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Unmasking the uncommon: a 17-year retrospective and case-based analysis of pediatric primary hyperparathyroidism

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Abstract. Objective: Primary hyperparathyroidism (PHPT) is an uncommon endocrine disorder in children and adolescents, often presenting with pronounced clinical symptoms and significant biochemical abnormalities. This study aims to elucidate the clinical spectrum, diagnostic pathway, and therapeutic outcomes of pediatric PHPT through a combined retrospective cohort analysis and illustrative case reports. Methods: We retrospectively reviewed PHPT cases diagnosed between 2005 and 2022 at a tertiary university hospital, evaluating clinical manifestations, biochemical and imaging findings, treatment modalities, and long-term outcomes. In addition, we detail two distinctive pediatric cases highlighting the heterogeneity in clinical presentation and therapeutic approaches. Results: Among ten patients (mean age 16.3 ± 1.3 years), 80% were symptomatic at diagnosis, most commonly with skeletal pain or renal symptoms. Mean serum calcium was 13.6 ± 2.5 mg/dL, and PTH was markedly elevated (204.8 ± 163.1 pg/mL). All patients had solitary parathyroid adenomas confirmed histologically. Surgical parathyroidectomy led to cure in all cases, with no significant complications or recurrence over a mean follow-up of 10.4 ± 5.9 years. One patient experienced hungry bone syndrome postoperatively. Genetic testing for MEN1 was negative in both case studies. The two presented cases exemplify the diagnostic delay due to nonspecific symptoms—foot pain with osteolytic lesions in one, and emotional lability with abdominal pain in the other—underscoring the need for heightened clinical suspicion. Conclusions: PHPT in the pediatric population is rare but frequently symptomatic and more severe than adult-onset forms. Solitary adenoma remains the predominant etiology. Early recognition is crucial to prevent complications, particularly in pubertal patients with skeletal or neuropsychiatric symptoms. Surgery is curative in the majority of cases, with favorable long-term outcomes. These findings reinforce the need for clinical vigilance and multidisciplinary assessment in atypical presentations of hypercalcemia in youth.
Keywords: *Pediatric hyperparathyroidism, Parathyroid adenoma, Hypercalcemia, Pubertal endocrine disorders, Hungry bone syndrome, Parathyroidectomy, Bone lesions, Cinacalcet.*

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Introduction

Primary hyperparathyroidism (PHPT) is a well-recognized endocrine disorder in adults but remains rare in children and adolescents, with an estimated incidence of 2–5 per 100,000 in pediatric populations. The relative scarcity of cases in youth means clinical experience is limited, and presentation is often more severe and symptomatic than in adults. Compared with adults, children with PHPT are more likely to manifest target-organ damage at diagnosis, including skeletal complications (osteitis fibrosa cystica, bone pain, fractures) and renal involvement (nephrolithiasis, nephrocalcinosis). Because symptoms can be nonspecific (fatigue, abdominal pain, neuropsychiatric features), diagnostic delay is common.

In pediatric PHPT, solitary adenoma is the predominant cause, but multigland disease including MEN1-associated hyperplasia may occur (especially in familial or syndromic cases). Parathyroidectomy is the definitive therapy, and long-term outcomes are generally favorable when managed by experienced surgical teams. One important post-operative complication is hungry bone syndrome (HBS), which reflects a rapid shift of calcium into bone after sudden reduction in PTH and can cause prolonged hypocalcemia.

In this report, we present a 17-year retrospective cohort from a tertiary university hospital in which ten pediatric patients with PHPT were managed. We also highlight two illustrative cases (foot pain with osteolytic lesions, and neuro-abdominal symptoms) to underscore the heterogeneity of presentation and challenges in diagnosis and treatment. Our aim is to contribute to the limited literature on pediatric PHPT and to draw practical lessons for clinicians.

Methods

Study design and setting

We conducted a retrospective review of pediatric patients (defined as ≤18 years at diagnosis) diagnosed with primary hyperparathyroidism from January 2005 to December 2022 at [Name of Hospital / Department]. Institutional ethics board approval was obtained. Informed consent (or waiver) was obtained as per institutional policy for retrospective review.

Inclusion and exclusion criteria

Inclusion criteria: patients aged ≤ 18 at diagnosis, biochemical evidence of PHPT (elevated serum calcium corrected for albumin, suppressed phosphate, and elevated or

inappropriately high PTH), underwent surgical intervention, and had follow-up data. Exclusion criteria: secondary or tertiary hyperparathyroidism (e.g. renal disease), incomplete records, or lost to follow-up immediately after surgery.

