Case Report

PHPT Masquerading as Rickets in Children and Presenting with Rare Skeletal Manifestations: Report of Three Cases and Review of Literature

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Abstract

Primary hyperparathyroidism (PHPT) is an uncommon condition in children and adolescents. However, rapid growth spurt during puberty may result in unmasking and development of certain skeletal manifestations of PHPT. We present three cases of PHPT associated with rare skeletal manifestations of rickets. All three patients had radiological evidence of rickets with primary hyperparathyroidism. All the three patients had single gland adenoma. Literature is sparse regarding reversal of features of rickets following parathyroidectomy. In all three patients of our series, there was a complete resolution of bone/joint pain. However, in two children only the genu valgum persisted but their growth was normal and they had no proximal muscle weakness. In another child multiple corrective surgeries were done to correct the deformities.

Keywords: Primary hyperparathyroidism, rickets, skeletal manifestations

Introduction

Primary hyperparathyroidism (PHPT) is an uncommon condition in children and adolescents. However, rapid growth spurt during puberty may result in unmasking and development of certain skeletal manifestations of PHPT. We present three cases of PHPT associated with rare skeletal manifestations of rickets.

Case Reports

Case 1

A fifteen-year-old girl, born at term of normal delivery second of three siblings, initially presented in the Orthopaedics OPD in 2010 with a history of progressive knee deforming of 1month and was referred to an endocrinologist for evaluation of metabolic bone disease. Dietary history was suggestive of adequate calcium and vitamin D intake and adequate sun exposure. No history of malabsorption or renal disorder. On examination, height 150 cm (5–10 percentile), weight 32 <5th percentile, US: LS = 0.96, percentile target height: 161.5 cm, genu valgum deformity noted, intermalleolar distance: 10.9 cm, bilateral wrist widening noted.

Biochemical evaluation revealed serum calcium: 14.2 mg/dl, phosphorus: 3.4 mg/dl, 25(OH) vitamin D: 25.10 nmol/L, iPTH: 1967 pg/ml, alkaline phosphatase: 1400 U/L, 24 hours urinary calcium: 282 mg/24 hours. Imaging: X-ray hand showed features of rickets [Figures 1-4]. CT neck: Features s/o left superior parathyroid adenoma. Lesion in lower pole of left lobe of thyroid Sestamibi scan: S/o functioning parathyroid adenoma on left side. She underwent left inferior parathyroidectomy in May 2010: however, on follow up after 1 year she was found to have elevated parathyroid hormone (PTH) and calcium and was then referred to SGPGI with a diagnosis of persistent hyperparathyroidism (HPT).

At evaluation in SGPGI there were no records of previous surgery; repeat methoxy iso butyl isonitrile (MIBI) revealed a superior parathyroid adenoma on left side and was

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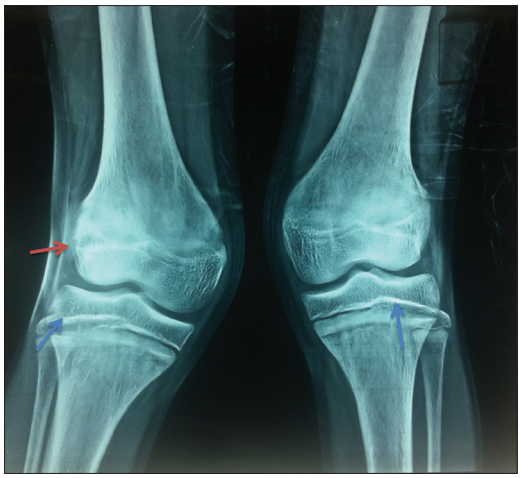

Figure 1: X-ray bilateral knee demonstrates bilateral genu valgum deformity with epiphyseal widening and metaphyseal marginal irregularity of bilateral tibial condyles. Lateral ends of bilateral femur and tibia show partial lucency of metaphysis with sharply defined margins (red arrow)

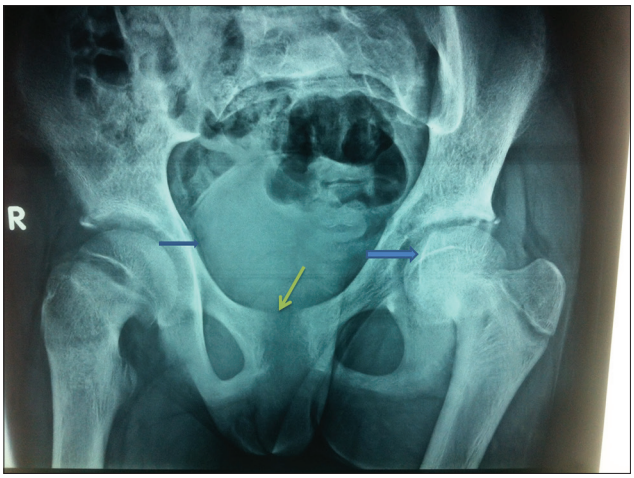

Figure 2: X-ray pelvis- AP view demonstrates , bilateral coxavera or SUFE (arrow) with increased pubic symphysis joint space (green arrow) and marginal irregularity

