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Pathological Fracture Femur In Primary Hyperparathyroidism - Uncommon Complications And Orthopaedic Challenges: A Case Report

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Abstract

Elevated levels of parathyroid hormone due to a hyperactive or ectopic parathyroid gland constitutes primary hyperparathyroidism. Hyperactivated osteoclastic resorption raises the levels of calcium that causes signs and symptoms, historically referred to as “stones, bones and groans.” as suggested by Fuller Albright. Multiple brown tumors (osteitis fibrosa cystica), salt and pepper skull are the common musculoskeletal manifestations seen. We report a case of pathological fracture femur in primary hyperparathyroidism to highlight the common to uncommon presentations, medical complications and the surgical challenges in its definitive management. A multidisciplinary team approach in a staged manner is essential to address the stormy pre-operative phase. Intramedullary nailing of the pathologically fractured femur restored the alignment and helped regain mobility after an extended period of rehabilitation.

Keywords: Primary hyperparathyroidism, Hyperparathyrotoxicosis seizures, Brown tumor, Osteitis fibrosa cystica, Myopathic foot drop

Introduction

Primary hyperparathyroidism (PHPT) is a condition characterized by elevated parathormone secondary to parathyroid adenoma (80%) or due to excessive secretion by one or more ectopic glands. The common presentations are nephrolithiasis, bony pain, brown tumor - unifocal or multifocal (osteitis fibrosa cystica), psychological symptoms like depression, anxiety and rarely pathological fractures. Seizures are more commonly a feature of hypothyroidism. Acute hypercalcemic crisis in parathyrotoxicosis is an Endocrine emergency. Diagnostic confirmation of PHPT is by Ultrasonogram and Tc-99-Sestamibi scan. The mainstay of treatment involves surgical excision of the abnormal gland and a staged fixation of the pathological fracture after Endocrine optimization, if necessary, in an Intensive Care Unit. This case study will highlight the uncommon presentation of a pathological fracture secondary to parathyroid adenoma induced primary hyperparathyroidism disguised as fibrous dysplasia and its associated diagnostic and surgical challenges.

Case Report :

A 42-year-old woman presented to us with a closed fracture femur following a trivial fall. She had insidious onset left-sided thigh pain and limp 3 months prior to her hospitalization. She had no other comorbidities but was severely malnourished. Her vitals were stable and had clinical signs of left

femoral shaft fracture without any distal neurovascular deficit. Plain radiographs showed severe osteopenia and confirmed a displaced femoral shaft fracture in an area of osteolytic lesion, which was also seen in the pre-injury radiograph, suggesting a pathological fracture. MRI showed heterogenous signal changes and intramedullary cystic lesions in bilateral femora – suggestive of fibrous dysplasia.

Blood values on admission showed anemia (Hb - 7.2 gm/dL), elevated alkaline phosphatase (174 IU/L) suggestive of high bone turnover, hypercalcemia (12.9 mg/dL), hypophosphatemia (2.3 mg/dL), hypomagnesemia (0.8 mg/dL), hypoalbuminemia (2.9 g/dL) with an A:G ratio of 1.1.

The fracture was temporarily stabilized by skin traction. While awaiting primary surgical fixation of the fracture, she had an episode of seizure and unresponsiveness, following which she was resuscitated and put on mechanical ventilation. Cardiac causes for collapse and cranial causes for seizures, sepsis were excluded. Serum PTH levels revealed hyperparathyroidism (2151pg/dL) while serum Prolactin was normal (10.86 µg/L). CT Brain showed acute intra-parenchymal hemorrhage with edema in right frontal, left frontal and occipital lobes in addition to acute subarachnoid hemorrhage in bilateral parietal lobes with mixed sclerotic and lytic appearing skull lesions. MR Brain confirmed the subarachnoid and intra-parenchymal hemorrhages and revealed a well-circumscribed expansile lesion in the skull – possibly suggestive of a Brown tumour or metastasis. PET CT showed diffusely increased density of bones with multiple lytic bone lesions; 30 x 21 mm non-FDG avid enhancing nodule in the supra-sternal region – inferior to the thyroid. Bone marrow biopsy was suggestive of metabolic bone disorder. ^{99m}Tc-Sestamibi parathyroid scintigraphy scan confirmed abnormal tracer uptake inferior to the lower pole of the left lobe of thyroid gland – in favour of hyperfunctioning ectopic parathyroid gland. Also, after the stormy phase of intensive care treatment, a foot drop in her left lower limb was noticed but she had intact sensations over the common peroneal nerve territory.

