

Bilateral Genu Valgum in an Adolescent with Primary Hyperparathyroidism: A Case Report and Review of Literature

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Abstract

Primary hyperparathyroidism in children and adolescents is rare and often symptomatic at presentation. A 15-year-old boy presented with bilateral genu valgum for two years. Biochemical results were consistent with primary hyperparathyroidism. Calcium levels normalized two months after removal of a left inferior parathyroid adenoma.

Key words: primary hyperparathyroidism, adolescent, genu valgum, parathyroid neoplasms

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a disorder of bone and mineral metabolism caused by autonomous secretion of parathyroid hormone (PTH). It is mainly seen in adults between 50 and 60 years of age, with an annual incidence of 30 per 100,000 and a lifetime prevalence of one per 1,000. The female to male ratio is approximately 3:1.¹ On the other hand, PHPT in children and adolescents is rare, with a prevalence of two to five cases per 100,000 and no apparent sex predilection.^{1,2} In contrast to adults who are often asymptomatic and commonly recognized during routine biochemical screening, children and adolescents with PHPT are mostly clinically symptomatic with end-organ damage. These include skeletal abnormalities and/or nephrolithiasis at presentation.²

Genu valgum is an unusual manifestation of PHPT in children and adolescents. To date, there is a limited number of published reports describing such presentation. We report a young patient who had bilateral genu valgum as a result of a parathyroid adenoma.

CASE

A 15-year-old boy presented in October 2018 with bilateral knock-knee for two years. He had an uneventful antenatal history and normal developmental milestones. He did not have any knee pain, swelling or stiffness. He had no history of injury, fracture or infection to his knees or legs. None of his family members had disorders related to multiple endocrine neoplasia type 1 (MEN 1) or type 2A (MEN 2A), hyperparathyroidism-jaw tumor (HPT-JT) syndrome or familial isolated hyperparathyroidism (FIHPT).

Physical examination revealed short stature (below 5th percentile) and bilateral genu valgum (Figure 1). There were no bony deformities including those typical of rickets. He had no polydactyly, joint laxity or lumbar kyphosis to suggest skeletal dysplasia. The knee joints were not swollen, tender or warm. Laboratory evaluation showed hypophosphatemia and elevated levels of calcium, alkaline phosphatase and intact parathyroid hormone (iPTH), consistent with the diagnosis of primary hyperparathyroidism (Table 1). Neck ultrasonography revealed a well-defined hypoechoic lesion measuring 1.2x1.5x2.7 cm at the inferior pole of left thyroid lobe. Kidney and liver function tests were normal. Unfortunately, serum vitamin D, urinary calcium, kidney ultrasonography and bone mineral density scan were not performed in this case.

He subsequently underwent left inferior parathyroidectomy in December 2018. Histopathologic examination of the resected parathyroid gland confirmed a parathyroid adenoma. His immediate postoperative serum calcium was 1.9 mmol/L, for which he received oral calcium and calcitriol for a month. His calcium levels normalized two months after surgery (Table 1). Meanwhile, corrective osteotomy is currently being contemplated by the pediatric orthopedic surgery team.

DISCUSSION

Our adolescent patient presented with bilateral genu valgum as a result of excessive parathyroid hormone secretion from a parathyroid adenoma. His age at presentation corresponds to those with a similar deformity described in literature (Table 2). Majority of reported cases presented during the adolescent period—between 11 to 17

Table 1. Preoperative and postoperative biochemical profile

Parameters	Preoperation (October 2018)	Two months post-operation (February 2019)	Six months post-operation (June 2019)	Reference range
Corrected calcium, mmol/L	2.97	2.14	2.13	2.10-2.55
Phosphate, mmol/L	1.03	1.64	1.3	1.45-2.10
Alkaline phosphatase, U/L	1354	560	377	116-468
Intact PTHa, pmol/L	154	–	–	1.5-7.6
Creatinine, μ mol/L	33	55	–	50-77

^aPTH, parathyroid hormone

Table 2. Primary hyperparathyroidism presenting as genu valgum: A summary of case reports and case series from published literature

