Genu valgum and primary hyperparathyroidism in children

Ramkumar S, Devasenathipathy Kandasamy, Vijay MK, Madhavi Tripathi, Jyotsna VP

ABSTRACT

Introduction: Bony deformity due to primary hyperparathyroidism is a rare entity in children. Case Series: We describe two children who presented with genu valgum to the Endocrine Department. Ten children with primary hyperparathyroidism presenting with genu valgum have been reported in literature and have been reviewed by us. Biochemical investigations revealed parathyroid hormone dependent hypercalcemia despite a deficiency of vitamin D in both children. A single parathyroid adenoma was identified by ultrasonography and (99mTc)-sestamibi (MIBI) scan. Both children underwent resection of the solitary parathyroid lesion which was confirmed as adenoma by histopathological examination. All cases reported in literature had solitary parathyroid adenoma and had onset around puberty consistent with our observation that pubertal growth spurt is responsible for the occurrence of genu valgum in children with previously undiagnosed primary hyperparathyroidism. Conclusion: Genu valgum is a common skeletal deformity in children with primary hyperparathyroidism. Solitary parathyroid adenoma was identified in all reported cases and all underwent parathyroidectomy. Pubertal growth spurt seems to contribute to the occurrence of genu valgum in children with primary hyperparathyroidism.

Keywords: Genu valgum, Hypercalcemia, Hyperparathyroidism, Parathyroid adenoma, Technetium-99m sestamibi

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INTRODUCTION

Primary hyperparathyroidism (PHPT) is one of the most common causes of hypercalcemia and metabolic bone disease in adults but it is a relatively uncommon disorder in children. Parathyroid adenomas are the most common cause of PHPT, other causes being four gland hyperplasia and rarely parathyroid carcinoma. Parathyroid adenoma can occur sporadically or as part of multiple endocrine neoplasia type 1 or type 2A (MEN-1/MEN-2A). Primary hyperparathyroidism presenting with bony deformities such as genu valgum has rarely been reported in children its mechanism is not understood. We report two cases of hyperparathyroidism who presented to the endocrine outpatient department with genu valgum.
CASE SERIES

Case 1: A 16-year-old boy was presented with symptoms of progressively increasing bowing of the legs for four years and bilateral leg pain for two years. He also had generalized arthralgia and polyuria. There was no history of recurrent fractures, recurrent vomiting, constipation or neck swelling. There was no past history of native treatment, the use of anti-tubercular or anti-epileptic drugs, jaundice or renal problems. There was no family history of renal calculi, hypertension or multiple endocrine neoplasia (MEN) related disorders. His height, weight and body mass index were 177 cm, 67 kg and 21.38 kg/cm², respectively. Apart from genu valgum (Figure 1A), no other skeletal deformity was noted. He was in Tanner’s stage 4. Hemogram, electrolytes, renal and liver functions test were normal. Serum prolactin was 11.2 (normal range 4.6–21.4 ng/mL) and serum albumin was 4.4 g/L. Radiological evaluation showed a brown tumor in the right proximal humerus (Figure 1C). His base line calcium and vitamin D status are given in Table 1. He was vitamin D deficient and after treatment of vitamin D deficiency, his hypercalcemia worsened and parathyroid hormone remained high. 24 hours urinary calcium excretion was 570 mg per day. Ultrasonogram (Figure 1D) and Tc-99m MIBI (Figure 2) scan showed presence of a left inferior parathyroid adenoma. No thyroid nodule was seen in the neck ultrasonogram.

