Multiple pathological fractures with a hidden aetiology

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Abstract

Bone disease is a well-recognised complication of primary hyperparathyroidism (PHPT). With early diagnosis of PHPT, florid bony changes such as brown tumours, lytic lesions and pathological fractures are rarely seen now. Here, we report an unusual presentation of PHPT in the current era. A 47-year-old lady was evaluated for multiple fragility fractures. Biochemical assessment confirmed primary hyperparathyroidism. DEXA scan showed severe osteoporosis. Left parathyroid adenoma was localised with imaging. She had multiple brown tumours. She underwent parathyroid adenoma excision and recovered after surgery with improved quality of life. Proper evaluation for secondary causes of osteoporosis is vital especially in premenopausal women. Early diagnosis and treatment of PHPT prevent disastrous complications.

Keywords: primary hyperparathyroidism, brown tumour, parathyroid adenoma, osteoporosis

Introduction

Primary Hyperparathyroidism (PHPT) is a common disorder of calcium characterised by hypercalcaemia and inappropriately normal or elevated parathyroid hormone (PTH) concentration. It is due to excessive secretion of PTH from one or more of the parathyroid glands. Early detection of PHPT during the asymptomatic phase has become very common especially in developed countries where biochemical screening is routinely recommended. Therefore, hypercalcaemia is usually mild, overt kidney stone disease occurs in less than 20% of patients and radiologically evident bone disease has become even less common. Fractures as the presentation of PHPT has become an unusual presentation. Unfortunately, target organ damage at presentation predominates in countries like China and India where the routine screening is not being practised.(1) In Asia, PHPT is more likely to present with overt hypercalcaemia and target organ damage compared to other parts of the world.(2) With the practice of routine screening, another variant of asymptomatic PHPT has been described; it is “normocalcemic PHPT”. Patients with symptomatic PHPT should undergo surgery unless contraindicated.

More than half of the premenopausal women with osteoporosis have a secondary cause.(3) So, it is critical to exclude the secondary causes of osteoporosis in patients with fragility fractures in the absence of traditional risk factors for osteoporosis, especially in premenopausal women, men younger than 50 years and in all patients with low bone density for age and sex (Z-score ≤ -2). With prompt identification of the cause and treatment, secondary osteoporosis is often reversible.

Case presentation

A 47-year-old, previously healthy premenopausal woman was evaluated for multiple fragility fractures over 2 months. She developed right sided tibia-fibula fracture followed by left sided femur shaft fracture. She had polyuria and polydipsia associated with...
constipation. She denied any bone pain. She was not on any medications, specially steroids. Family history was not significant for recurrent young onset fractures, hypercalcaemia, neck surgeries or other features suggestive of MEN syndrome. She had a palpable neck mass.

Initial biochemical assessment revealed moderate hypercalcaemia (13 mg/dL) with low phosphate and elevated ALP (415 U/L). PTH dependent hypercalcaemia was confirmed with an intact PTH level of 2513.9 pg/mL. She had vitamin D deficiency as well. “Symptomatic primary hyperparathyroidism with vitamin D deficiency” was diagnosed. Renal function was normal and there was no ultrasonic evidence of nephrolithiasis or nephrocalcinosis. DEXA scan revealed severe osteoporosis with a T-score of -4.3 for total lumbar spine and a Z – score of -3.2 suggestive of probable secondary osteoporosis.

Hypercalcaemia was managed with adequate hydration. Vitamin D replacement was started with careful monitoring of calcium levels. Parallely, imaging studies for localisation were arranged. USS scan of the neck showed a nodule of the left lobe of the thyroid gland. No separate parathyroid lesion was reported. Thyroid function test was normal. 99M Tc – Sestamibi scan revealed an active left parathyroid adenoma. For further anatomic characterisation, 4D CT scan was arranged, it showed left parathyroid neoplasm measuring 4.4 cm (CC) × 2.7 cm (Tr) × 2.6 cm (AP). Bony changes such as brown tumours at left clavicle, mandible and bilateral maxillary sinuses and lytic lesions at cervical vertebrae were also noted in the CT scan (see figure 1). Though she had PTH dependent hypercalcaemia, in the presence of lytic lesions, the possibility of multiple myeloma was evaluated and excluded. Taking into account the very high PTH level with significant target organ damage and the large parathyroid tumour, the possibility of parathyroid carcinoma was considered.

