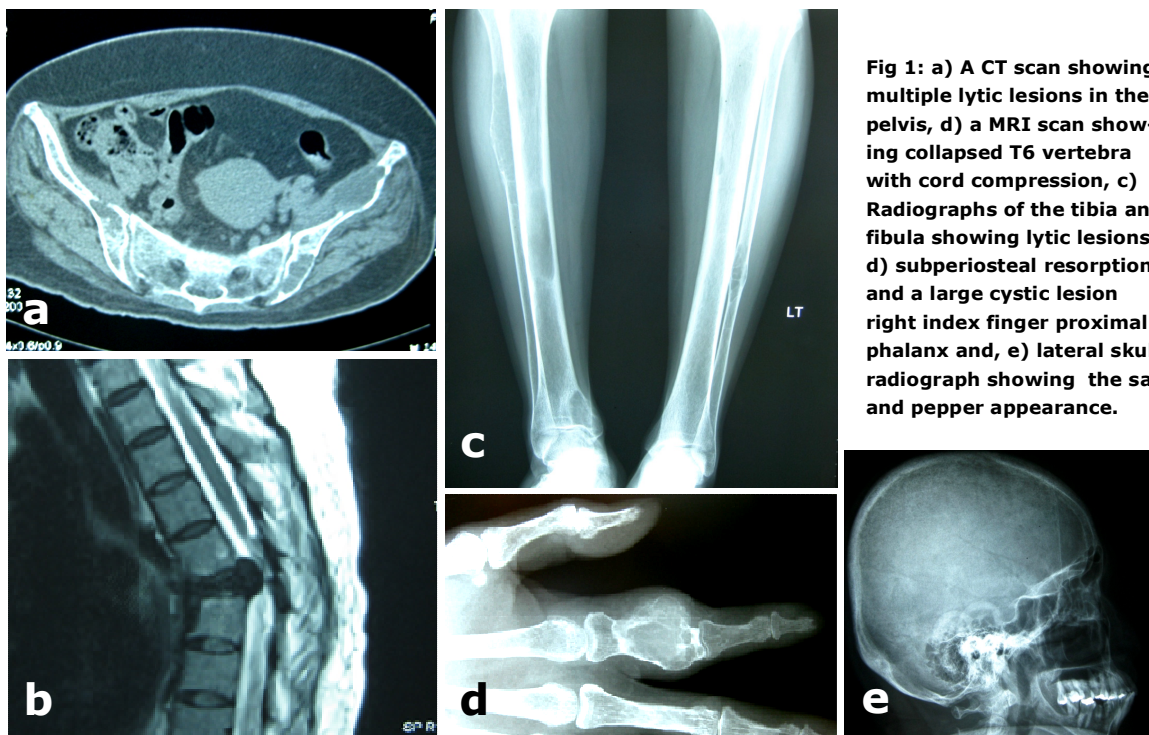


Fig 1: a) A CT scan showing multiple lytic lesions in the pelvis, d) a MRI scan showing collapsed T6 vertebra with cord compression, c) Radiographs of the tibia and fibula showing lytic lesions, d) subperiosteal resorption and a large cystic lesion right index finger proximal phalanx and, e) lateral skull radiograph showing the salt and pepper appearance.

x 1.7cm left superior parathyroid mass. A CT scan however did not show any parathyroid adenoma or lymphadenopathy. The skeletal screening showed multiple cystic, lytic lesions of the phalanges (Fig 1c), tibia, fibula (Figure 1d), and salt and pepper appearance of the skull (Figure 1e).

The hypercalcaemia was treated with intravenous hydration and a course of intravenous pamidronate. In view of the cord pressure and risk of progression, a transpedicular screw fixation of the spine was done. Six weeks later, this was followed by parathyroid excision with the suspicion of a parathyroid tumour. Intra-operatively, there were no findings suggestive of a parathyroid cancer. The frozen section was reported as only parathyroid adenoma. The tumour was excised in toto. Post-surgical specimen histopathology established the diagnosis of a parathyroid cancer.

On the second post-operative day, the patient had mild hypocalcaemia and was treated with oral calcium and vitamin D. When the diagnosis was confirmed to be parathyroid cancer based on histological findings, she was advised to proceed with a left thyroid lobectomy and node dissection. Unfortunately, the patient declined. After four months of follow up, the serum iPTH level was normal and she was still on replacement with calcium and vitamin D. She remained pain- and recurrence-free and was able to mobilise independently.

