Section: Medicine

Case Series and Review

HYPERPARATHYROIDISM WITH UNUSUAL SKELETAL PRESENTATIONS: A CASE SERIES AND REVIEW

Prashant Gaikwad[1], Mayur Garg[1], Yash Anarase[2], Samata Dongare[3]

[1]Assistant Professor, Department of Medicine, MGMIHS, Kamothe, Navi Mumbai, India.
[2]Junior Resident, Department of Medicine, MGMIHS, Kamothe, Navi Mumbai, India.
[3]Assistant Professor, Department of Gyanecology and Obstetrics, JJ Hospital, Mumbai, India.

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Corresponding Author:
Dr. Yash Anarase,
Junior Resident, Department of Medicine, MGMIHS,Kamothe,Navi Mumbai, İndıa.
Email: yash.anarase.123@gmail.com

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ABSTRACT

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by excessive secretion of parathyroid hormone leading to hypercalcemia and disturbances in calcium–phosphate metabolism. Although many cases are detected incidentally during routine biochemical screening, symptomatic disease with skeletal involvement continues to be encountered, particularly in regions where diagnosis is delayed. Classical skeletal manifestations include osteitis fibrosa cystica, decreased bone mineral density, and pathological fractures. However, rare skeletal presentations may mimic neoplastic or metastatic bone disease, posing diagnostic challenges. This case series highlights three patients with unusual skeletal manifestations of PHPT and discusses the diagnostic and therapeutic considerations associated with these presentations.

The first case involved a 23-year-old male presenting with progressive swelling of the right jaw. Biochemical evaluation revealed severe hypercalcemia and markedly elevated parathyroid hormone levels. Imaging studies confirmed a right inferior parathyroid adenoma with a mandibular brown tumor. The second case described a 31-year-old female with severe bone pain and advanced osteoporosis due to PHPT. Following parathyroidectomy, she developed symptomatic hypocalcemia consistent with hungry bone syndrome, requiring intensive calcium and vitamin D supplementation. The third case involved a 49-year-old male presenting with bilateral lower limb weakness and vertebral compression fractures. Imaging revealed multiple osteolytic lesions mimicking metastatic malignancy; however, biochemical findings confirmed PHPT due to a parathyroid adenoma.

These cases illustrate the diverse skeletal manifestations of PHPT and emphasize the importance of biochemical evaluation in patients presenting with unexplained bone lesions or hypercalcemia. Early recognition and appropriate imaging are essential for accurate diagnosis and surgical planning. Parathyroidectomy remains the definitive treatment and leads to significant clinical and biochemical improvement. Careful postoperative monitoring is crucial, particularly for complications such as hungry bone syndrome. This case series highlights the need for heightened clinical awareness to prevent diagnostic delay and reduce morbidity associated with advanced PHPT.

Keywords: Primary hyperparathyroidism; Brown tumor; Hungry bone syndrome; Parathyroid adenoma; Vertebral compression fracture; CKD; Secondary hyperparathyroidism.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by excessive and autonomous secretion of parathyroid hormone (PTH), resulting in hypercalcemia and disturbances in calcium and phosphate metabolism. The condition is most commonly caused by a solitary parathyroid adenoma, although parathyroid hyperplasia and

carcinoma may also occur. PHPT is one of the most common endocrine disorders, with an estimated prevalence of approximately 1–7 cases per 1000 individuals in the general population, and it occurs more frequently in women and in older adults. In many developed countries, PHPT is often detected incidentally during routine biochemical screening before significant clinical symptoms develop.[1–3]

Classically, PHPT affects multiple organ systems, particularly the skeletal and renal systems. Skeletal manifestations result from increased osteoclastic activity leading to bone resorption and include osteitis fibrosa cystica, decreased bone mineral density, pathological fractures, and bone pain. Renal manifestations such as nephrolithiasis and nephrocalcinosis are also commonly observed.[4–6]

