Case Series

Genu valgum in children with primary hyperparathyroidism: A case series with a review of the literature

Harshal Sakale, Ankit Kumar Garg, Shubham Bhardwaj, Alok Chandra Agrawal

Department of Orthopaedics, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India

Abstract

Primary hyperparathyroidism (PHPT) is relatively uncommon in children, and skeletal deformities due to it are even rarer in this age group. Less than 20 such cases have been reported in the English literature. We describe a case series of three patients who presented with genu valgum deformity and were found to have primary hyperparathyroidism on further evaluation. The cases were primarily managed by removing the adenoma and later taken up for correction of the skeletal deformity. Genu valgum deformity in children can occur secondary to hyperparathyroidism due to a pubertal growth spurt.

Keywords: Genu valgum, parathyroid adenoma, primary hyperparathyroidism

Introduction

Hyperparathyroidism is a clinical condition characterized by an increase in the production of parathormone (PTH). It can be primarily due to an intrinsic change in the parathyroid gland (adenoma, hyperplasia, carcinoma, or in association with MEN syndrome), secondary due to dysregulation of physiological stimulus in conditions such as chronic renal disease, vitamin D deficiency, calcium malabsorption syndromes, or tertiary where there is an autonomous secretion of the PTH in prolonged secondary cases.[1-3]

Primary Hyperparathyroidism (PHPT) is a fairly common endocrine disorder with a female preponderance (3:1). PHPT is relatively uncommon in children, and skeletal deformities associated with it are even rarer in this age group.[2,3] Deformities around the knee joint, such as genu valgum, are rare, and less than 20 cases reported. The mechanism of these deformities in PHPT is unknown. We report three such cases where growing children having PHPT presented with Genu valgum deformity.

Address for correspondence: Dr. Shubham Bhardwaj, Department of Orthopaedics, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India.
E-mail: bhardwajshubham15081995@gmail.com

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Case Presentation

Case 1

A 14-year-old male boy presented to our outpatient department with a progressive deformity of the bilateral knee for the last six months [Figure 1]. He also had somatic growth retardation and Pes Carinatum [Figure 1]. There was no history of recurrent fractures, arthralgia, polyuria, vomiting, constipation, malabsorption, diarrhea, jaundice, treatment with antitubercular or antiepileptic drugs, or the use of native treatment. There was no family history of hypertension, renal stones, or MEN-related disorders. There was no history of malabsorption, recurrent

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diarrhea, native treatment, antitubercular or antiepileptic drug intake, jaundice, or renal problems.

On examination, there was a minor cystic swelling palpable on the anterior aspect of the neck, just to the right side of the midline. On further radiological and biochemical evaluation, we found raised serum calcium (14.5 mg/dl) and raised serum parathyroid hormone (1022.2 pg/ml). We raised the alkaline phosphatase level (1890 U/L), with a normal thyroid profile, serum vitamin D, magnesium, and phosphorus levels. USG neck revealed a Hyperechoic mass in the right inferior lobe of the Thyroid gland. CECT also revealed an avoid mass in the left inferior thyroid. A TC-99 m scan showed an avid MIBI lesion in the right inferior lobe of the thyroid. The patient underwent removal of the mass under general anesthesia, and the surgical pathology was consistent with a recurrence of benign hyperparathyroid adenoma. The patient was later followed up with biochemical investigations, which showed normal levels with an overall improved general condition.

The patient is now planned for the correction of bilateral genu valgum.

Case 2

A 12-year-old girl presented to our outpatient department with a progressive deformity of both knees over the last 3 months [Figure 2]. She also has a history of short stature for age, delayed puberty, and an absence of secondary sexual characteristics, along with Primary amenorrhea (Tanner stage 1). The family also noticed a midline swelling in the neck for the last 1 year. The patient also complained of generalized body aches and associated fatigue during the presentation.

There was no history of recurrent fractures, polyuria, vomiting, constipation, malabsorption, diarrhea, jaundice, treatment with antitubercular or antiepileptic drugs, or native treatments. There was no family history of hypertension, renal stones, or MEN related disorders. There was no history of malabsorption,

