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Case Report

Teriparatide for the treatment of primary hypoparathyroidism in children

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Abstract: In this retrospective case series, the clinical data of four pediatric patients with primary hypoparathyroidism (PHPT) treated with teriparatide at the Endocrinology Department of Capital Center for Children's Health, Capital Medical University, from May 2018 to May 2025, were analyzed. All patients were male and from four unrelated families. The ages at onset were 8 months, 12 years, 3 days, and 8 years plus 9 months, respectively, with time from onset to diagnosis ranging from several days to 1 year. The primary clinical manifestations of PHPT included seizures, tetany, and limb numbness. Seizures were observed in the two younger patients, whereas tetany or limb numbness were noted in the two older patients. Physical examination revealed positive Trousseau's sign or facial nerve signs. Laboratory test results showed hypocalcium, hyperphosphatemia, and decreased parathyroid hormone (PTH). Imaging revealed basal ganglia calcification in one patient and multiple small renal calculi in another. A heterozygous pathogenic variant in the CASR gene was identified by whole-exome sequencing in three patients, confirming a diagnosis of autosomal dominant hypocalcemia type 1 (ADH-1). All four patients had poor responses to conventional therapy (calcium supplements + vitamin D or its derivatives) and were subsequently treated with teriparatide (20 μg/dose, subcutaneously, 1-2 doses daily), with dose frequency adjusted based on serum calcium levels. Following 1 to 6 months of treatment, all patients achieved favorable outcomes, including normalization of serum calcium levels and resolution of clinical symptoms. No known teriparatide-related side effects were observed during treatment. Upon treatment discontinuation, patients smoothly transitioned to conventional therapy. Serum calcium levels were maintained at the lower limit of normal. Three patients experienced resolved clinical symptoms, while one patient experienced occasional tetany and numbness when the medicine was taken irregularly. Teriparatide (rhPTH1-34) effectively corrected hypocalcemia and alleviated clinical symptoms in pediatric PHPT, with a favorable safety profile. Therefore, teriparatide can be considered for children with refractory PHPT who do not respond adequately to conventional therapies.

Keywords: Teriparatide (recombinant human parathyroid hormone 1-34), primary hypoparathyroidism, hypocalcaemia

Introduction

Primary hypoparathyroidism (PHPT) is a rare endocrine disorder in childhood, characterized by hypocalcemia and hyperphosphatemia. Clinically, it primarily manifests as tetany, convulsions, and numbness [1-3]. Conventional treatment involves oral calcium supplements and vitamin D or its derivatives. However, some pediatric patients, particularly infants and young children, experience unstable serum calcium levels under stress conditions despite increased doses. This leads to frequent seizure episodes, harming quality of life [4]. Teriparatide (rhPTH1-34) is currently the only recombinant PTH formulation available in China [5]. International studies have confirmed its efficacy in treating refractory PHPT in both adults and children [6], though domestic clinical data on its pediatric use remain limited. This study retrospectively analyzed the treatment course of teriparatide in four pediatric patients with refractory PHPT, supplemented by a literature review, to evaluate its short-term efficacy, safety, and clinical management strategies, providing references for the treatment of pediatric PHPT.

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Methods

Four pediatric patients with PHPT treated with teriparatide at the Endocrinology Department of Capital Center for Children's Health, Capital Medical University between May 2018 and May 2025 were enrolled. All the four patients were male and from four unrelated families. General information and whole-exome sequencing results are shown in **Table 1**. This study was reviewed and approved by the Ethics Committee of the Capital Center for Children's Health, Capital Medical University. Due to the retrospective nature, informed consent was waived.

Case presentation and results

Case 1

Case 1 was admitted for recurrent seizures. Initial treatment included oral calcium carbonate and intravenous calcium gluconate, with a total daily calcium dose of 1800 mg, along with calcitriol (1,25-dihydroxyvitamin D) 0.75 μg/day and vitamin D 400 IU/day. However, serum calcium remained unstable. When seizure frequency exceeded 10 episodes per day, teriparatide 20 μg was administered subcutaneously once daily after obtaining informed consent from the family. By the second day, serum calcium rose to 2.25 mmol/L, seizures improved, intravenous calcium supplementation was gradually discontinued, and oral calcium dose was reduced. As condition improved, the dose of teriparatide was tapered to every other day on day 8, and treatment continued for 1 month. During follow-up, the patient remained seizure-free, although hypercalciuria was noted. Renal ultrasound revealed bilateral nephrocalcinosis. Intellectual and motor development, as well as growth indices, were normal.

