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Recombinant Parathyroid Hormone Therapy for Severe Neonatal Hypoparathyroidism

Yoon Hi Cho, BSc(Med), MBBS, FRACP, Michel Tchan, BMedSc, MBBS, PhD, FRACP, Bithi Roy, MBBS, MD, Robert Halliday, BSc(Med), MBBS, FRACP, Meredith Wilson, MBBS, FRACP, Mbioeth, Shoma Dutt, MBBS, PhD, FRACP, Susan Siew, MBBS (Hons), FRACP, Craig Munns, MBBS, PhD, FRACP, Neville Howard, MBBS, FRACP, FRCP(C)

Children's Hospital at Westmead, Sydney, Australia

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Recombinant Parathyroid Hormone Therapy for Severe Neonatal Hypoparathyroidism

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Hypoparathyroidism-retardation-dysmorphism (HRD) syndrome (OMIM 241410), also known as Sanjad-Sakati syndrome, is a rare autosomal recessive disorder characterized by hypoparathyroidism, growth failure, developmental delay, and characteristic facies. We describe the effective short-term use (tapered over 12 days) of recombinant parathyroid hormone (PTH) (teriparatide) in an unusual genetic condition characterized by hypoparathyroidism.

Standard treatment for hypoparathyroidism involves oral vitamin D analogues and calcium, often in large doses to achieve sufficient intestinal calcium transport to overcome the hypercalciuria and concomitant malabsorption.[1] Despite its known physiological benefits,[2] recombinant PTH is not usually considered in the treatment algorithm for hypoparathyroidism in the pediatric population.

Case Report

Approval for this case report was obtained from the Human Research Ethics Committee of The Children's Hospital at Westmead. Informed consent was obtained from the family. A female infant was born to first-cousin Iraqi parents at 31 weeks gestation, after an antenatal course that included oligohydramnios and fetal growth restriction. The parents had previously experienced 2 first-trimester miscarriages and fetal death at 30 weeks, and the current pregnancy was conceived after in vitro fertilization. She had a birth weight of 1190 g (SDS, −1.02), length of 36.5 cm (SDS, −1.77), and head circumference of 25.4 cm (SDS, −1.61). Dysmorphic features included deep-set eyes, large ears with hypoplastic posterior helices, and a thin nose (Figure 1). The newborn period was complicated by respiratory distress syndrome, treated with surfactant, mechanical ventilation, and continuous positive airway pressure. Significant feeding intolerance and vomiting were present from the first week of life. Upper gastrointestinal studies showed gastric hypomotility and delayed passage into the duodenum with no mechanical obstruction. Transpyloric tube feeding was started at 4 weeks after birth. Fat malabsorption was confirmed by fecal fat analysis and low serum vitamin A and E levels. Results of a sweat test were normal. Pancreatic enzyme replacement and fat-soluble vitamin supplementation was instituted.

Hypocalcemia (corrected plasma calcium, 6.7 mg/dL; normal range, 8.4-10.6 mg/dL) was first detected on day 3. Empirical treatment with calcium and cholecalciferol was started for presumed vitamin D deficiency, given that the mother was veiled and had documented vitamin D deficiency. Subsequently, an inappropriately low PTH level was found on multiple occasions (<2.8 pg/mL; normal range, 9.5-66.5 mg/dL). The infant had a high urine calcium:creatinine ratio (1.5 mM/mM) despite hypocalcemia, an elevated plasma phosphate level (11.7 mg/dL; normal range, 3.7-6.5 mg/dL), and a normal 25-hydroxy vitamin D level (36 ng/mL; normal, >19 ng/mL). Ultrasound did not reveal nephrocalcinosis. Normal parental calcium and PTH levels excluded maternal hyperparathyroidism and inherited calcium-sensing receptor defects. Fluorescence in situ hybridization for 22q11 deletion was negative. X-rays in the neonatal period did not show skeletal abnormalities.

HRD syndrome was suspected on the basis of persistent hypoparathyroidism, prenatal and postnatal growth restriction, and dysmorphic facial features. Analysis of the tubulin-specific chaperone E (TBCE) gene (*TBCE*) confirmed the presence of homozygous 12-bp deletions in exon 2 (c.155-166del12; p.del52-55). Analysis of parental DNA confirmed that both parents were heterozygous for the same mutation.

Recurrent episodes of severe hypocalcemia (nadir total corrected calcium, 3.8 mg/dL) and poor postnatal growth continued. Calcitriol therapy was introduced, and doses were rapidly escalated to 800 ng/kg/day (usual maximum 90 ng/kg/day), delivered via both oral and transpyloric routes to maximize absorption. Magnesium supplementation was started for hypomagnesemia (1.1 mg/dL; range, 1.6-2.4 mg/dL). At 2 weeks corrected gestational age, hypocalcemia refractory to high-dose calcitriol prompted a trial of recombinant PTH (PTH 1-34; teriparatide). A starting dose of 1 μg/kg delivered subcutaneously, followed by twice-daily dosing, minimized fluctuations in ionized calcium levels (Figure 2). Levels achieved the normal range

HRD	Hypoparathyroidism-retardation-dysmorphism
PTH	Parathyroid hormone
TBCE	Tubulin-specific chaperone E

From the Children's Hospital at Westmead, Sydney, Australia

The authors declare no conflicts of interest.

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HRD (Hypoparathyroidism-retardation-dysmorphism), PTH (Parathyroid hormone), TBCE (Tubulin-specific chaperone E)

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