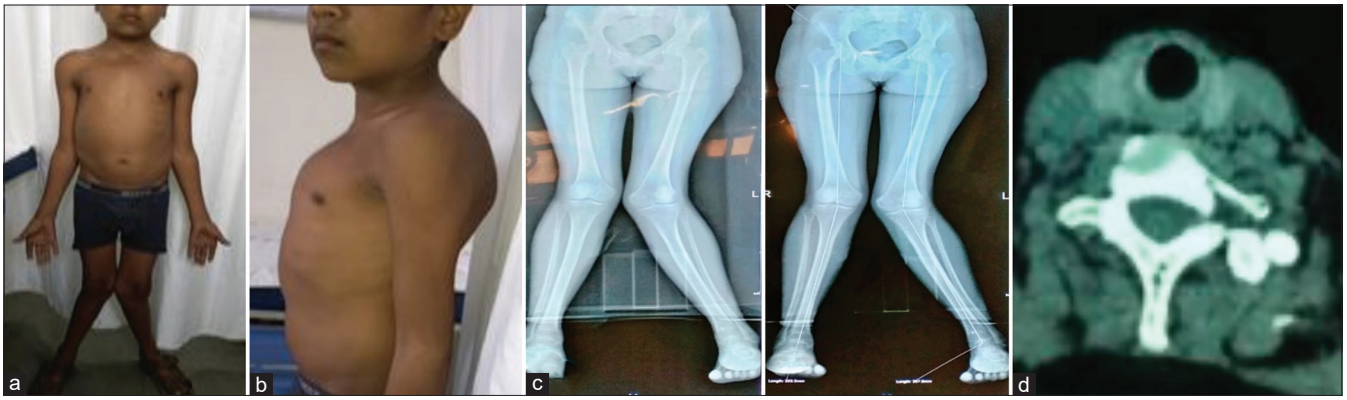

Figure 1: (a and b) show clinical photographs of the patient with genu valgum and pectus carinatum deformity, (c) shows a scannogram with bilateral genu valgum deformity, and (d) shows an axial CT image with a mass located posteroinferior to the right lobe of the thyroid gland

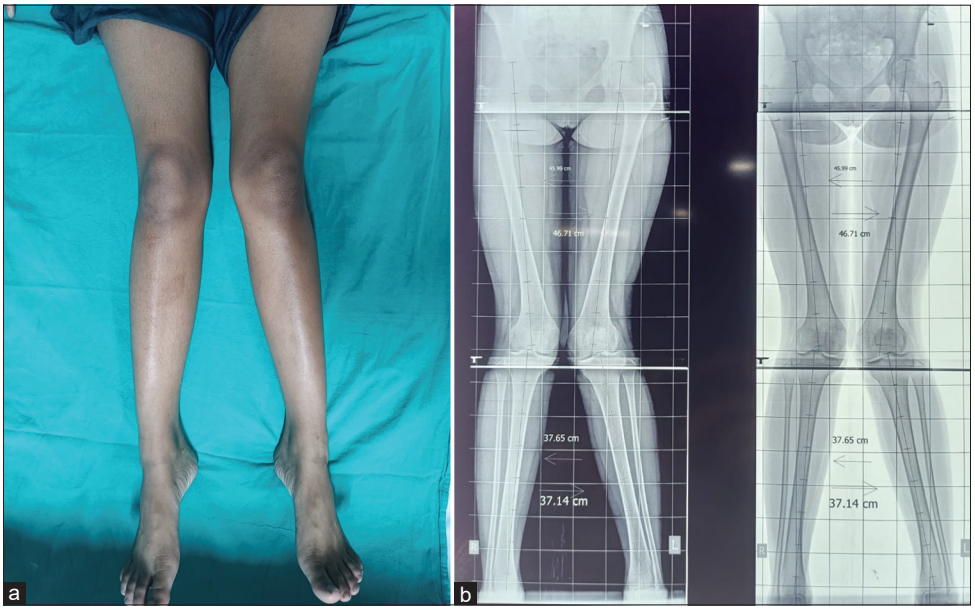

Figure 2: (a) Shows clinical photographs of the patient with bilateral genu valgum deformity, and (b) shows a scannogram with bilateral genu valgum deformity

recurrent diarrhea, native treatment, antitubercular or antiepileptic drug intake, jaundice, or renal problems.

On detailed examination, stunting was noted, and Tanner's staging was significantly below her chronological age. A small, cystic, palpable midline neck swelling was present, which moved with deglutition and adhered to the underlying thyroid gland.

The biochemical workup revealed Serum Hypercalcemia (13.7 mg/dl) with hypomagnesemia, along with raised levels of Serum Parathyroid (567.4 pg/ml), Serum Estrogens, and LH, which were within normal limits (towards the upper limit).

Plain radiographs showed generalized osteopenia in the skeletal long bones and vertebrae.