Excisional biopsy of the hyperactive parathyroid gland along with parathyroidectomy was done by our General Surgery team a month later once her general condition improved. Histopathological examination of the excised tissue showed a well-circumscribed lesion with lesional cells arranged in nests, cords and clusters in a palisading pattern with round to oval cells, vesicular nuclei, nuclear grooving and scant to moderate cytoplasm – suggestive of parathyroid tissue. After correcting the 'Hungry Bone Syndrome' induced hypocalcemia, left shaft of femur fixation was planned. Given the delayed fixation, open reduction and intramedullary interlocking nail fixation was carried out in a lateral decumbent position. Post-operatively, she had extended rehabilitation and delayed full weight bearing due to her metabolic musculoskeletal dysfunction and foot drop. The delayed wound infection at 3 weeks post-operatively was caused by Pseudomonas aeruginosa that needed wash out, debridement and local Vancomycin beads therapy. In her post-operative phase, she had critical monitoring of her electrolytes, calcium and vitamin D levels and were corrected as advised by the Endocrinologist. At 6 months follow-up, wound and the fracture healed well, foot drop completely recovered and she regained unaided full weight-bearing walking.

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Date		S. Calcium (in mmol/L)
25-04-2022	Day of admission	13.6
01-05-2022	After correction	8.3
15-05-2022	Recurrence	13.2
25-05-2022	Day of surgical excision of parathyroid adenoma	13.3
05-06-2022	Hungry Bone Syndrome	5.5
29-06-2022	After correction	8.4
20-08-2022	3 months follow up	8.6

Table 1 – Serial serum Calcium levels

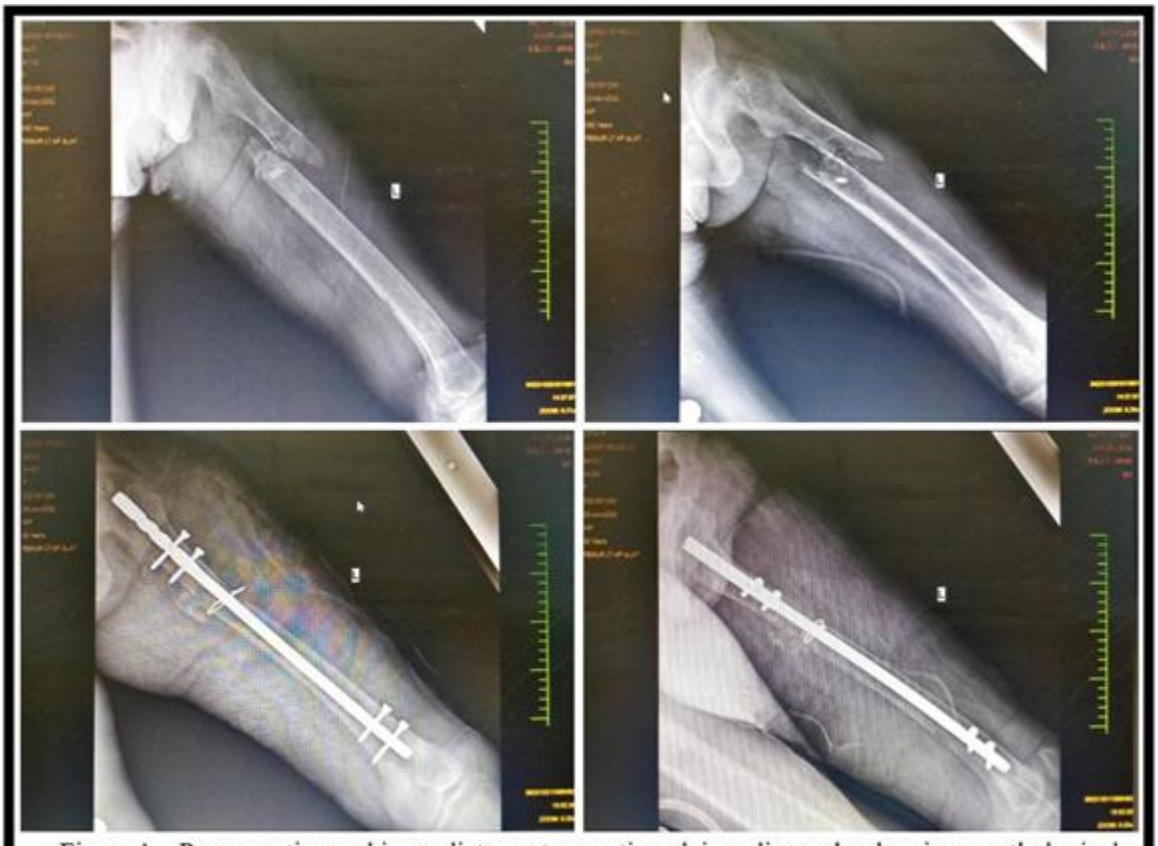

Figure 1 – Pre-operative and immediate post-operative plain radiographs showing a pathological fracture shaft of femur fixed with intramedullary interlocking nail