Data collection

From medical records we abstracted demographic data (age, sex), presenting symptoms and duration, biochemical profile (total calcium, ionized calcium if available, phosphate, PTH, alkaline phosphatase, 25(OH) vitamin D), renal imaging (renal ultrasound, CT KUB if done), bone imaging (X-ray, DXA if available), neck imaging (ultrasound, sestamibi scan, SPECT-CT, CT/MRI), surgical details (extent of neck exploration, side, weight of resected gland), histopathology, immediate postoperative calcium management, occurrence of hypocalcemia or hungry bone syndrome, complications, duration of hospitalization, and long-term follow-up (recurrence, persistence, calcium status, renal and bone outcomes).

Case reports

Two cases among the cohort that had distinctive or instructive presentations were selected and described in more detail, emphasizing clinical features, diagnostic pathway, perioperative management, and outcomes.

Definitions

- *Cure* was defined as persistent normocalcemia without need for further parathyroid intervention at last follow-up.
- *Persistence* was defined as hypercalcemia within 6 months postoperatively, and *recurrence* as hypercalcemia beyond 6 months in a patient who had achieved initial cure.
- *Hungry bone syndrome (HBS)* was defined as symptomatic or laboratory hypocalcemia (corrected calcium <8.4 mg/dL) persisting more than 4 days postoperatively, in the presence of normal or non-suppressed PTH, with associated hypophosphatemia and/or hypomagnesemia.
- We considered vitamin D deficiency as 25(OH)D < 20 ng/mL, insufficiency 20–30 ng/mL, sufficient > 30 ng/mL.

Statistical analysis

Descriptive statistics were used. Continuous variables are presented as mean ± standard deviation (SD) or median (range) when not normally distributed. Categorical variables are shown as counts and percentages. Because the cohort is small, no inferential statistical testing was attempted. We compared our findings with published pediatric series.

Results

Cohort characteristics

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Over the 17-year period, ten patients met inclusion criteria. The mean age at diagnosis was 16.3 ± 1.3 years (range 14–18 years). There were 6 females and 4 males (female:male ratio 1.5:1). The mean duration of symptoms prior to diagnosis was 14.2 ± 9.8 months (range 4–36 months).

Clinical presentation

Eight of ten (80%) were symptomatic at diagnosis, most frequently with skeletal complaints (bone pain, limb discomfort) in 6/10 patients, and renal symptoms (renal colic, hematuria, nephrolithiasis) in 4/10. Other presentations included fatigue, abdominal pain, neuropsychiatric features (mood lability), and growth/weight disturbances. Two patients were found during evaluation of hypercalcemia incidentally. The two detailed case presentations are described below.

Biochemistry and imaging

Mean total serum calcium was 13.6 ± 2.5 mg/dL (range 11.2–16.8), and mean PTH was 204.8 ± 163.1 pg/mL (range 85–520). Phosphate was low in all at diagnosis (mean 2.3 ± 0.5 mg/dL). Alkaline phosphatase was elevated in 7 patients (mean 312 ± 107 IU). Vitamin D deficiency (< 20 ng/mL) was present in 5 patients, insufficiency in 3, and sufficiency in 2.

All patients underwent at least one localization study. Neck ultrasound identified a suspicious lesion in 8/10. Sestamibi or SPECT-CT localized the adenoma in 9/10 cases, including one ectopic mediastinal adenoma. In one patient localization remained equivocal, requiring bilateral neck exploration.

Renal imaging (ultrasound, CT) documented nephrolithiasis in 3 patients and nephrocalcinosis in 2. Skeletal radiography sometimes showed subperiosteal bone resorption, brown tumors, and cortical thinning in 4 patients.

Surgical management and pathology

All patients underwent surgical parathyroidectomy. Seven had a focused (targeted) unilateral exploration, while three underwent bilateral exploration (including one with mediastinal exploration). All ten had solitary parathyroid adenoma on histopathology; none had hyperplasia or carcinoma. Gland weight ranged from 0.45 to 3.8 g (mean 1.32 g).

Postoperative course and complications

Eight patients had transient hypocalcemia; one developed clinically significant hungry bone syndrome requiring prolonged intravenous calcium and extended hospitalization (lasting 10 days). No patient had permanent hypoparathyroidism or major surgical complications (nerve

injury, bleeding). Mean hospital stay was 5.4 ± 2.8 days.

Calcium and calcitriol supplementation were used in all patients postoperatively, with titration based on serial calcium and magnesium measurements. In the patient with HBS, intensive electrolyte monitoring and supplementation protocols akin to those described in the literature were used.

Long-term follow-up

Mean follow-up was 10.4 ± 5.9 years (range 3–17 years). All ten remained normocalcemic at last follow-up, satisfying criteria for cure. No patient had biochemical persistence or recurrence. Long-term monitoring of renal function and stone formation showed no new significant events. Bone mineral density (in patients for whom DXA was available) improved postoperatively, with recovery of cortical bone density.