USG and CECT of the neck revealed a mass consistent with a Parathyroid adenoma in the right superior Parathyroid gland, and Histopathology revealed tissue consistent with a benign Parathyroid mass. The patient underwent excision of the right parathyroid gland along with the adenoma under GA. A multidisciplinary team under Ear, Nose, Throat, Endocrinology, Orthopedics, and Gynecology, followed up with the patient. The patient achieved menarche and attainment of secondary sexual growth in the subsequent follow-up, along with an improved general condition and somatic growth. The patient has been planned for subsequent correction of bilateral knee deformities.

Case 3

A 14-year-old boy presented to the orthopedic outpatient department with a progressive deformity of the bilateral knee for the last 4 months. He also had a history of generalized weakness, indigestion, and loss of appetite for the last 2 years. There was no history of recurrent fractures, arthralgia, polyuria, vomiting, constipation, jaundice, treatment with antitubercular or antiepileptic drugs, or alternative treatments. There was no family history of hypertension, renal stones, or MEN-related disorders. There was no history of native treatments, antitubercular or antiepileptic drug intake, jaundice, or renal problems.

Bilateral Genu valgum was appreciated during the general physical examination, without other gross skeletal deformities. There was no appreciable neck swelling or delay in the appearance of Secondary sexual characteristics. Upon investigations, the boy was found to have hypercalcemia and hypophosphatemia, along with normal vitamin D. This led to further workup, wherein blood levels of Serum Parathyroid hormone were found to be significantly elevated.

Ultrasound of the neck revealed a solitary swelling in the left upper Parathyroid gland, which was later found to be an Adenoma of the Parathyroid gland on further workup, including a sestamibi scan.

The Head and neck surgeons operated on the child and showed a remarkable improvement in the child's general condition.

Later, the child was referred to the orthopedic outpatient department, where a workup for the Genu valgum deformity, and the condition was later operated on by performing hemiepiphysodesis on the affected side.

Discussion

Parathormone, an 84-amino-acid polypeptide, is secreted by the chief cells of the parathyroid glands and plays a vital role in calcium homeostasis in the human body. It activates vitamin D and increases calcium absorption via its effects meditated on the kidneys and gastrointestinal tract, as well as increased absorption from bones.[4-6]

The incidence of PHPT varies from 0.1% to 0.3% in the general population and has a rarely occurrence in the paediatric population.[3] The clinical presentation of Hyperparathyroidism in children lacks specificity and is characterized by bone disease, renal stones, or vague signs and symptoms such as fatigue, anorexia, nausea, vomiting, constipation, irritability, and impaired concentration. These manifestations are attributed to the presence of hypercalcemia. Approximately 50% of affected children experience polyuria and polydipsia. It is essential to evaluate the 25-hydroxyvitamin D levels in all patients suspected of having primary Hyperparathyroidism.

Furthermore, any detected vitamin D deficiency should be cautiously addressed.[1,3,4,7] The Endocrine Society guidelines specify that serum 25-hydroxy vitamin D levels should be measured in all patients with PHPT. Additionally, it is recommended that vitamin D depletion be addressed before making any medical or surgical management decisions. While genu valgum is not a common presenting feature of primary Hyperparathyroidism, it is considered one of the skeletal deformities seen in children with this condition.[2]

To our knowledge, there have only been 12 reported cases of this phenomenon in the literature. The clinical features, biochemical parameters, and radiological findings of these cases are summarized in Table 1. Of the twelve cases, seven were females, and three were males. Most of these cases presented with genu valgum, which suggests an etiological connection. All 12 cases were attributed to a solitary parathyroid adenoma. It is worth noting that vitamin D deficiency can manifest as genu valgum and can also lead to tertiary hyperparathyroidism. However, none of the reported cases exhibited a deficiency in vitamin D.[3]

Biochemically, the disease correlates with high serum calcium levels, hypophosphatemia, increased alkaline phosphatase, and raised intact parathyroid hormone (iPTH) levels. Modern imaging and diagnostic tools, such as the 4D CT scan, have higher sensitivity and specificity than MRI scans in diagnosing parathyroid adenoma. Ultrasonography, though user-dependent, has a 73% sensitivity and almost 100% specificity in diagnosing parathyroid lesions. A nuclear scan, such as 99 m Tc Sestamibi

Table 1: The clinical features, biochemical parameters, and radiological findings of reported cases

