Intraoperative Parathyroid Hormone Monitoring in Neonatal Severe Primary Hyperparathyroidism

Authors: Emilio García-García, MD, Inmaculada Domínguez-Pascual, MD, Mercedes Requena-Díaz, MD, Rosa Cabello-Laureano, MD, Israel Fernández-Pineda, MD, and María J. Sánchez-Martín, MD

Virgen del Rocío Hospital, Sevilla, Spain

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Abstract

Neonatal severe primary hyperparathyroidism presents in the first days of life with severe life-threatening hypercalcemia. It is associated with an inactivating homozygous mutation of the calcium sensing receptor gene. Total parathyroidectomy is the treatment of choice, so the surgeon must identify all the parathyroid tissue, including supernumerary and ectopic glands. We present the case of an infant who underwent total parathyroidectomy at age 4 months in which intraoperative parathyroid hormone monitoring provided immediate confirmation of surgical cure. Pediatrics 2014;134:e1203–e1205

CASE REPORT

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Neonatal severe primary hyperparathyroidism (NSPH) is a life-threatening condition that presents within days of life with marked hypercalcemia, relative hypocalciuria, and serum parathyroid hormone (PTH) concentrations as much as 10-fold higher than normal. It is associated with an inactivating homozygous mutation of the calcium sensing receptor (CaSR) gene.\(^1\)\(^-\)\(^5\)

Total parathyroidectomy is the treatment of choice. Residual or ectopic parathyroid tissue explains persistence of hyperparathyroidism after surgery; any parathyroid remnant quickly becomes hyperplastic.\(^4\)\(^-\)\(^6\)

In other types primary hyperparathyroidism, intraoperative PTH monitoring provides real-time confirmation of surgical cure and indicates to the surgeon when all hyperfunctional parathyroid tissue has been adequately excised.\(^7\) To our knowledge, this is the first report of intraoperative PTH assessment in NSPH.

**PATIENT PRESENTATION**

A male infant was referred to our institution for parathyroidectomy at 3.5 months of age. He was admitted to another hospital at 18 days of age with severe global hypotonia, poor feeding, failure to thrive, signs of dehydration, and lethargy. The initial analysis revealed severe hypercalcemia with a total serum calcium level of 2.0 mmol/L (normal values 2.0–2.6 mmol/L) and PTH of 526 pg/mL (normal values 15–70 pg/mL). The parents were cousins. The genetic test revealed a homozygous mutation in exon 5 in the patient’s CaSR gene, which was heterozygous in both progenitors, so diagnosis of NSPH was confirmed in the infant. Parathyroid gland localization tests including \(^{99m}\)Tc-sestamibi scintigraphy, as well as ultrasonography, were negative.

A total parathyroidectomy was conducted at 4 months of age. Intact PTH was measured by a rapid assay (Elecsys, Roche Diagnostics, Mannheim, Germany; detection limits 1.20–5000 pg/mL) that requires ~20 minutes to obtain a result. Before the operation, the PTH value was 190.0 pg/mL, and 10 minutes after excision of 4 parathyroid glands, the PTH value fell to 19.8 pg/mL. Thirty-six hours later, he started to require calcium supplements for hypocalcemia. Histology revealed parathyroid chief cell hyperplasia.

At 30 months of age, the patient was following a normal diet with calcidiol supplements, psychomotor development and growth are appropriate, and serum analysis reveals PTH of 3.1 pg/mL and total calcium of 2.0 mmol/L.

**DISCUSSION**

CaSR regulates calcium homeostasis through its ability to modulate PTH secretion and renal calcium reabsorption. NSPH is most commonly an autosomal recessive condition produced by an inactivating homozygous mutation in CaSR gene. By contrast, more common heterozygous mutations are associated with a benign variant termed familial hypocalciuric hypercalcemia, which generally requires no specific treatment.\(^1\)\(^-\)\(^3\)

Total parathyroidectomy is the standard treatment of NSPH\(^1\)\(^-\)\(^4\) and leads to significantly greater survival than subtotal parathyroidectomy or medical treatment.\(^2\)

Individual variations of the location and number of glands may pose difficulties because unidentified extra parathyroid tissue will complicate the patient’s course.\(^15\)

Seven percent of the normal population has supernumerary glands that can be found along the mediastinum, thyroid or thymus, requiring thymectomy or hemithyroidectomy.\(^1\)\(^,\)\(^15\)\(^,\)\(^16\)

Preoperative localization tests, including scintigraphy, ultrasonography, and magnetic resonance imaging, are useless, so the parathyroid tissue must be identified during the surgery.\(^8\)

Intraoperative PTH monitoring takes advantage of the short plasma half-life (3–5 minutes) of PTH and a rapid assay technique that allows measurements while the patient is still in the operating room. A relative drop in PTH level into the normal range is suggestive of adequate removal of hyperfunctioning parathyroid tissue. For localization of an occult gland, bilateral jugular venous sampling for PTH can be performed at the time of exploration. A unilateral elevation is suspicious for a missing hyperfunctioning gland on that side.\(^7\)

We conclude that intraoperative PTH monitoring is useful providing real-time confirmation of surgical cure in NSPH.

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