CASE REPORT

Osteitis fibrosa cystica masquerading as bone neoplasm

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SUMMARY

A 50-year-old female patient with no significant medical history presented with left knee pain. Radiographs of the knee showed a circumferential swelling of the distal femur suggestive of neoplasia. Further evaluation revealed multiple lesions in the left iliac bone and proximal femur. Biopsy was suggestive of a reparative granuloma or an aneurysmal bone cyst. Laboratory assessment showed hypercalcaemia and elevated parathyroid hormone consistent with severe primary hyperparathyroidism. Osseous survey was significant for salt and pepper appearance of the skull. Ultrasound of the neck and ^{99m}Tc-sestamibi parathyroid scintigraphy localised a left parathyroid adenoma/carcinoma. Parathyroidectomy was successful, and a large parathyroid adenoma was excised. Six months later, the patient was doing fine with her gait returning to normal. On follow-up 2 years later, she had no recurrence of the lesions.

BACKGROUND

Over the years, the clinical presentation of hyperparathyroidism has undergone significant changes. The presentation of hyperparathyroidism previously included bone pain, nephrolithiasis and abdominal pain; these days, hyperparathyroidism is mostly asymptomatic and detected on routine laboratory evaluation.¹ Osteitis fibrosa cystica (OFC) or brown tumour is a collection of osteoclasts and poorly woven bone which has been described in association with severe hyperparathyroidism.² Due to its radiographic and histological appearance, it is often mistaken for metastatic disease or bone neoplasms.³ Although not seen commonly, it may

be the presenting manifestation of hyperparathyroidism. Physicians need to be aware and consider OFC in the differential diagnosis; otherwise, this may lead to unnecessary diagnostic and treatment procedures.

CASE PRESENTATION

A 50-year-old female patient with left knee pain of 3-month duration presented to her primary care physician. She did not report any trauma; however, she had trouble ambulating and had to use a knee brace. She had no history of polyuria, polydipsia, nephrolithiasis or low trauma fractures. She had no significant medical or surgical history. Physical examination was significant for tenderness on the anterior and medial aspects of the knee along with decreased range of motion.

INVESTIGATIONS

Radiographs of the knee showed no fracture but a circumferential soft-tissue swelling was noted. This was suspicious for a bone neoplasm and she was referred to orthopaedics for further evaluation. MRI showed a rounded area of signal abnormality in the distal femur with cortical thinning and defects, suggestive of a neoplastic process (figure 1). CT scan of the chest, abdomen and pelvis showed a 4.2 cm lytic bone lesion in the left iliac bone and 2.2 cm lytic lesion in the left proximal femur (figure 2).

As this pattern was suspicious for metastatic disease, a biopsy of iliac and femoral lesions along with prophylactic intramedullary nailing of the left femur was done. Pathology revealed abundant giant cells and spindle cells with reactive bone formation consistent with a giant cell reparative granuloma or

Figure 1 MRI femur showing an area of signal abnormality (red arrow).

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Figure 2 (A) CT pelvis showing an osteolytic lesion in the left iliac bone. (B) CT femur showing an osteolytic lesion in the left femoral head.

an aneurysmal bone cyst. (figure 3). Laboratory assessment showed hypercalcaemia of 12.3 (8.5–10.2 mg/dL) which was suspected to be secondary to hypercalcaemia of malignancy. Further evaluation revealed a high parathyroid hormone (PTH) of 1810 (15–65 pg/mL) consistent with severe primary hyperparathyroidism and a low vitamin D of <13 (>30 ng/mL). Bone survey showed diffuse osteopenia, salt and pepper appearance of the calvarium (figure 4). Ultrasound of the neck showed a 3.8 cm solid hypoechoic mass inferior to the pole of the left lobe of the thyroid. ^{99m}Tc -sestamibi parathyroid scintigraphy revealed a persistent large uptake in the inferior aspect of the left thyroid lobe consistent with a large parathyroid adenoma or carcinoma. (figure 5).

DIFFERENTIAL DIAGNOSIS

Although multiple osteolytic lesions are most consistent with metastatic disease, important differential diagnosis includes: lymphoma, fibrous dysplasia of the bone, multiple myeloma and hyperparathyroidism (with OFC).⁴ However, a close examination of the zone of transition between the osteolytic lesion and

normal bone on X-ray can help to differentiate between benign and malignant lesions. Benign lesions have a sharp well-defined zone of transition whereas malignant ones have a wide and irregular zone.⁵ Hypercalcaemia can also be seen in all the aforementioned entities although through different mechanisms. Assessing the level of PTH can differentiate hyperparathyroidism from the others. While the PTH is high in hyperparathyroidism, it is suppressed in hypercalcaemia secondary to malignancy.⁶ The histological picture of OFC is similar to other osseous pathologies like an aneurysmal bone cyst, giant cell tumours, giant cell granulomas and low-grade osteosarcomas. Therefore, a high index of suspicion is needed to prevent misdiagnosis.⁴

TREATMENT

Parathyroidectomy was performed with the intraoperative PTH monitoring. With excision of the parathyroid adenoma, the PTH dropped from 1826 pg/mL to 144.7 pg/mL (92%). Pathology showed a hypercellular parathyroid consistent with a parathyroid adenoma. Postoperatively, the patient experienced transient

Figure 3 (A) H&E stain showing parathyroid adenoma (weight 12 g). (B) Parathyroid adenoma showing chief cells. (C) and (D) Left femoral biopsy showing nodular spindle cell formation with scattered osteoclast like giant cells and reactive bone formation.