Publication	Year	Age, yr	Gender	End-organ damage	Etiology	Outcome after parathyroidectomy
McClure RD et al ⁶	1945	14	Female	Skeletal abnormalities	Left inferior parathyroid adenoma	Biochemical normalization and spontaneous correction of genu valgum
Balch HE et al ³	1953	21	Female	Skeletal abnormalities	Left inferior parathyroid adenoma	Hungry bone syndrome in immediate post-operative period, followed by biochemical normalization and recalcification of demineralized bones
Lloyd HM et al ⁷	1965	14	Male	Skeletal abnormalities	Left inferior parathyroid adenoma	Biochemical normalization and skeletal improvement
Rapaport D et al ⁴	1986	15	Female	Skeletal abnormalities, nephrolithiasis	Right inferior parathyroid adenoma	Clinical and biochemical resolution
		15	Male	Skeletal abnormalities, nephrolithiasis	Right inferior parathyroid adenoma	Clinical and biochemical resolution
Kauffmann C et al ⁸	1993	13	Female	Skeletal abnormalities	Left inferior parathyroid adenoma	Biochemical normalization and resolution of bone demineralization
Menon PS et al ⁹	1994	14	Female	Skeletal abnormalities, nephrolithiasis	Left superior parathyroid adenoma	Normalization of calcium and phosphate
Harman CR et al ¹⁰	1999	14	Female	Skeletal abnormalities	–	–
Walczyk A et al ¹¹	2011	15	Male	Skeletal abnormalities	Right inferior parathyroid adenoma	Biochemical resolution and improvement of BMD ^a
Dutta D et al ²¹	2013	12	Female	Skeletal abnormalities	Right inferior parathyroid adenoma	Clinical and biochemical resolution
Ratnasingam J et al ¹²	2013	15	Female	Skeletal abnormalities	Right parathyroid adenoma	Biochemical resolution
Ramkumar S et al ¹³	2014	16	Male	Skeletal abnormalities	Left inferior parathyroid adenoma	Biochemical resolution
		13	Male	Skeletal abnormalities	Right inferior parathyroid adenoma	Biochemical resolution
Sharma S et al ¹⁴	2016	15	Female	Skeletal abnormalities	Left inferior parathyroid adenoma	Biochemical resolution
Zil-E-Ali A et al ¹⁵	2016	14	Female	Skeletal abnormalities	Right inferior parathyroid adenoma	Biochemical resolution
Arambewela MH et al ¹⁶	2017	12	Female	Skeletal abnormalities	Right inferior parathyroid adenoma	Resolution of primary hyperparathyroidism
Kamath SP et al ¹⁷	2018	11	Female	Skeletal abnormalities	Left superior parathyroid adenoma	Normalization of iPTH ^b
		12	Male	Skeletal abnormalities, nephrolithiasis	Left superior parathyroid adenoma	Normalization of iPTH ^b
Khan KA et al ²²	2019	17	Male	Skeletal abnormalities	Left inferior parathyroid adenoma	Biochemical resolution
Paruk IM et al ¹⁸	2019	17	Male	Skeletal abnormalities	Left inferior parathyroid adenoma	Clinical and biochemical resolution
		13	Male	Skeletal abnormalities	Right superior parathyroid adenoma	Clinical and biochemical resolution
Rao KS et al ¹⁹	2019	12	Female	Skeletal abnormalities, nephrolithiasis	Right inferior parathyroid adenoma	Hungry bone syndrome in immediate post-operative period, long term outcome not reported
Yanrismet Y et al ²⁰	2019	13	Male	Skeletal abnormalities	Right inferior parathyroid adenoma	Hungry bone syndrome in immediate post-operative period, long term outcome not reported

^aBMD, bone mineral density

^biPTH, intact parathyroid hormone

years old— except for one who came for medical attention at the age of 21.³ Out of these 23 patients with PHPT who manifested either unilateral or bilateral genu valgum, 13 were females. The underlying reason for the occurrence of such deformity in this particular age group remains unclear. It has been postulated that the direct effect of elevated parathyroid hormone on the epiphyseal plate and bone remodeling during the pubertal growth spurt could be the main contributing factor.⁴