Case 2

Case 2 received oral calcium and alfacalcidol daily after admission; however, serum calcium remained between 1.61 and 1.83 mmol/L, and tetany and numbness persisted. After obtaining informed consent from the family, teriparatide 20 μg was administered subcutaneously twice daily, then reduced to once daily after 5 days. Treatment was discontinued after one month, followed by gradual transition back to conventional therapy. Serum calcium remained stable, with no recurrence of tetany. No adverse reactions occurred during treatment. At the last follow-up, serum calcium was 2.08 mmol/L, with normal urinary calcium-to-creatinine ratio.

Case 3

Following admission, Case 3 received calcium and calcitriol, but hypocalcemia persisted. Recurrent seizures occurred despite repeated intravenous calcium supplementation. Hence, subcutaneous injection of teriparatide 20 μg was given once daily. After two injections, total calcium and ionized calcium reached 2.12 mmol/L and 1.16 mmol/L, respectively, and seizures ceased. Serum calcium remained within normal range. After 2 months, teriparatide was discontinued and replaced with conventional calcium and vitamin D therapy. No adverse reactions occurred during treatment.

Case 4

Despite oral calcium supplementation at 3600 mg/day and calcitriol at 0.75 μg/day, serum calcium remained low (lowest ionized calcium 0.66 mmol/L) with recurrent tetany. Subcutaneous injection of teriparatide 20 μg once daily was initiated. By day 2, total calcium increased to 2.07 mmol/L, tetany resolved, and serum calcium remained stable. During the 1-month treatment period, total serum calcium was maintained at 2-2.2 mmol/L, serum phosphorus were normal, and serum magnesium was maintained around 0.6 mmol/L. No serious adverse reactions occurred during treatment. The patient maintained stable serum calcium and normal growth and development during follow-up. Regular monitoring of urinary calcium, renal ultrasound, and cranial CT has not yet been performed.

Discussion

The primary treatment goal for primary hypoparathyroidism (PHPT) is to alleviate clinical symptoms and signs while preventing complications such as hypercalcemia, hypercalciuria, nephrocalcinosis/renal stones, and other extraosseous calcifications. Serum calcium levels should be maintained slightly below the normal range or around the lower limit of normal [7, 8]. Therefore, preventing hypercalciuria to avoid complications is equally important as alleviating clinical symptoms.

PTH1-34 has been studied in multiple trials involving adults and children with PHPT. These

Table 1. Clinical manifestations, laboratory findings, genetic results, and follow-up of four pediatric patients