With the increasing availability of biochemical testing, severe skeletal complications have become less common in developed countries. However, in developing regions, delayed diagnosis and coexisting vitamin D deficiency often lead to advanced disease with prominent skeletal involvement.[7]

Rare or unusual skeletal presentations of PHPT may mimic other serious conditions such as metastatic bone disease or hematological malignancies, posing diagnostic challenges. Manifestations such as mandibular brown tumors, severe osteoporosis leading to postoperative hungry bone syndrome, and vertebral compression fractures may represent the initial presentation of PHPT in some patients.[8–10]

Early recognition of these atypical presentations is essential to ensure timely diagnosis and appropriate management, particularly because surgical removal of the hyperfunctioning gland is curative in the majority of cases.[11] This case series presents four patients with unusual skeletal manifestations of primary hyperparathyroidism, highlighting diagnostic challenges and management strategies.

CASE SERIES

Case 1: Hyperparathyroidism with Jaw Brown Tumor

A 23-year-old male was referred from the dental outpatient department with complaints of progressive swelling over the right side of the jaw associated with pain for the past two months. The swelling had gradually increased in size over time. The patient also had a history of left-sided renal calculi two years earlier for which he had undergone DJ stenting, suggesting a possible underlying metabolic cause. On clinical examination, a firm swelling was noted over the right mandibular region with localized tenderness.

Laboratory investigations revealed significant biochemical abnormalities suggestive of primary hyperparathyroidism. The patient had markedly elevated serum calcium levels of 14.8 mg/dL and low serum phosphorus levels of 2.3 mg/dL. Serum intact parathyroid hormone (PTH) levels were significantly elevated at 1488 pg/mL. Additionally, 24-hour urinary calcium excretion was elevated at 544 mg/24 hours. These findings were consistent with the diagnosis of primary hyperparathyroidism.

Imaging studies were performed to localize the source of excess parathyroid hormone secretion. Ultrasonography of the neck revealed a well-defined hypoechoic lesion measuring 3.4 × 2.3 cm with internal cystic areas in the region of the right inferior parathyroid gland, suggestive of a parathyroid adenoma. A technetium-99m sestamibi scan demonstrated increased tracer uptake in the right inferior parathyroid region, confirming the presence of a parathyroid adenoma and aiding preoperative localization. Imaging of the jaw showed a lytic lesion consistent with a brown tumor, a rare skeletal manifestation of primary hyperparathyroidism.

The patient was diagnosed with primary hyperparathyroidism secondary to a right inferior parathyroid adenoma with an associated mandibular brown tumor. Definitive management was performed with surgical excision of the right inferior parathyroid adenoma. Postoperatively, the patient showed significant biochemical improvement with reduction in serum calcium and PTH levels. The patient was advised regular follow-up with biochemical monitoring and imaging to assess recovery and regression of the skeletal lesion.

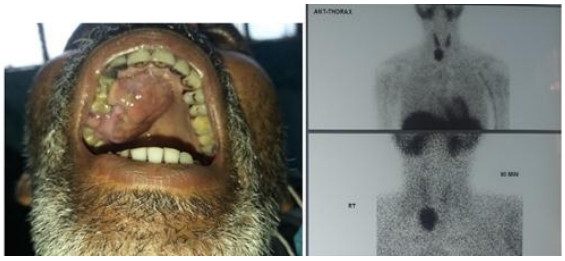

Figure 1a: Right jaw brown tumor. 1b: TC 99 Sestamibi scan showing right inferior Parathyroid

Case 2 – Hyperparathyroidism with Hungry Bone Syndrome

A 31-year-old female presented with complaints of severe generalized bone pain, lethargy, and difficulty in walking with a limp on the right side. Biochemical evaluation revealed significant hypercalcemia with a serum calcium level of 14 mg/dL and hypophosphatemia with serum phosphorus of 1.2 mg/dL. Serum intact parathyroid hormone (PTH) levels were markedly elevated at 1385 pg/mL, and serum alkaline phosphatase was greater than 1500 IU/L, indicating severe skeletal involvement due to primary hyperparathyroidism. Localization studies using technetium-99m sestamibi scan revealed a left inferior parathyroid adenoma.