Primary hyperparathyroidism in children and adolescents is caused by either parathyroid adenoma (solitary or multiple) or hyperplasia, which may be sporadic or familial. Parathyroid carcinoma in this age group is rarely reported.² Familial causes encompass MEN 1 or MEN 2A,

HPT-JT and FIHPT. Our patient most likely has sporadic PHPT due to the absence of a family history of the aforementioned disorders. Moreover, additional screening revealed a normal prolactin level and a normal pituitary gland on magnetic resonance imaging. Solitary parathyroid adenoma appears to be the etiology in all the reported cases, including our patient (Table 2).

Our patient presented with isolated bilateral genu valgum with no other symptoms attributable to hypercalcemia. This piece of information has to be taken with a pinch of salt because it is well-known that children and adolescents with PHPT may have vague and non-specific symptoms involving the gastrointestinal, renal, musculoskeletal and neurological systems.^{1,2} These non-specific complaints

may potentially be dismissed as trivial and hence fail to raise the alarm unless a calcium level, which is often not part of routine blood tests in children, is checked. As a consequence, delayed diagnosis of PHPT and end-organ damage at presentation are common in this age group.

Interestingly, the lack of routine biochemical screening in children and adolescents may not exclusively justify the more severe presentations of PHPT in this juvenile population compared to their adult counterparts. This is because symptomatic PHPT remains uncommon at the fourth and fifth decades of life, as it is detected mainly by routine biochemical tests.¹ The question of whether juvenile PHPT and adult PHPT represent two separate entities remains unanswered. A meta-analysis of 16 studies that included 268 juvenile and 2,405 adult patients with PHPT demonstrated that the former had greater hypercalcemia and hypercalciuria, despite similar serum iPTH levels. Decreased parathyroid adenoma sensitivity to negative feedback by calcium and increased target tissue responsiveness to the effects of parathyroid hormone in juvenile PHPT were suggested to be the key differences between these two age groups, providing the basis for future research.⁵

In addition to genu valgum, most patients reported in literature also manifested with other radiologic changes typical of primary hyperparathyroidism.^{3,6-20} These include subperiosteal bone resorption especially over the phalanges, acro-osteolysis, subchondral resorption

around specific joints, brown tumors, salt-and-pepper radiologic appearance of the skull and osteopenia. It is noteworthy that three patients were initially treated as vitamin D deficiency rickets before the final diagnosis of PHPT was made.²⁰⁻²² In fact, genu valgum is one of the known clinical features of nutritional rickets.²³ In these patients, the lack of clinical improvement and new onset of hypercalcemia coupled with persistent elevation of parathyroid hormone following vitamin D repletion eventually unveiled the diagnosis of PHPT. On a different note, concomitant nephrolithiasis seems infrequent, as only four out of twenty-three total cases in literature exhibited the said complication.^{4,9,17}

Parathyroidectomy is the mainstay of treatment in children with PHPT.¹ Treatment goals include immediate and permanent cure of excessive calcium and parathyroid hormone secretion, mitigation of symptoms as well as reversal of end-organ damage.² All reported cases including ours underwent successful parathyroidectomy. Hungry bone syndrome during the immediate post-operative period, which constituted a significant risk in this age group due to the greater disease severity, was reported in a handful of cases.^{3,19,20} Long-term outcomes post-parathyroidectomy are favorable as evidenced by clinical and/or biochemical resolution in majority of patients. Our patient's calcium levels remained within normal range six months after surgery without any calcium or vitamin D supplement (Table 1). However, he will still require osteotomy to correct his bilateral genu valgum.



Figure 1. Clinical (A) and radiologic (B) evidence of bilateral genu valgum.

In conclusion, primary hyperparathyroidism in children and adolescents is rare and often diagnosed late, with genu valgum being an unusual manifestation of this disorder. Nevertheless, a high index of suspicion is warranted, as prompt parathyroidectomy may lead to cure and reversal of debilitating complications.

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Ethical Consideration

Patient consent was obtained before submission of the manuscript.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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