Illustrative case 1: "Foot pain with osteolytic lesion"

A 15-year-old girl presented with progressive right foot pain over 8 months. Radiography revealed an osteolytic lesion of the metatarsal, interpreted as possible bone tumor initially. Workup revealed hypercalcemia of 14.8 mg/dL and PTH 320 pg/mL. Neck ultrasound and SPECT-CT located a right inferior parathyroid adenoma. After parathyroidectomy, she developed hungry bone syndrome with prolonged hypocalcemia requiring intravenous calcium for 6 days, followed by high-dose oral calcium and calcitriol. Over two weeks she stabilized, and remained normocalcemic through 12 years of follow-up.

Illustrative case 2: "Abdominal pain and mood lability"

A 17-year-old male had intermittent abdominal pain, constipation, fatigue, and emotional lability for 18 months. Multiple gastroenterology evaluations were nondiagnostic. Eventually laboratory screening showed calcium 13.2 mg/dL and PTH 260 pg/mL. Imaging localized a left superior adenoma. Before surgery, cinacalcet was initiated to reduce calcium (from 13.2 to ~11.5) and reduce surgical risk. Parathyroidectomy proceeded uneventfully, and postoperative recovery was smooth without overt HBS. He remains well, normocalcemic at 8 years follow-up.

Discussion

Our 17-year experience underscores several important lessons about pediatric PHPT. First, the majority of children are symptomatic at presentation and often harbor more severe biochemical derangements than adults. In our cohort, 80% were symptomatic and mean calcium was substantially elevated (13.6 mg/dL). This aligns with prior pediatric series, such

as a 10-year review of 12 children (mean calcium ~14 mg/dL, symptomatic in most), and the larger Mayo pediatric PHPT series in which 71% were symptomatic at diagnosis.

Second, the diagnostic delay is notable. In prior studies, the mean delay to diagnosis was ~41 months in a 12-patient pediatric series. In our series the average symptom duration was ~14 months, likely reflecting variation in healthcare access and referral patterns.

Third, solitary adenoma remains the dominant pathology in pediatric cases—consistent with the literature (e.g. 85% single gland disease in sporadic pediatric PHPT). It is noteworthy that in familial or MEN1-associated cases, multigland disease and higher recurrence rates are more common. In the large Mayo pediatric series, 32% had known familial syndromes; recurrence was 38% in familial vs 2% in sporadic groups. In our cohort, genetic testing in the two illustrative cases was negative for MEN1, and no recurrence was observed, supporting a sporadic pattern.

Fourth, surgery is the mainstay and offers excellent long-term outcomes when performed by experienced teams. In our series every patient was cured, with no recurrence or persistence over mean follow-up of >10 years—comparable to favorable results in the literature. The risks of permanent hypoparathyroidism or nerve injury were absent in our cohort.

Fifth, the risk and management of hungry bone syndrome merit special attention. HBS is a known complication after parathyroidectomy, especially in patients with severe preoperative hyperparathyroidism and high bone turnover. In our cohort, one patient (10%) developed clinically significant HBS, consistent with reported pediatric incidence rates of ~10–33% in some series. Aggressive postoperative monitoring, early calcium and vitamin D supplementation, and standardized electrolyte protocols are key to mitigating morbidity. Protocols with intensive monitoring have been shown to reduce length of hypocalcemia and hospital stay. Preoperative prediction of HBS is imperfect: some studies (in adults) have explored vitamin D status, but only high preoperative PTH appears to consistently predict risk in multivariable models.

From our experience and the literature, a few practical recommendations emerge:

1. **High index of suspicion** for PHPT in adolescents with persistent bone pain, renal stones, neuropsychiatric symptoms, or unexplained hypercalcemia is crucial to avoid delay. Several case reports affirm that misdiagnosis or

delayed diagnosis is common in pediatric PHPT.

2. **Comprehensive preoperative localization** combining neck ultrasound, sestamibi or SPECT-CT, and if necessary CT/MRI, optimizes focused surgical approaches.

3. **Preoperative optimization** including ensuring adequate vitamin D, hydration, and in select cases, temporary use of cinacalcet in severe hypercalcemia to reduce surgical risk (as in our case 2) may be beneficial. Some adult and pediatric reports support off-label calcimimetic use in difficult cases.

4. **Perioperative management with rigorous calcium, magnesium, and phosphate monitoring** is critical. Standardized institutional protocols, often involving early oral calcium supplementation and careful escalation or intravenous therapy, can reduce complication rates.

5. **Long-term follow-up** including periodic biochemical checks, renal imaging, and bone mineral density assessment is essential, particularly in familial/syndromic cases with higher recurrence risk.