Case 2: A 13-year-old boy was presented with bowing of legs (Figure 3A) which was noted in last three months and was slowly progressive. Apart from myalgia, nausea and occasional abdominal pain, there was no other history of hypercalcemic symptoms, bone pain or fractures. There was no history of malabsorption, recurrent diarrhea, native treatment, anti-tubercular or antiepileptic drug intake, jaundice or renal problems. There was no family history of renal calculi, hypertension or MEN related disorders. His height, weight and body mass index were 154 cm, 50 kg and 21.08 kg/cm², respectively. Apart from genu valgum, no other skeletal deformity was noted. He was in Tanner stage 2. His hemogram, electrolytes, renal and liver functions test were normal. Serum prolactin was 11.6 (normal range 4.6–21.4 ng/mL) and serum albumin was 4.9 g/L. Radiological evaluation showed brown tumor in the distal femur and patella (Figure 3B–C). Patient was initially suspected of rickets by a private practitioner and treated with injection arachitiol six lac units stat. Baseline calcium and vitamin are given in Table 1. Similar to the first case, his hypercalcemia worsened and parathyroid hormone remained high. Urine showed calcium oxalate crystals. A 24-hour urinary calcium excretion was 520 mg per day. Ultrasonogram (Figure 3D) and (99m) Tc-sestamibi (MIBI) (Figure 4) scan showed presence of a right inferior parathyroid adenoma. No thyroid nodule was seen in neck ultrasonogram.

Both the children underwent resection of the parathyroid lesion. Biopsy in both cases was consistent with parathyroid adenoma. Cut section of both the
Table 1: Serum total calcium, phosphate, alkaline phosphate, intact parathyroid hormone (iPTH) and 25-hydroxy vitamin D levels in both patients

| Patient | Total Calcium (mg%) | Phosphate (mg%) | SAP (IU/mL) | iPTH (pg/mL) | 25-OH Vit-D (ng/mL) |
|---------|---------------------|----------------|-------------|--------------|-------------------|
| **At presentation** | | | | | |
| Case 1  | 11                  | 3.7            | 2416        | 760.2        | 9.0               |
| Case 2  | 10.7                | 3.7            | 1001        | 1136         | 5.1               |
| **After correction of vitamin D deficiency** | | | | | |
| Case 1  | 14.5                | 2.7            | 1099        | 569.9        | 21                |
| Case 2  | 14.7                | 4.3            | 1673        | 644          | 47.9              |
| **After surgical removal of parathyroid adenoma** | | | | | |
| Case 1  | 8.4                 | 2.0            | 646         | 23.9         |                   |
| Case 2  | 8.2                 | 2.7            | 970         | 24           |                   |

specimen showed grayish brown lobulated lesion surrounded by a thin connective tissue capsule. Microscopically, the tumor was encapsulated with a rim of compressed non-neoplastic parathyroid tissue at the periphery. The tumor was hypercellular and predominantly comprises chief cells (Figure 5). No nuclear atypia, mitotic activity or necrosis was identified. Postoperatively, both had symptomatic hypocalcemia secondary to transient hypoparathyroidism and were managed with calcium and calcitriol.

**DISCUSSION**

Primary hyperparathyroidism in children is uncommon and usually presents with bone disease or renal stones [1–3]. The clinical spectrum of hyperparathyroidism in children is non-specific with vague signs and symptoms such as fatigue, anorexia,
children. The second case described by us had evidence of genu valgum in hyperparathyroidism in deficiency alone is insufficient to explain the isolated occurrence of rickets. Vitamin D deficiency in children. These children rarely manifest with other features of rickets. They have elevated parathyroid hormone levels with radiological features like brown tumors favoring hyperparathyroidism. Ultrasonogram and technetium 99M sestamibi scan are useful in localizing the parathyroid adenoma. Though the exact mechanism for development of genu valgum in PHPT still needs to be defined, a possible explanation could be due to the direct effect of elevated parathyroid hormone on the growth plates during pubertal growth spurt.

CONCLUSION

Genu valgum is a rare presentation of PHPT in children. These children rarely manifest with other features of rickets. They have elevated parathyroid hormone levels with radiological features like brown tumors favoring hyperparathyroidism. Ultrasonogram and technetium 99M sestamibi scan are useful in localizing the parathyroid adenoma. Though the exact mechanism for development of genu valgum in PHPT still needs to be elucidated, it is proposed that elevated parathyroid hormone levels may have a direct effect on the growth plates during pubertal growth spurt resulting in genu valgum.

