Unchecked hyperparathyroidism and von recklinghausen's disease of bone: Great mimicker in diagnosis

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ABSTRACT

Incidence of new cases of a severe form of unchecked primary hyperparathyroidism is decreasing day by day. Here, we report the case of a 40-year-old female patient of primary hyperparathyroidism with a maiden visit to the hospital with multiple osteolytic lesions and multiple pathological fractures. The diagnosis was installed and managed accordingly.

Keywords: *Cystic, Osteolytic, Primary hyperparathyroidism.*

The primary hyperparathyroidism (PHPT) has an overt action on cortical bones and skeletal display. The parathyroid hormone binds to osteoblasts, which further differentiates to osteoclasts and hereafter cortical bone resorption [1]. Literature is in support that the incidence of unchecked hyperparathyroidism has a dramatic downfall in recent years [2]. Osteitis fibrosa cystica (von Recklinghausen's disease of bone) is a bony pathology, where the bone mass is decreased and replaced by fibrous tissue, and it is a feature of advanced (unchecked hyperparathyroidism) stage [3].

Here, we are presenting a case of the severest form of osteitis fibrosa cystica in a female, which presented to the hospital with the dependent and crippling stage and here got managed to the independent stage. The rationale behind reporting the case report is to mention the treatment option of pathological fracture as well of PHPT by multidisciplinary teamwork.

CASE REPORT

A 40-years-old female presented to us with the chief complaints of inability to walk (even with support) and multiple bony deformities since five years. Family and personal history were insignificant.

On general examination, the patient had anemia, conspicuous look, lean and thin body with multiple swelling over all the limbs and abnormal mobility of the right thigh. On vital examinations, respiratory rate was16 per minutes, blood pressure was 128/76 mm Hg, pulse rate was 88 beat per minutes and temperature was normal. The patient also had a single diffuse swelling over the thyroid region and anterolateral bowing of the left tibia (Fig. 1). She was able to sit with support but unable to do active straight leg raising (SLR) test. Initially, she managed to walk with support but since 1 year she is limited to bed and now due to pain and deformity in the left thigh, she came to the Hospital.

Skeletal survey of the patient was sought, which revealed the multiple cystic bony lesions in all long bone, spine, iliac bone and pathological fracture of bilateral neck of femur (Fig. 2). After clinico-radiological workup, the differential diagnosis of fibrous dysplasia (Mazabraud syndrome), metastasis and hyperparathyroidism were installed. Ultrasonography of the abdomen and pelvis was done. This showed the multiple hypoechoic fluid-filled cavities in both sides of the iliac bone.

Magnetic resonance imaging (MRI) was done for the pelvis and neck area. MRI pelvis (plain + contrast) revealed the bilateral fracture neck of femur and post contrast-enhancing cystic cavity in both iliac bone with solid component and multiple fluid-filled levels. Computed tomography (CT) scan of the face and neck showed the eccentric, heterogeneous swelling from the posterior right lobe of the thyroid. The lesion was abutting the trachea and

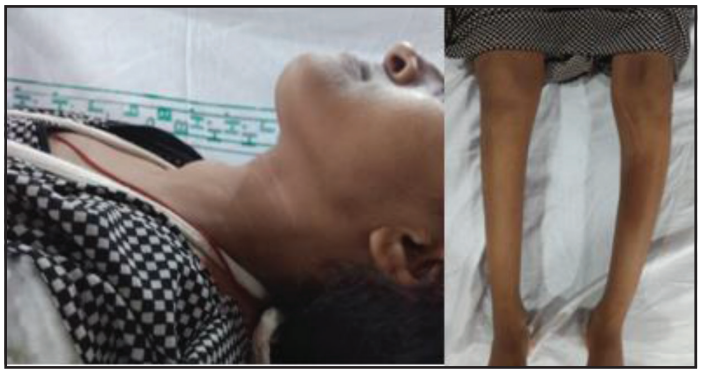

Figure1: Clinical image of the patient showing swelling over thyroid area and bowing of leg.