Bone mineral density was assessed using dual-energy X-ray absorptiometry (DEXA), which demonstrated severe osteoporosis involving multiple skeletal sites. The lumbar spine (L1–L4) showed a bone mineral density (BMD) of 0.611 with a T-score of −4.0. The femoral neck showed severe bone loss with BMD values of 0.388 on the left side and 0.393 on the right

side, corresponding to T-scores of −4.2 and −4.1 respectively. Total femur measurements also demonstrated osteoporosis with BMD values of 0.512 on the left side and 0.452 on the right side, with T-scores of −3.5 and −4.0 respectively. The most severe involvement was observed in the forearm, where the right radius showed a BMD of 0.284 with a T-score of −6.9 and the left radius showed a BMD of 0.290 with a T-score of −6.8. According to the World Health Organization classification, all measured sites were consistent with severe osteoporosis, indicating advanced skeletal disease related to prolonged hyperparathyroidism.

The patient received preoperative treatment with zoledronic acid to reduce bone resorption and subsequently underwent surgical resection of the parathyroid adenoma. On the third postoperative day, she developed symptoms of hypocalcemia including perioral numbness, carpopedal spasms, and positive Chvostek and Trousseau signs. Laboratory investigations showed a sharp decline in serum calcium to 5.9 mg/dL, with serum phosphorus of 1.5 mg/dL, serum magnesium of 1.1 mg/dL, intact PTH of 90.3 pg/mL, and alkaline phosphatase of 600 IU/L. These findings were consistent with hungry bone syndrome, a postoperative complication resulting from rapid remineralization of previously demineralized bone.

The patient was treated with intravenous calcium infusion along with phosphorus and magnesium supplementation and high-dose calcitriol therapy. Gradual stabilization of biochemical parameters was achieved; however, even six months after surgery, she continued to require high-dose oral calcium and calcitriol supplementation, indicating prolonged hungry bone syndrome associated with severe preoperative skeletal disease.

Case 3: Hyperparathyroidism Presenting with Vertebral Compression Fractures

A 49-year-old male presented with complaints of progressive weakness of both lower limbs and severe backache for the past two weeks. The symptoms were associated with difficulty in walking and worsening spinal pain. On neurological examination, motor power in both lower limbs was reduced to 3/5, and ankle clonus was present, indicating possible spinal cord involvement. Magnetic resonance imaging (MRI) of the spine revealed an anterior wedge compression fracture of the D2 and D3 vertebrae with associated spinal cord compression, explaining the neurological deficits.

Laboratory investigations showed marked biochemical abnormalities suggestive of primary hyperparathyroidism. The patient had hypercalcemia with a serum calcium level of 13.3 mg/dL, low serum phosphorus of 2.4 mg/dL, and significantly elevated intact parathyroid hormone (PTH) levels of 1241 pg/mL, consistent with the diagnosis of primary hyperparathyroidism. Further imaging was performed to localize the hyperfunctioning parathyroid gland. A technetium-99m sestamibi (MIBI) scan demonstrated a right inferior parathyroid adenoma measuring 2.4 × 2 × 2.5 cm.

To further evaluate the skeletal involvement, SPECT-CT imaging was performed, which revealed multiple lytic lesions involving the cranium, facial bones, appendicular skeleton, sternum, ribs, and vertebrae. The radiological appearance closely mimicked metastatic malignancy or multiple myeloma, posing a significant diagnostic challenge. However, the markedly elevated PTH levels along with hypercalcemia confirmed the underlying diagnosis of primary hyperparathyroidism with extensive skeletal involvement. This case highlights the importance of biochemical evaluation in differentiating advanced hyperparathyroid bone disease from malignant skeletal disorders.