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Author Contributions

Ramkumar S – Substantial contribution to conception, design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Devasenathipathy Kandasamy – Substantial contribution to conception, design, Acquisition of data, Drafting and revising article critically for important radiology related content, Final approval of the version to be published

Vijay MK – Substantial contribution to conception, design, Acquisition of data, Drafting the article and revising it critically for important Pathology related content.

Figure 5: Microscopic section examined (Case 1 (A, B) and case 2 (C, D)) showing a well-encapsulated tumor predominantly comprises of chief cells. A compressed rim of normal parathyroid tissue is evident at the periphery.
| Author            | Age/gender | Clinical features                                      | Total calcium (mg%) | iPTH (pg/mL) | 25-OH Vitamin D (ng/mL) | Radiological features reported                                      |
|-------------------|------------|--------------------------------------------------------|--------------------|--------------|--------------------------|---------------------------------------------------------------------|
| 1 Harman et al.   | 14/F       | Genu valgum at age 11                                   | Not available**    | No material  | Not available**           | Multiple brown tumors in metacarpal bones                           |
| 2 Kauffman et al. | 13/F       | Genu valgum (1 yr duration), backache, pain in legs,   | 3.66 mmol/l, 1066  | 125          |                          | Subperiosteal resorption, demineralization of skull vault, bilateral coxa vara and zones of calcification on knee metaphyses |
|                   |            | became lame later                                       | 3.8mmol/l          |              |                          |                                                                     |
| 3 PS Menon [6]    | 14/F       | Genu valgum (6 yr duration), rachitic features, renal  | 2.69 - 2.89        | 760 - 790    |                          | Generalised osteopenia, erosions of lateral ends of clavicles, subperiosteal resorption, bilateral femoral epiphyseal displacement and irregular destruction of metaphyses, bilateral brown tumours in femur and tibia |
|                   |            | calculi                                                | mmol/l             |              |                          |                                                                     |
| 4 Ratnasingham    | 15/F       | Only genu valgum                                       | 12.4               | 1649         | 28                       | Osteopenia, subperiosteal resorption, terminal resorption of distal tufts |
| 5 Hary E. Balch   | 21/F       | Genu valgum, fever, nausea, vomiting, loin pain,       | 21.2               | -            | -                        | Osteitis fibrosa generalisata                                       |
|                   |            | headache, nocturia                                     |                    |              |                          |                                                                     |
| 6 Arne Bjernulf   | 14/F       | Tiredness, genu valgum                                 | 15                 | 2.6          | -                        | Osteoporosis                                                        |
| 7 Arne Bjernulf   | 15/M       | Genu vaglum                                            | 17                 | 2.8          | -                        | Osteoporosis                                                        |
| 8 Arne Bjernulf   | 15/M       | Genu valgum, apathy                                    | 12                 | 1.1          | -                        | Deficient lamina dura, osteoporosis, subperiosteal resorptions, brown tumor in left fifth metacarpal |
| 9 Rapaport et al. | 15/F       | Weight loss, irritability, constipation, polyuria      | 17.6               | 1.6          | -                        | Moth eaten skull, tibial cyst                                        |
| 10 Rapaport et al.| 15/M       | Painless hematuria, genu valgum                         | 13.7               | 3.3          | -                        |                                                                     |
| 11 Case 1         | 16/M       | Genu valgum noted for last 4 years, bone pains         | 11*                | 760.2*       | 9.0*                     | Brown tumor in right upper humerus                                   |
| 12 Case 2         | 13/M       | Genu valgum noted last 3 months, myalgia, abdominal    | 10.7*              | 1136*        | 5.1*                     | Brown tumor in lower femur and patella                              |
|                   |            | pain                                                   |                    |              |                          |                                                                     |

*values mentioned are at the time of presentation, ** mean serum calcium of 12.1 mg% and iPTH of 22.1 pg/mL reported in case series of 33 case
content, Final approval of the version to be published.

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Jyotsna VP – Substantial contribution to conception, design and acquisition of data, Drafting the article and revising it critically for important intellectual content, Final approval of the version to be published.

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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