Figure 4 Bone survey revealing salt and pepper appearance of the skull (white arrow).

Figure 5 (A) Ultrasound of the neck showing an enlarged parathyroid gland (red arrow). (B) ^{99m}Tc -sestamibi parathyroid scintigraphy of the neck showing intense uptake on the left side consistent with a hyperactive parathyroid gland.

hypocalcaemia secondary to hungry bone syndrome (HBS) and needed calcium supplementation.

OUTCOME AND FOLLOW-UP

She underwent physical rehabilitation and on follow-up in the clinic at 6 months the patient was doing fine with her gait returning to normal. On follow-up 2 years later, the patient continued to do well and radiographic assessment showed no osseous abnormalities.

DISCUSSION

The clinical picture of hyperparathyroidism has undergone a vast change since the 1960s with the invention of the multi-channel autoanalyser and measurement of serum calcium became commonplace.² With earlier detection of hyperparathyroidism, many of the severe and chronic manifestations of hyperparathyroidism are rarely seen anymore. Cope found skeletal manifestations in 23% in their series of patients (preautoanalyser) while Silverman *et al* found that skeletal manifestations in less than 2% of patients.^{7,8} The estimated prevalence of primary hyperparathyroidism is 0.04/1000.²

The action of PTH on bone is a unique one with intermittent secretion favouring bone formation and continuous secretion favouring bone resorption.⁹ It also differs from postmenopausal osteoporosis as it affects cancellous bone more than trabecular bone.⁸ It is high bone turnover state with increased formation and resorption. PTH1 receptors are present on osteoblast lineage cells. PTH increases the formation and decreases the apoptosis of osteoblasts. It can also decrease the synthesis of sclerostin which is an inhibitor of the Wnt signalling pathway. It can also decrease the synthesis of osteoprotegerin and increase production of RANK-L which can increase resorption.^{10–12}

OFC or brown tumour is a bone lesion which represents the final stage of hyperparathyroidism.¹³ It was initially described in 1891 by Von Recklinghausen.¹⁴ It is most commonly seen in the jaw bone, clavicle, pelvis ribs and ends of long bones.⁵ Due to the rapid bone loss, haemorrhage, granulation tissue and fibrous tissue replace the bone marrow; the brownish discolouration is due to haemosiderin deposition. Imaging shows a lytic or multilobular cystic lesion known as OFC often misdiagnosed as bone neoplasms or metastatic disease. Histologically, it consists of giant cells, spindle cells, fibrous tissue and poorly woven bone; however, certain giant cell granulomas/tumours, and aneurysmal bone cysts may have the same picture.¹⁵ They can cause bone pain, pathological fractures and compression of surrounding structures.¹⁶

OFC and neoplastic/metastatic disease may be differentiated by assessing the PTH level which is elevated in hyperparathyroidism-induced hypercalcaemia and normal/low in hypercalcaemia of malignancy.¹³ OFC resolves with the surgical treatment of hyperparathyroidism making its recognition crucial to avoid unnecessary diagnostic and therapeutic procedures. However, local excision or curettage may be done especially if there are functional problems. Rarely steroids have been used to decrease the size of the tumour if they do not resolve postparathyroidectomy.^{17–20}

HBS is the sudden and prolonged hypocalcaemia secondary to the decrease in PTH levels which can be seen after parathyroidectomy. Risk of developing HBS includes older age, larger parathyroid glands and radiographic bone involvement.²¹

Other radiological manifestation in hyperparathyroidism is described in table 1.²²

Table 1 Radiological manifestations of hyperparathyroidism

Salt and pepper appearance of skull	Skull bones show a marked stippling with pin head-sized opaque areas.
Codfish vertebra	Smooth biconcave deformity of the vertebral bodies, squared-off end plates and compression of adjacent discs.
Loss of lamina dura	Lamina dura is thin plate of cortical bone forming the tooth socket which is seen normally as a thin white line on X-ray.
Subperiosteal resorption	Pathognomic, best seen on the radial side of the second and third digits. Can also be seen in the lateral one-third of the clavicles.
Rugger-jersey spine	Subendplate hyperdensities causing an alternating sclerotic and lucent appearance.
	Generalised demineralisation of bone with coarsening of trabecular pattern
	Bone cysts in pelvis, ribs and metacarpals

Learning points

- ▶ Osteitis fibrosa cystica (OFC) is the classic skeletal manifestation of hyperparathyroidism which is rarely seen in the developed world.
- ▶ OFC needs to be considered in the differential diagnosis when there are osteolytic lesions and hypercalcaemia. They are most common in the jaws, pelvis, long bones, skull and ribs.
- ▶ OFC can be differentiated from malignancy by measuring parathyroid hormone; it is markedly increased in hyperparathyroidism and suppressed in hypercalcaemia of malignancy. It typically resolves after the surgical treatment of hyperparathyroidism.
- ▶ Skeletal manifestations of hyperparathyroidism though rare are reflective of chronic hyperparathyroidism. They may be the presenting features and merit immediate recognition and treatment.

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