DISCUSSION

Primary HPT occurs secondary to a parathyroid adenoma in more than 85% of cases and multi-glandular hyperplasia in 5-10%. Carci-

noma accounts for less than 3%.⁵ HPT causes loss of cortical bone and predisposes to micro-fractures and secondary haemorrhage. This leads to influx of multinucleated macrophages and ingrowth of reparative fibrous tissue resulting in a reactive tissue mass known as the Brown tumour. The vascularity, haemorrhage, and haemosiderin deposition gives rise to the characteristic colour of a Brown tumour. They can cause deformities of the bone and simulate a neoplastic process. Although the overall incidence of Brown tumours is greater in primary than with secondary HPT, spinal Brown tumours have been reported more in secondary HPT.⁶ Brown tumours occur in 5% of patients with HPT and there have been only 15 reported cases of spinal brown tumours in the literature. Of these 15 patients, only five had primary HPT with the rest having secondary HPT, mostly due to chronic kidney disease on dialysis.⁴ A likely explanation for this is that HPT usually affects the cortical bone more than the cancellous bone, unlike malignancy where vertebral involvement is more common.

HPT presents as diffuse osteopaenia as well as circumscribed lucent bone areas. Erosion of the tufts of the phalanges is an associated finding and is more pronounced on the radial than the ulnar side. Other areas of resorption include symphysis pubis, distal clavicle, pelvis, ribs extremities and mandible. The calvaria may have a granular appearance typically described as the 'salt and pepper' skull. Lytic lesions are more often found in women than in men and have increased incidence with age.⁷

Clinical presentations of hypercalcaemia are myriad involving many organ

Table 1: Clinical features suggestive of parathyroid cancer with primary hyperparathyroidism.

| Clinical features | Incidence |
|---|------------|
| Age: less than 50 years | |
| Severe hypercalcaemia and markedly iPTH levels (>10 times ULN), including parathyroid crisis | 12% |
| Severe symptoms of bone (osteitis fibrosa cystica) | 40% to 70% |
| Renal disease (renal stones, nephrocalcinosis) | 30% to 60% |
| Recurrent laryngeal palsy from direct tumour invasion | |
| A palpable (parathyroid) neck mass | 30% to 50% |
| Operative features | |
| Large gland; a mean of 3.3 cm in diameter in some series (7), | |
| Firm or hard gland and appears pale in colour, | |
| Local invasion of adjacent structures e.g., thyroid, strap muscle, recurrent laryngeal nerve, | |
| Lymph node involvement may be present in about 15% of cases; in such cases, en bloc resection that includes the ipsilateral thyroid gland, adjacent lymph nodes and adherent tissue is the only curative treatment. | |

systems (Table 1). Our patient experienced mainly backache and was found to have renal stones and lytic bones lesions. Interestingly, our patient did not complain of any gastrointestinal symptoms. She was also treated for depression in the previous five years. Depression in association with hypercalcaemia has been well documented.¹² However, it is uncertain in our case whether this could have been related especially given the duration of the depressive illness.

It is important to consider primary HPT in the differential diagnosis of multiple lytic bone lesions and fractures. Fine needle aspiration cytology (FNAC) and bone biopsy are important investigations to exclude malignancy. Serum iPTH will assist in diagnosing HPT. Bone scintigraphy is a highly sensitive test for detection of the altered local bone metabolism. However, it lacks specificity to differentiate bone metastasis from metabolic bone disease. Histology remains important for diagnosis confirmation.⁸ In our patient the initial clinical, biochemical and radiological impression was that of metastatic bone disease. The localisation of the parathyroid tumour by ultrasound imaging is generally

useful before surgery. Ultrasound has a sensitivity of 70 to 80% whereas technetium (Tc-99m) sestamibi scan has a sensitivity of 86 to 90% in detecting primary HPT.⁹

Once HPT is diagnosed, the challenge is to differentiate between parathyroid carcinoma and adenoma before surgery. FNAC is not sensitive and specific for this purpose. The *sine qua non* of parathyroid cancer is capsular or vascular invasion, a situation often detected after examination of the entire resected gland. It is of great importance that parathyroid carcinoma is considered in iPTH dependent hypercalcaemia, as the morbidity and mortality associated are substantial, and optimal outcomes are associated with complete resection of the tumour at the initial surgery.¹ The optimal surgical treatment for a carcinoma is *en bloc* resection with ipsilateral thyroid lobectomy and removal of any enlarged or abnormal lymph nodes. Frozen section may assist but should not be used alone in diagnosis.

Our case is interesting for several reasons. With the iPTH level of more than 10 times, severe metabolic bone disease and the

nephrocalcinosis, carcinoma was very likely. However in the absence of locally invasive disease, local lymph node involvement and a negative frozen section, only parathyroid excision was done. The parathyroid carcinoma was only diagnosed during the examination of the resected specimen. Unfortunately our patient declined to proceed with hemithyroid resection as recommended in such a case. However, she has remained well.

After resection of a parathyroid adenoma or carcinoma, hungry bone syndrome and severe hypocalcaemia may be seen and may persist due to atrophy of the remaining parathyroid glands. Pre-operative pamidronate in combination with high doses oral alfacalcidol and calcium supplements can prevent symptomatic postoperative hypocalcaemia. This may also reduce the requirement for intensive monitoring of calcium, patient morbidity, and reduce hospital stay.¹⁰ Our patient was treated with intravenous pamidronate pre-operatively and hydration and she did not have severe hypocalcaemia post-surgery in spite of severe bone disease.

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