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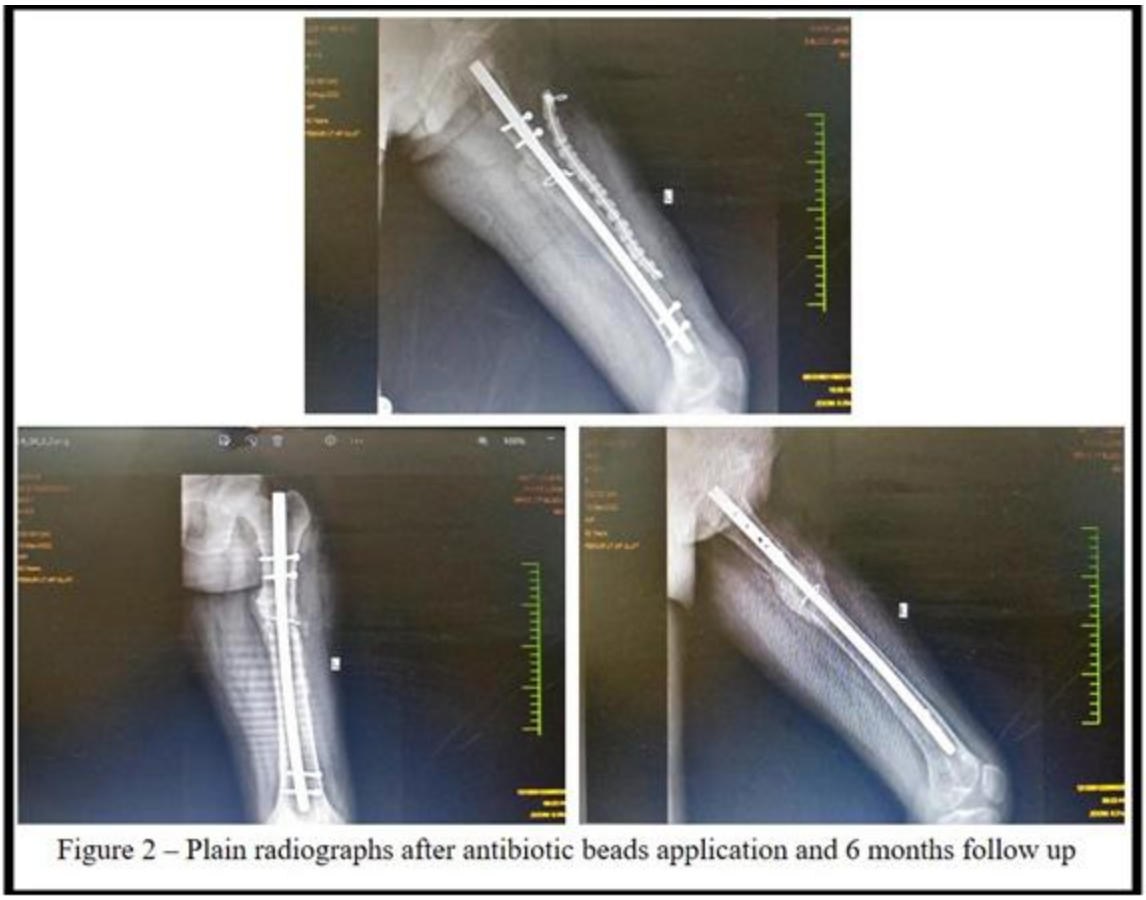

Figure 2 – Plain radiographs after antibiotic beads application and 6 months follow up

Figure 3 – Photographs showing satisfactory clinical outcome at 6 months follow up

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Discussion

Primary hyperparathyroidism (PHPT) presenting as a pathological fracture is a rare entity (1). The incidence of PHPT is 0.4 to 82 per 100,000 worldwide (1). Causes of PHPT are parathyroid adenomas (85%), hyperplasia (10%), cancer (<1%) (1) or a hyper-secreting ectopic gland. Rarely, PHPT can be familial due to germline mutation resulting in part of MEN (Multiple Endocrine Neoplasia) syndromes - type 1, 2a and 4. Based on the clinical manifestations, primary hyperparathyroidism is classified as kidney, bone, kidney-bone disease. The main symptoms are bone pain (46.02%), urolithiasis (41.59%), constipation (25.66%), fatigue (18.58%), and polyuria (15.93%). (1)

Chronic hyperparathyroidism upregulates osteoclastic resorption, granulation and fibrosis leading to cystic degeneration of bone called osteitis fibrosa cystica or "Brown tumor" (2, 8). It is a non-neoplastic cyst grouped under the giant cell tumor group (2). Prevalence of brown tumors is less than 2% in PHPT (3). They are common in women in their 3rd and 4th decades (2). The sites commonly involved are jaw, skull, clavicle, ribs, sacroiliac joint, femur and spine (3).