Author	Age/ gender	Clinical features	Total calcium (mg%)	iPTH (pg/mL)	25-oH Vitamin-D (ng/mL)	Radiological features reported
Harman *et al.*[8]	14/F	Genu Valgum at age 11	Not available	Not available	Not available	Multiple brown tumors in metacarpal bones
Kauffman *et al.*[9]	13/F	Genu valgum (1 yr duration), backache, pain in legs, became lame later.	3.66 mmol/l, 3.8 mmol/l	1066	125	Subperiosteal resorption, demineralization of the skull vault, bilateral coxa Vara, and zones of calcification on the knee metaphyses
Menon *et al.*[7]	14/F	Genu valgum (6 yr duration), rachitic features, renal calculi	2.69 mmol/l–2.89 mmol/l	760–790	-	Generalized osteopenia, erosions of the lateral ends of the clavicles, subperiosteal resorption, bilateral femoral epiphyseal displacement, and irregular destruction of the metaphysis, as well as bilateral brown tumors in the femur and tibia
Ratnasingham *et al.*[10]	15/F	Only genu valgum	12.4	1649	28	Osteopenia, subperiosteal resorption, and terminal resorption of the distal tufts
Balch *et al.*[11]	21/F	Genu valgum, fever, nausea, vomiting, loin pain, headache, and nocturia	21.2	-	-	Osteitis fibrosa generalist
Bjernulf *et al.*[12]	14/F	Tiredness, genu valgum	15	2.6	-	Osteoporosis
Bjernulf *et al.*[12]	15/M	Genu vaglum	17	2.8	-	Osteoporosis
Bjernulf *et al.*[12]	15/M	Genu valgum, apathy	12	1.1	-	Deficient lamina dura, osteoporosis, subperiosteal resorptions, brown tumor in the left fifth metacarpal
Rapaport *et al.*[13]	15/F	Weight loss, irritability, constipation, and polyuria	17.6	1.6	-	Moth-eaten skull, tibial cyst
Rapaport *et al.*[13]	15/M	Painless hematuria, genu valgum	13.7	3.3	-	-
S *et al.*[3]	16/M	Genu valgum noted for last four years, bone pains	11	760.2	9.0	Brown tumor in the right upper humerus
S *et al.*[3]	13/M	Genu valgum noted in last three months, myalgia, abdominal pain	10.7	1136	5.1	Brown tumor in lower femur and patella
CASE 1	14/M	Bilateral genu valgum, Pes carinatum, and somatic growth retardation	14.5	1022.2	65	Subperiosteal resorptions, Osteopenia, and Bilateral genu valgum
CASE 2	12/F	Bilateral genu valgum, short stature, delayed puberty, and absence of the secondary sexual characters	12.3	786.4	48	Osteopenia, bilateral genu valgum
CASE 3	14/M	Bilateral genu valgum, loss of appetite, indigestion	12.6	986.2	55	Bilateral genu valgum, osteopenia

scintigraphy, Iodine 123 Subtraction, and thallium technetium subtraction scan, can help localize the tumor and any ectopic lesions. It is often necessary to evaluate skeletal changes and bone mineral density using a DEXA scan to proceed further with treatment.[2,3,9]

Conclusion

Through this case series, we emphasize the need to keep PHPT as one of the possible aetiologies behind skeletal deformities in Paediatric patients wherein common causes, such as Rickets, have been ruled out. PHPT is rare in children, and its manifestation in the form of skeletal deformities is even rarer. Generally, Hyperparathyroidism is an incidental finding in children where regular blood workup reveals hypercalcemia and hypophosphatemia in the presence of Hypovitaminosis D. A high degree of suspicion helps in aiding the diagnosis at an early stage and prevents or treats the skeletal deformities occurring in the children. The condition is generally unmasked in puberty children, after hitting the growth spurt, and the diagnosis is most probable at this stage. A multidisciplinary approach, by engaging paediatricians, endocrinologists, orthopaedics, and head-neck specialists, helps manage such children holistically and achieve optimum outcomes.

Clinical message

A high degree of suspicion helps in aiding the diagnosis at an early stage of genu valgum deformity and prevent or treat skeletal deformities in children.

Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient consented to his or her images and other clinical information being reported in the journal. The patient understands that his or her name and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Learning point

PHPT is rare in children, and when it does manifest, it is even rare in the form of skeletal deformities. Generally, Hyperparathyroidism is an incidental finding in children, where regular blood workup reveals hypercalcemia and hypophosphatemia in the presence of Hypovitaminosis D. A high degree of suspicion helps in aiding the diagnosis at an early stage and prevents or treats skeletal deformities in children. The condition is generally unmasked in puberty children, after hitting the growth spurt, and it is at this stage that the diagnosis is most probable.

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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Conflicts of interest

There are no conflicts of interest.

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