She underwent parathyroid adenoma excision with intraoperative PTH monitoring. Intraoperative PTH dropped more than 50% from the baseline within 10 minutes. Being large tumour, severe hypercalcaemia, high PTH level, vitamin D deficiency and presence of skeletal abnormalities are predictors of hungry bone syndrome. However, she didn't develop it postoperatively. Post op period was uneventful. She

Figure 1 - 4D – CT images showing Brown tumours at left clavicle A; bilateral maxillary sinuses B; mandible C; lytic lesions at cervical vertebra D
was discharged on post op day 2 with calcium, vitamin D3 and active vitamin D supplements. Histology was compatible with parathyroid adenoma. Calcium supplements were tailed off gradually. She is awaiting a repeat assessment of bone mineral density with DEXA scan. She is free of symptoms with improved quality of life and has started to mobilise independently. Though a thyroid nodule was detected in the USS neck, a separate thyroid nodule was not identified in CT scan or during the surgery. It is likely that the USS neck detected the parathyroid lesion.

Discussion

Primary Hyperparathyroidism can present with three distinct clinical phenotypes: Overt target organ involvement, mild asymptomatic hypercalcaemia and normocalcaemic hyperparathyroidism. The important factors determining the predominant phenotype of presentation in a particular country are the extent of routine biochemical screening, prevalence of vitamin D deficiency and whether patients diagnosed with osteopenia or osteoporosis are screened for PHPT. Overall, the incidence of presentation with target organ damage has considerably reduced and it has become very rare in developed countries. In Sri Lanka routine screening for calcium or PTH level is not done. Vitamin D deficiency has been identified as a common under diagnosed entity.(4) Even though it is recommended to screen for secondary causes including PHPT after the diagnosis of osteoporosis is made, it is less widely practised. Screening for osteoporosis and evaluation of secondary causes don't occur in most settings where patients present with fractures. It indicates a wide care gap in the management of osteoporosis. Fortunately, our patient was evaluated for the secondary causes and the hidden aetiology was identified.

Bone is a major target organ affected in PHPT. Patients can present with bone pain; fragility fractures or skeletal deformities and various characteristic radiographic changes have been described. The classic imaging appearance is osteitis fibrosa cystica (OFC) in which brown tumours, lytic lesions, subperiosteal resorption of phalanges and bony cysts are seen. Brown tumours are identified in around 3% of patients.(5) Parathyroid surgical management results in complete regression of brown tumours in most of the patients.(6)

Osteopenia and osteoporosis are well – recognised skeletal manifestations of PHPT. PHPT preferentially affects the peripheral skeleton rather than axial skeleton in comparison to postmenopausal osteoporosis where the opposite happens. Early diagnosis of PHPT can prevent progression into osteoporosis and incidence of pathological fractures which increase mortality and impair quality of life. Thus, evaluation of patients with PHPT includes assessment with DEXA scans (lumbar spine, hip and distal radius) and vertebral spine assessment.

After the biochemical diagnosis of PHPT is made, preoperative localisation is important to allow more accurate and potentially curative minimally invasive treatment for the patients with single gland disease. Approximately 80% of patients have single parathyroid adenoma.

Conclusion

It is crucial to evaluate secondary causes of osteoporosis in all patients, especially in premenopausal women and young men less than 50 years old, when they are diagnosed with osteoporosis or present with fractures. Patients with PHPT manifesting severe skeletal and other end organ damage are still observed due to delayed diagnosis of severe disease. Prompt diagnosis and management can cure the disease with reversal of the skeletal damage and improvement in quality of life.

Declarations

Conflicts of interest
The authors declare that they have no conflicts of interest

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