Musculoskeletal symptoms are bone pain with or without pathological fractures, especially of weight-bearing hips and lower limbs (3). The rate of pathological fractures in primary hyperparathyroidism is 15 per 1000 person-years (3). Myopathy associated with hyperparathyroidism is a rare phenomenon that, we believe, is the cause of delayed foot drop involving the dorsiflexors of the ankle while the sensations remained intact.

Adult seizures due to metabolic causes account for 10%. Literature provides enough evidence for seizures induced by severe hypocalcemia but our patient threw a seizure during the hypercalcemic crisis, which we attribute to the hypercalcemia-induced hypertensive metabolic encephalopathy or hypomagnesemia. Strict correction of the electrolyte imbalance is the mainstay of the treatment than anticonvulsive agents but has poor prognosis (10).

Delayed diagnosis of PHPT is usually due to uncommon presentations such as a pathological fracture (3). Blood values usually reveal hypercalcemia, hypophosphatemia, high ALP and significantly elevated serum parathormone (3). Thus, serum calcium and parathormone levels screening should be considered in pathological fracture cases with a high index of suspicion.

In PHPT, plain radiographs show osteolytic lesions (brown tumors), rugger jersey spine, salt and pepper skull, and subperiosteal resorption of phalanges (3). Long bones usually exhibit thinned-out cortices, cystic changes and osteopenia (2). 'Brown tumor' has similarities to benign cystic lesions like aneurysmal and simple bone cysts (3). The pre injury MRI of our patient done at outside hospital showed features suggestive of "fibrous dysplasia", which is in complete discordance to the actual diagnosis. On MRI, brown tumors are characterized by hypointensity in T1 and hyperintensity in T2 (2). PET-CT and ^{99m}Tc-Sestamibi scan have high specificity in PHPT. Histopathological features seen are osteoclasts, diffuse fibrosis, neo-angiogenesis and hemosiderin (brown color) deposition (3).

The mainstay of treatment of parathyroid adenoma is parathyroidectomy, evident by the cure rate of 95% to 98% (3, 7). However, there is no consensus regarding the management of secondary pathological fractures, especially in the weight-bearing lower limb (2). Fixation of fractures before or after the excision of the parathyroid lesion is contentious, although literature supports post-parathyroidectomy fixation owing to the probable hypercalcemic crisis (3,9).

For femur diaphyseal fractures, intramedullary nailing is shown to be superior to load-bearing extramedullary devices (5, 6), as it allows for good pain control, biomechanical stability and immediate weight bearing (4).

Following the excision of parathyroid adenoma, a swift and prolonged phase of hypocalcemia, hypophosphatemia and hypomagnesemia may ensue, which is known as Hungry Bone Syndrome. Robust Endocrinology monitoring and management of Calcium, Magnesium and Vitamin D levels is warranted.

Calcium, when tested for, is usually the total calcium level. However, 50% of calcium is albumin bound and only the free ionic calcium is the active metabolite. Hence in the management of a hypercalcaemic crisis, corrected calcium has to be calculated for precise control. Corrected calcium can

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be calculated by the formula [Serum calcium + (4 .0 - Albumin level)] where serum calcium is measured in mg/dl and Albumin in g/dl.

Conclusion

Pathological fractures of a long bone with severe generalized osteopenia should raise the suspicion of underlying metabolic bone disorder. As a differential diagnosis, malignancy and metastasis need to be excluded. However, parathyrotoxicosis can have atypical presentation like pathological fractures with hypercalcaemic seizures and myopathy. Musculoskeletal features masquerading as fibrous dysplasia, as in our case, can mislead the treating surgeons. Bone mineral profile including serum PTH is a useful screening tool that helps in timely diagnosis and management of suspected "Brown tumor". In PHPT associated pathological fracture, the root cause of it i.e. parathyroid adenoma needs excision and subsequent electrolyte dysfunction needs robust management prior to Orthopaedic stabilization. A multi-disciplinary approach is warranted to ensure swift diagnosis and comprehensive management for a successful outcome.

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