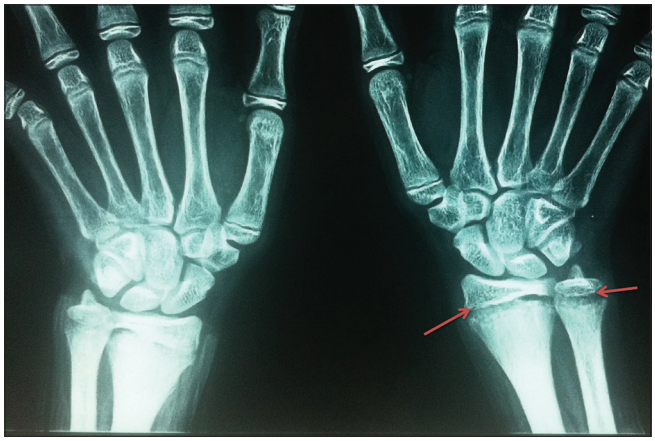

Figure 3: X-ray bilateral wrists AP view- demonstrates mild irregularity and widening of the growth plates of both radius and ulna

Figure 4: Bilatereal genu valgus deformity

concordant with the ultrasonography (USG) finding of a left superior parathyroid adenoma. Bilateral neck exploration was performed with intraoperative parathyroid hormone (IOPTH) monitoring. At operation, both right parathyroid glands were found to be grossly normal; a left superior parathyroid adenoma was found which was excised (2.2 × 1.6 × 1.6 mm, weight 2.2 gm). However, left inferior parathyroid gland could not be found. IOPTH according to Miami criteria was curative, as there was >50% drop from the pre-excision value of 2130 to 231 at 10 minutes. Histophalogical examination was suggestive of parathyroid adenoma. At the last follow up, in 2016, her biochemical parameters including calcium and iPTH were within normal limits and she was free of bone pains, though her genu valgum persisted.

Case 2

A 15-year-aged young adolescent girl presented with history of pain in both legs since 3 years followed by stiffness in both knees with limping gait and dislocation of hip joint with deformities in both hands (widening of the wrist) and chest (kyphosis and rachitic rosary) [Figures 5-9]. There was history of fracture left clavicle and left hand by trivial trauma. Since last 1 year she was bedridden. She consulted an orthopaedic when it was detected that she had high serum alkaline phosphatase levels and low vitamin D levels. She was put on vitamin D and calcium supplements but then she developed an episode of pancreatitis which required hospitalization, though she recovered on conservative treatment. She was evaluated during her admission for pancreatitis and serum calcium was found to be raised and hence was referred to our institute. She was found to have raised serum calcium along with high intact PTH of 1250 pg/ml. Her localization investigations were concordant, therefore, she underwent focused parathyroidectomy under cervical block. Postoperatively patient was given prophylactic calcium infusion because of the severe bone disease. Histopathology turned out to be parathyroid adenoma.

Case 3

A 11-year-old boy presented with difficulty in walking and bowing of knees since 10 months. Patient also had severe

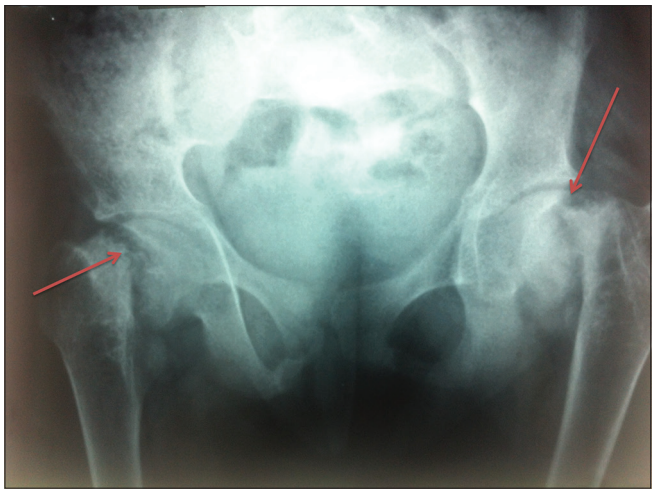

Figure 5: Radiograph of pelvis AP view - demonstrates diffuse osteoporosis with coarse trabecular pattern. Coxavera deformity and pathological fractures of bilateral femoral neck