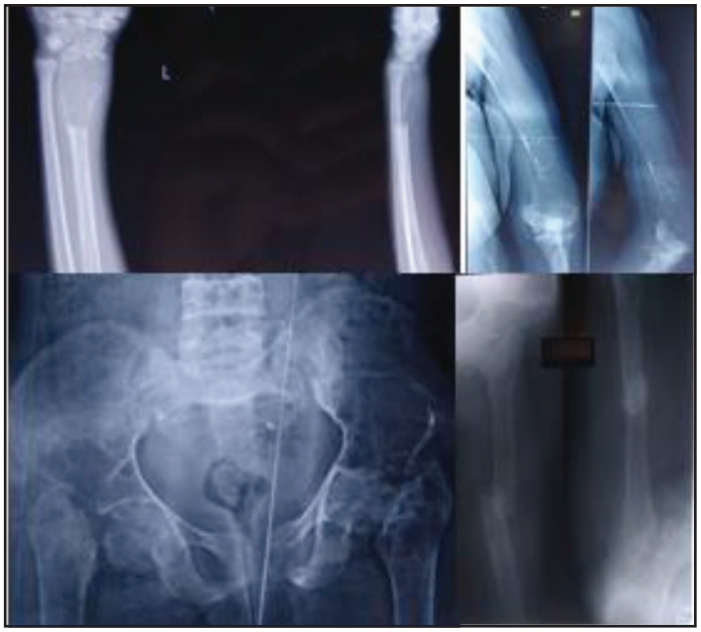

Figure 2: Skeletal survey of the patient showing cystic lesion of left distal end of radius (top left side), involvement of whole of the humerus (top right side), pathological fracture of both neck of femur (lower left side) and pathological fracture of shaft of the femur (top right side).

displacing the right common carotid artery and right internal jugular vein (Fig. 3). There were also multiple cystic lesions of clavicle, skull and facial bone.

Her blood chemistry showed alkaline phosphate – 900 U/L (normal range - 245-770 U/L), serum calcium 12.9 mg/dL (normal range- 9 to 11 mg/dL), serum phosphate 2.6 mg/dL (normal range 2 to 4 mg/dL) and increased serum PTH 1008 pg/mL (normal range-11.1-79.5 pg/mL)]. A biopsy was taken from distal end radius and sent for the histopathological examination. Section revealed the diffuse sheets of the polygonal cell of clear cytoplasm with uniform nuclei. These findings were consistent with the finding of osteitis fibrosa cystica (Fig. 4). For the fractured shaft of the femur, the patient got managed conservatively by applying the hip spica for 10 weeks.

Based on clinical, radiological and biochemistry profile, the diagnosis of unchecked primary hyperparathyroidism was installed and planned for the surgery. The right inferior parathyroid gland was found, enlarged and got dissected out. Histopathological examination was consistent with the chief cell adenoma. Postoperatively, calcium and magnesium profile was maintained in close observation. The parathyroid hormone level fell down and restricted to normal range (66.1 pg/m). In a follow-up,the patient was counseled for long term treatment. She was kept on oral calcium, calcitriol and alendronate. After 1 year of follow-up (serum calcium 10.0 mg/dL),the patient was able to walk with support and managed to do her day to day activity.

DISCUSSION

Sir Richard Owen (1850) picked out the parathyroid glands in an Indian rhinoceros. The parathyroid gland is the latest organ to be recognized in the mammalian kingdom. Later on, the term

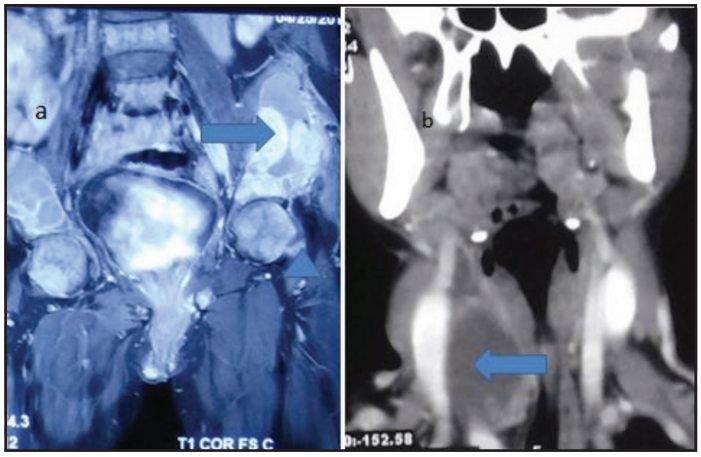

Figure3: MRI pelvis showing the bilateral fracture neck of femur and enhancing cystic cavity in both iliac bone (a) and CT scan (b) showing the eccentric, heterogeneous mass from posterior right lobe of thyroid abutting to trachea and displacing carotid artery and right internal jugular vein.

hyperparathyroidism was coined by Fuller Albright in 1940s to narrate the occurrence of an excess of parathyroid hormone [4]. Assessment of serum calcium level has become popular in practice since 1970. So, obviously the incidence of early diagnosis of primary hyperparathyroidism (PHPT) became easier [5].