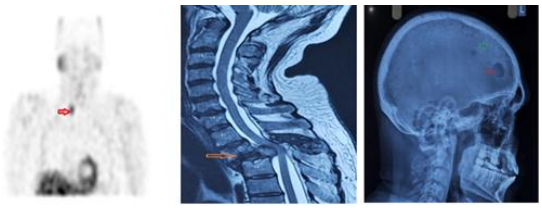

Figure 2a: MIBI scan showing right inferior parathyroid adenoma. 2b: MRI spine suggestive of D2-D3 wedge compression fracture. 2c: X-ray skull suggestive of lytic lesion (red arrow), salt and pepper appearance (green arrow)

Case 4: Tertiary Hyperparathyroidism in a case of Dialysis Dependent CKD

A 35-year-old female presented with pedal oedema and shortness of breath of 3 days' duration. She was a known case of chronic kidney disease (CKD) and had been on maintenance haemodialysis for the past 5 years. In addition, she reported progressive difficulty sitting up from a lying position over the last 6 months, suggestive of a significant functional limitation.

On physical examination, she was found to have marked deformities involving both upper and lower limbs [Figure 3a], indicating a chronic underlying skeletal pathology. The deformities were associated with impaired mobility and reduced functional capacity.

Laboratory investigations revealed: Serum calcium: 10.3 mg/dL; Serum phosphorus: 12.1 mg/dL; Intact parathyroid hormone (iPTH): 2029 pg/mL

The presence of markedly elevated iPTH with deranged mineral metabolism raised suspicion of severe hyperparathyroidism with renal osteodystrophy. MRI neck demonstrated an enlarged thyroid gland with a few focal altered signal intensity lesions posterior to the thyroid gland, suggestive of parathyroid enlargement/adenoma.

Subsequently, a Tc-99m sestamibi (MIBI) scan revealed increased tracer uptake in all four parathyroid glands, confirming the presence of hyperfunctioning parathyroid tissue and suggesting multigland disease. Skeletal imaging showed advanced bone involvement: X-ray lower limbs:

features suggestive of severe osteoporosis [Figure 3c]. Skull X-ray: classical salt-and-pepper appearance [Figure 3b], consistent with hyperparathyroid bone disease

A diagnosis of severe tertiary hyperparathyroidism with skeletal involvement in the setting of CKD on maintenance haemodialysis was made, consistent with advanced renal osteodystrophy due to hyperparathyroidism. The patient was initiated on medical therapy, including Tablet Cinacalcet 30 mg twice daily and Injection Denosumab 60 mg subcutaneously, planned once every 6 months. Given the severe biochemical abnormalities, radiological findings, and disabling skeletal manifestations, she was planned for total parathyroidectomy.

This case highlights an unusual presentation of severe tertiary hyperparathyroidism with marked limb deformities and advanced skeletal changes, including severe osteoporosis and salt-and-pepper skull, emphasizing the need for early recognition and aggressive management of metabolic bone disease in dialysis-dependent CKD patients.

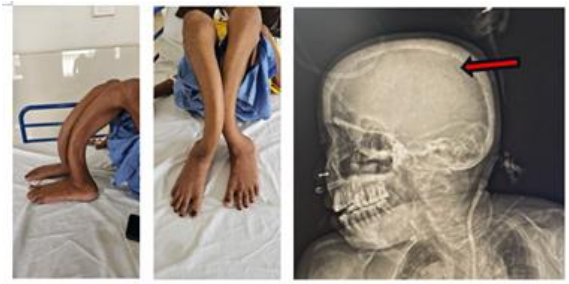

Figure 3a: Images showing lower limb deformity. b: Xray Skull showing Salt and Pepper appearance

DISCUSSION

Primary hyperparathyroidism (PHPT) is diagnosed by demonstrating elevated or inappropriately normal parathyroid hormone (PTH) levels in the presence of hypercalcemia. Measurement of 24-hour urinary calcium excretion and the calcium/creatinine clearance ratio is important to differentiate PHPT from familial hypocalciuric hypercalcemia (FHH), which may present with similar biochemical abnormalities but requires a different management approach. In borderline cases or when serum albumin levels are abnormal, measurement of ionized calcium may provide additional diagnostic clarity. Imaging modalities such as neck ultrasonography and technetium-99m sestamibi scanning are commonly used for localization of hyperfunctioning parathyroid tissue and are important for preoperative planning. Ultrasonography is often used as the first-line imaging modality due to its accessibility and cost-effectiveness, especially in resource-limited settings.[1,2,12]