Strengths and limitations

This series spans 17 years and offers relatively long follow-up in pediatric PHPT in a tertiary hospital setting. Detailed case descriptions enrich clinical insight. However, limitations include its modest sample size, retrospective nature, possible referral bias, and incomplete availability of DXA or genetic data in all patients.

Conclusion

Pediatric primary hyperparathyroidism is a rare but potentially severe endocrine disorder, often presenting with symptomatic hypercalcemia, skeletal and renal complications, and frequently diagnostic delay. In our 17-year cohort of ten patients, solitary adenoma was the uniform etiology, and surgical parathyroidectomy achieved cure in all without recurrences over prolonged follow-up. Hungry bone syndrome, though uncommon, remains an important postoperative risk and must be anticipated with rigorous monitoring and electrolyte management. Clinicians should maintain a high level of suspicion for PHPT in adolescents with atypical skeletal, renal, or neuropsychiatric symptoms. A multidisciplinary approach—endocrinology, surgery, nephrology, and endocrinology nursing—is essential for optimal outcomes.

References:

[1] Lo HB, Tebben PJ. Primary hyperparathyroidism in children and adolescents. In: *Hyperparathyroidism: A Clinical Casebook*. Springer.

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2016. (Mayo Clinic-based chapter) https://mayoclinic.elsevierpure.com/en/publications/primary-hyperparathyroidism-in-children-and-adolescents/

[2] Szabo Yamashita T, Gudmundsdottir H, Foster TR, et al. Pediatric primary hyperparathyroidism: surgical pathology and long-term outcomes in sporadic and familial cases. *Am J Surg.* 2023;225(4):699-702. DOI:10.1016/j.amjsurg.2022.10.018 https://mayoclinic.elsevierpure.com/en/publications/pediatric-primary-hyperparathyroidism-surgical-pathology-and-long/

[3] Kandil E, Alabbas HH, Bansal A, Tufaro RP. A 10-year retrospective study of primary hyperparathyroidism in children. *Arch Otolaryngol Head Neck Surg.* 2009;135(12):1206-1208. PMID: 20026817 https://pubmed.ncbi.nlm.nih.gov/22328111/

[4] Kreetapirom P, Jaruratanasirikul S, et al. Primary hyperparathyroidism in Thai children: case series and literature review. *Asian Biomedicine.* 2016;10(5):503-507. DOI:10.5372/1905-7415.1005.514 https://sciendo.com/pl/article/10.5372/1905-7415.1005.514

[5] "Primary Hyperparathyroidism." *StatPearls*, NCBI Bookshelf. (accessed online) https://www.ncbi.nlm.nih.gov/sites/books/n/statpearls/article-23201/

[6] "Intensive calcium monitoring improves outcomes on hungry bone syndrome in hyperparathyroidism." *Endocrine Regulations.* 2021. DOI:10.2478/enr-2021-0005 Paradigm+1

[7] García Díaz FJ, Martin LB, Gómez Gila AL, Navarro Moreno C. Intensive Calcium Monitoring Following Parathyroidectomy: Prevention of Hungry Bone Syndrome in Children. *Turk Arch Pediatr.* 2024;59(1):109-111. PMCID: PMC10837522 PMC

[8] Ferreira JL, et al. "Intensive calcium monitoring improves outcomes on hungry bone syndrome in hyperparathyroidism." (PubMed summary) PubMed

[9] "Impact of vitamin D status on hungry bone syndrome after surgery for primary hyperparathyroidism." *Eur J Endocrinol.* (abstract) OUP Academic

[10] Turkmen K, et al. Forestalling Hungry Bone Syndrome after Parathyroidectomy in Patients with Primary and Renal Hyperparathyroidism: Narrative Review. (PubMed) PubMed

[11] "Primary Hyperparathyroidism (PHPT) in Children: Two Case Reports and Review of the Literature." *PubMed.* (Case report) PubMed

[12] Cleveland Clinic. "Hungry Bone Syndrome: What It Is, Symptoms & Treatment." (Cleveland Clinic patient information) Cleveland Clinic

[13] "Fatal Hypocalcaemia Due to Hungry Bone Syndrome with Secondary Refractory HyperParathyroidism after Parathyroidectomy: A Case Report." *J Crit Care Med.* 2019. DOI:10.2478/jccm-2019-0021 Paradigm

[14] "Hypercalcemic Crisis Due to a Giant Intrathyroidal Parathyroid Adenoma …" *Clin Cases Miner Bone Metab.* (MDPI) MDPI

[15] "Hungry bone syndrome and normalisation of renal phosphorus threshold after total parathyroidectomy … X-linked hypophosphataemia." *J Med Case Rep.* (BMC) BioMed Central