Persistent high parathormone (PTH) leads to osteopenia, followed by osteoporosis. Later on, it succumbs to cyst formation and fibrosis ensues and the severe stage is precipitated and called as osteitis fibrosa cystica. The hyperparathyroidism, either present as renal stone or bony involvement but never simultaneously, due to unascertained reasons. It has the incidence of 1% to 4% and the preponderance for the female in the third to a fifth decade [6].

The occurrence of PHPT is mainly sporadic. A solitary adenoma is responsible for 80%–85% of the cases of PHPT. Rarely double adenoma has been found in 4% of the cases. The general hyperplasia of all four parathyroid glands represents the rest of the cases [7]. Parathyroid carcinoma is a very rare cause of PHPT and appears in less than 1% [8]. The familial parathyroid disorder accounts for 5% of the PHPT. Family history also plays an important role in rule out the familial form of PHPT, particular to the multiple endocrine neoplasia (MEN) 1and MEN 2A, so that the genetic testing could be done [9].

In a typical hyperparathyroidism case, exaggerated osteoclastic function leads to resorption of bone and accumulation of innocuous spindle cells and multinucleated giant cells as a compensatory mechanism. Along poorly formed woven bone and this is typified by the name brown tumor [10]. Multiple locations of the brown tumor are uncommon; hence, the fibrous dysplasia and metastatic lesion are the closest differential diagnosis of it. The PHPT is classically diagnosed as high serum calcium associated with increased PTH level. On the contrary, the other causes of hypercalcemia are in association with low PTH level due to the intact axis of calcium (negative feedback) and PTH metabolism [11].

Medical treatment of PHPT has not been favored by most of the authors. It possesses cumbersome longer follow-up and costlier treatment. It's recommended only in few conditions like

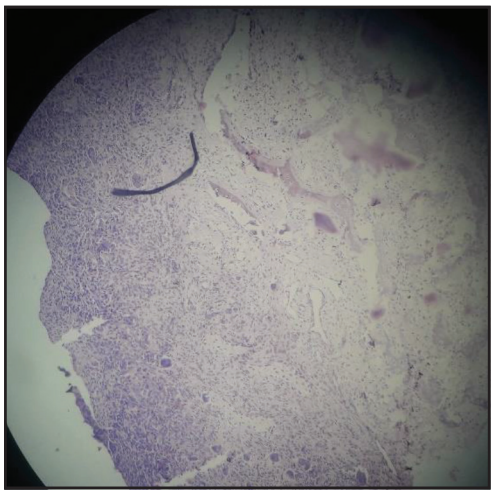

Figure4: Hematoxylin and eosin (HE) depicting (10X) that cyst is wall deficient (pseudocyst) and the lumen is filled with necrotic material and macrophages.

a refusal of surgery, pregnancy and failure cases of surgery. On the contrary, the surgical measure is cost-effective and easier in observation, in the management of symptomatic as well as asymptomatic patients of life expectancy of ≥ 6.5 years [12]. Now the general consensus has recommended the parathyroidectomy in all symptomatic as well as in asymptomatic patients of age ≤ 50 years, vertebral fracture, with osteoporosis, serum Ca^{++} ≥1 mg above the normal upper range, creatinine clearance of <60 ml/min and presence of renal stones [13].

Successful management is conceded if the normocalcemia has been achieved after the six months of the parathyroidectomy. Then the annual follow-up is done with normal calcium level [14]. Sometimes (40%) the PTH level remains still high even the eucalcemia has been achieved after parathyroidectomy. In such situation, the repercussion of higher PTH level is still an enigma, but it can be due to low vitamin D level, hungry bone syndrome, lower dose of calcium, renal failure (inadequate vitamin D synthesis), end-organ resistant to vitamin D [15].

CONCLUSION

The patient presenting with multiple osteolytic lesions due to primary hyperparathyroidism should not be missed by an orthopedist. If the typical bony feature of primary hyperparathyroidism is associated with elevated calcium level, then the parathyroid hormone must be obtained to ascertain the diagnosis. Other departments (general surgery) should be involved actively for holistic management.

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