	Case 1	Case 2	Case 3	Case 4
General data				
Sex	Male	Male	Male	Male
Age at onset	8 months	12 years	3 days	8 years and 9 months
Age at diagnosis	8 months	13 years	1 month	8 years and 11 months
Primary clinical manifestations	Convulsions	Tetany and numbness	Convulsions	Tetany
Laboratory test results				
Total calcium (2.25-2.74) mmol/L	1.57	1.59	1.53	1.5
Free calcium (1.18-1.32) mmol/L	0.85	0.77	0.7	0.62
Serum phosphorus (1.29-1.94) mmol/L	3.15	2.73	2.73	2.03
Total parathyroid hormone (14.9-56.9) pg/mL	5.5	7.3	3.15	1.36
Alkaline phosphatase (0-400) U/L	220	153	190	103
25-hydroxyvitamin D3 (75-200) nmol/L	96.85	78.23	72.55	81.8
Serum magnesium (0.66-1) mmol/L	0.61	0.8	0.57	0.58
Serum sodium (135-145) mmol/L	140	138	139	140
Serum potassium (3.5-5.5) mmol/L	3.6	4.47	4.1	3.69
Serum chloride (98-110 mmol/L)	103	101	102	99
Blood gas pH (7.35-7.45)	7.41	7.36	7.45	7.44
HCO3 (22-27) mmol/L	24	23	25	26.3
Random urine calcium/urine creatinine	0.203 (<0.6)	0.01 (<0.21)	3.54 (<0.8)	0.22 (<0.21)
24-hour urine calcium (<0.1 mmol/kg.d)	0.06	0.081	0.6	0.368
Humoral immunity and cellular immunity	normal	Normal	Normal	Normal
Head CT	Punctate calcifications in bilateral basal ganglia regions	Normal	Normal	Normal
Urinary system ultrasound	Normal	Normal	Multiple small stones in both kidneys	Normal
Video EEG	Normal pediatric EEG	-	Normal pediatric EEG	-
Gene	CASR c.2495T>G	CASR c.1377+5G>A (variant of uncertain significance)	CASR c.374T>C	Negative
Treatment type				
Calcium (mg)	1800	3000	750	3600
Calcitriol or Alfacalcidol (ug)	Calcitriol 0.75	Alfacalcidol 2.4	Calcitriol 0.25	Calcitriol 0.75
Vitamin D3 (U)	400	-	-	-
rhPTH (ug)	20, once daily	20, twice daily	20	20
Treatment duration with rhPTH	1 month	1 month	6 months	1 month
Total calcium after PTH treatment	1.9-2.68	2.3	2.48	2.07
Follow-up and last result				
Calcium (mg)	1200	2400	1500	1200
Calcitriol or Alfacalcidol (ug)	Calcitriol 0.5	Calcitriol 0.5	Calcitriol 0.25	Calcitriol 0.25
Vitamin D3 (U)	400	400	-	-
Total calcium (2.25-2.74) mmol/L	2.19	2.08	2	2.01
Random urine calcium/urine creatinine (<0.21)	-	0.0054	-	-
24-hour urine calcium (<0.1 mmol/kg.d)	0.14	-	0.09	-
Urinary system ultrasound	Renal ultrasound revealed clustered hyperechoic areas in both renal pyramids.	-	Multiple small stones in both kidneys	-
Other	No seizure episodes; normal growth parameters	Tetany and numbness during irregular medication	No seizure episodes	No tetany

studies demonstrated that a single daily subcutaneous injection of PTH 1-34 exerts distinct pharmacodynamic effects on the kidneys, including a rapid increase in cyclic adenosine monophosphate (cAMP) levels, enhanced phosphorus excretion, and reduced urine calcium excretion, thereby maintaining stable calcium concentrations in both blood and urine [9]. In pediatric patients, twice-daily injections of PTH 1-34 reduced the total daily dose required to maintain calcium homeostasis by more than 50%. Furthermore, twice-daily injections demonstrated superior efficacy compared to once-daily injections in maintaining serum calcium levels within the normal range in children [10].

The safety of PTH 1-34 therapy has been confirmed, with no considerable difference from conventional treatments in terms of adverse reaction rates. In China, however, this drug has not yet been approved for the treatment of pediatric PHPT, and high cost prevents its widespread use in clinics. The dosages used in this study were guided primarily by existing adult dosing guidelines and sporadic case reports, employing an individualized dose-titration strategy based on frequent monitoring of serum calcium levels.

In the present study, four pediatric patients with PHPT, presenting with severe and refractory hypocalcemia, recurrent seizures, or tetany, were included. Each of them received teriparatide (rhPTH1-34) for 1 to 6 months, achieving favorable outcomes. These findings indicate that teriparatide may be a viable treatment option with favorable efficacy and safety profiles for children with refractory PHPT who do not respond adequately to conventional therapy.

However, this study had certain limitations. First, the retrospective design inevitably introduced selection bias, and the completeness and accuracy of data depend on the quality of historical medical records, which may have affected reliability of the findings. Second, the small sample size limited the statistical power. Third, the lack of long-term follow-up data restricted the applicability of conclusions, as evidence on long-term safety and efficacy was insufficient. Finally, teriparatide use in children with PHPT was off-label, and authoritative dosage guidelines are lacking. Notably, this study did not employ a weight-based dosing regimen, which warrants further exploration. Therefore, prospective, multi-center studies with larger sample sizes and longer follow-up are needed to validate these findings.

Conclusion

Teriparatide may be considered a treatment option for pediatric patients with refractory hypocalcemia in PHPT when conventional therapy is ineffective, demonstrating favorable efficacy and safety profiles.

Disclosure of conflict of interest

None.

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