Skeletal manifestations of PHPT occur due to chronic osteoclastic bone resorption caused by elevated PTH levels. Brown tumors represent localized osteolytic lesions formed by excessive bone resorption and replacement with fibrovascular tissue and hemosiderin deposition. These lesions can occur in the mandible, ribs, pelvis, and long bones and may radiologically resemble neoplastic lesions.[4,9] In the present case series, one patient presented with a mandibular brown tumor, an uncommon but well-recognized manifestation of severe PHPT. Recognition of the underlying metabolic disorder is essential to avoid misdiagnosis as a primary bone tumor or metastatic disease. Surgical removal of the parathyroid adenoma usually leads to regression of brown tumors and normalization of bone metabolism.[1]

Hungry bone syndrome (HBS) is a well-known postoperative complication of parathyroidectomy and is characterized by severe and prolonged hypocalcemia resulting from rapid remineralization of previously demineralized bone.[10,13] Patients with severe skeletal disease, markedly elevated alkaline phosphatase levels, and prolonged hyperparathyroidism are at increased risk of developing HBS. In our second case, the patient developed symptomatic hypocalcemia with classical clinical signs including perioral numbness and carpopedal spasms shortly after surgery. Early identification and prompt treatment with intravenous calcium, magnesium, phosphate supplementation, and active vitamin D analogues are essential to prevent complications and ensure recovery.[14]

The third patient in our series presented with vertebral compression fractures and multiple lytic skeletal lesions that mimicked metastatic malignancy or multiple myeloma on imaging studies. Advanced skeletal involvement in PHPT can produce extensive osteolytic lesions due to severe bone demineralization and increased osteoclastic activity.[4] Such presentations can pose significant diagnostic challenges, and biochemical evaluation remains crucial for establishing the correct diagnosis and avoiding unnecessary oncological investigations. According to the guidelines from the Fifth International Workshop on the Management of Primary Hyperparathyroidism, surgical intervention is recommended in patients with symptomatic disease, significant hypercalcemia, osteoporosis, vertebral fractures, nephrolithiasis, or impaired renal function.[11] Parathyroidectomy is considered the definitive treatment and has a cure rate exceeding 95% when performed by experienced surgeons.[15] In our patients, surgical removal of the parathyroid adenoma resulted in significant clinical and biochemical improvement.

Postoperative management is particularly important in patients with severe skeletal disease who are at risk of developing hungry bone syndrome. Preoperative correction of vitamin D deficiency and adequate postoperative calcium and vitamin D supplementation have been shown to reduce the severity and duration of hypocalcemia.[16] Regular biochemical monitoring and patient education regarding symptoms of hypocalcemia are essential to ensure optimal postoperative recovery.

CONCLUSION

Primary hyperparathyroidism is a clinically diverse disorder that may present with a wide range of manifestations, from asymptomatic hypercalcemia to severe skeletal complications. Unusual presentations such as mandibular brown tumors, hungry bone syndrome, and vertebral compression fractures can create significant diagnostic challenges and may mimic other serious conditions such as malignancy.

This case series highlights the importance of maintaining a high index of suspicion and performing appropriate biochemical evaluation in patients presenting with unexplained skeletal lesions or hypercalcemia. Early diagnosis and timely surgical intervention with parathyroidectomy remain the cornerstone of treatment and are associated with excellent outcomes. Careful postoperative monitoring, particularly for complications such as hungry bone syndrome, is essential to ensure optimal recovery and reduce morbidity.

Patient Consent: Written informed consent was obtained from the patients for publication of this case series and the accompanying clinical details and images. All patient information has been anonymized to maintain confidentiality and protect patient privacy.

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