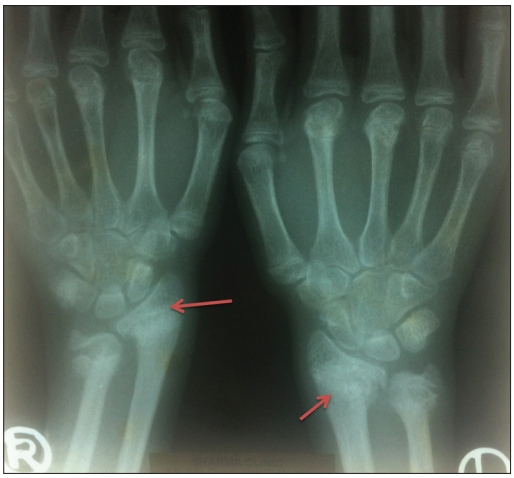

Figure 6: Radiograph of bilateral wrists - demonstrates irregularity and widening of growth plate with metaphyseal cupping and fraying of both radius and ulna

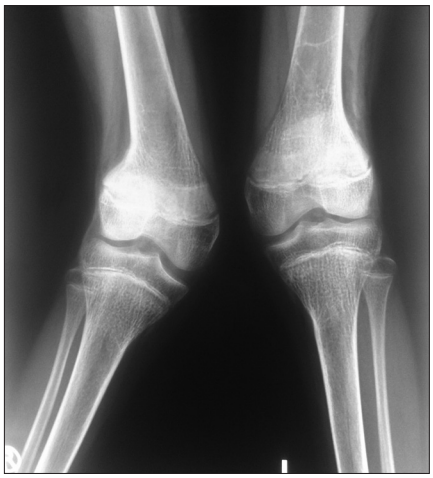

Figure 7: X-ray bilateral knee demonstrates generalised osteopenia, increased trabecular pattern, genu valgum deformity and increased zone of provisional calcification involving distal metaphyseal ends of bilateral femur

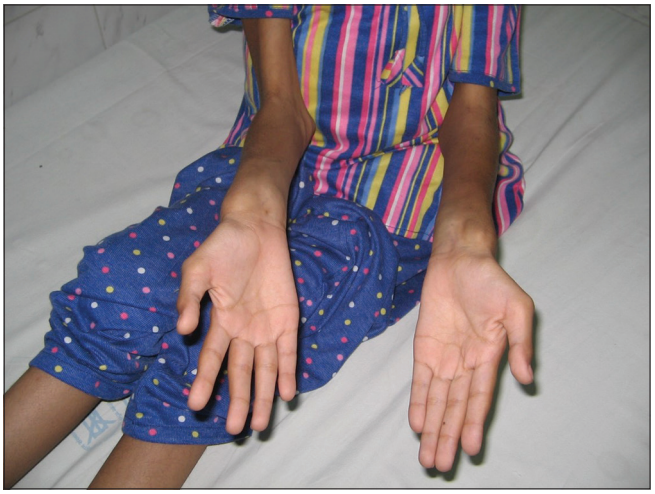

Figure 8: Widening of wrists

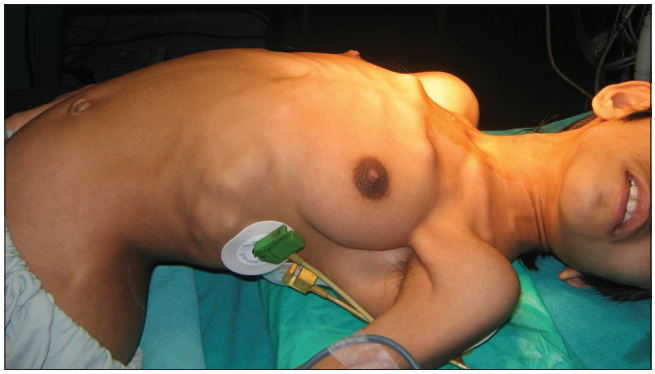

Figure 9: Chest deformity

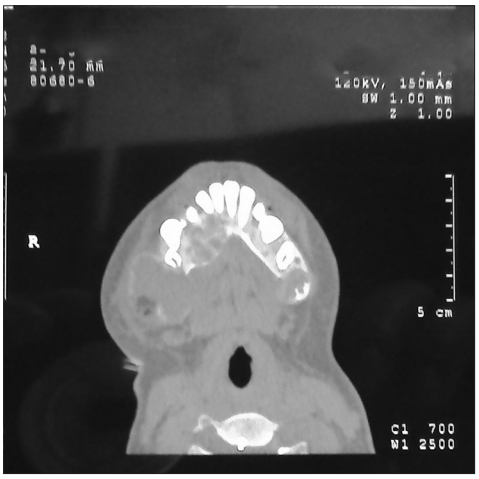

Figure 10: Brown tumor of the mandible

proximal muscle weakness with multiple bony swellings over face [Figure 10]. Patient was evaluated with magnetic resonance imaging of knee and given calcium and vitamin D supplements during his evaluation elsewhere with suspicion of rickets. However, when patient did not improve further

investigations were done. On biochemical evaluation, serum calcium was high on three occasions and intact PTH was 607 pg/ml. Localization studies done revealed concordant findings on USG and MIBI. Patient underwent focused parathyroidectomy. Postoperatively patient developed clinical and biochemical hypocalcemia which was managed with calcium infusion and oral calcium and vitamin D. Histopathology came out to be parathyroid adenoma. Biopsy from bony swellings of face was osteitis fibrosa cystica (OFC).

Discussion

Rickets as presenting feature of PHPT in children is extremely rare with only 23 cases reported till date.[1,2] PHPT is typically a disease of post-menopausal women in Caucasian population. However, in areas of vitamin D deficiency and calcium deficiency, PHPT may be seen in young patients and even in children and adolescents.[3–6]

Unlike the Western world, the classic presentation of PHPT in the form of OFC and nephrolithiasis is still commonly seen in developing countries and one of the reasons for this has been severe vitamin D deficiency in these regions.[7]

In a review by Pitukcheewanont *et al*.[2] common presenting signs and symptoms of PHPT with rickets in children include knock-knees or genu valgum (70%), rachitic rosary (50%), widened wrist and ankle (31.5%), bone/joint pain (37.5%) and anorexia (31.25%). All three children in our report had radiological findings consistent with rickets. It can be speculated that the severe skeletal abnormalities seen in children may be due to synergistic effect of vitamin D deficiency along with deleterious effect of elevated PTH. A state of malabsorption leading to vitamin D deficiency is unlikely because there were no overt gastrointestinal symptoms in any of the patients.

Two radiological findings in rickets with PHPT require special mention. Genu valgum can also manifest in vitamin D deficiency states and these cases may be thought of having tertiary HPT, but all of the 23 cases mentioned in literature including ours had a single gland enlargement, whereas the classic picture of tertiary HPT is of parathyroid hyperplasia. Most of the cases of PHPT with genu valgum described so far have occurred in the period of adolescence when there is a rapid growth spurt combined with direct effect of elevated PTH on the growth plate.[8,9]

Another finding is of slipped upper femoral epiphisis (SUFE). In the review of 85 children with SUFE,[10] the etiological factors of SUFE included hypothyroidism (40%), growth hormone deficiency (25%) and miscellaneous causes including PHPT (35%). Thus PHPT causing SUFE is extremely rare with only nine cases reported worldwide. In SUFE there is displacement of capital femoral epiphysis caused by shear stress on a vulnerable physis during rapid growth in adolescence.[11] In the series by Ganie *et al*.[12] one child had short stature also. All our three children had short stature.

Regarding the biochemical findings in such children, in the literature review by Pitukcheewanont *et al*.[2] 13 children had hypercalcemia and only three children were normocalcemic at presentation but who became hypercalemic after vitamin D supplementation. In a review by Roizen and Levin[13] it was reported that young PHPT has greater incidence of hypercalcemia and hypercalciuria as compared to adult PHPT at similar levels of PTH. The highest recorded PTH was 1659 pg/ml[12] while in one child the PTH level was still higher 1967 pg/ml.

In the report by Ganie *et al*.[12] all four children had single adenoma; in the series by Pitukcheewanont *et al*.[2] 13 out of 14 children had adenoma and only one child had multiglandular disease. In the case reported by Dutta *et al*.[1] their patient also had a single adenoma. In all our three children there was a single adenoma. The PHPT in developing countries is also associated with large and heavy adenomas with a higher mean weight.[7,14]

Literature is sparse regarding reversal of features of rickets following parathyroidectomy. In all three patients of our series, there was complete resolution of bone/joint pain. However, in two children only the genu valgum persisted but their growth was normal and they had no proximal muscle weakness. In another child multiple corrective surgeries were done to correct the deformities.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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