Successful Parathyroidectomy with Intraoperative Parathyroid Hormone Monitoring in a Neonate with Severe Primary Hyperparathyroidism Caused by Homozygous Mutation in *CASR*

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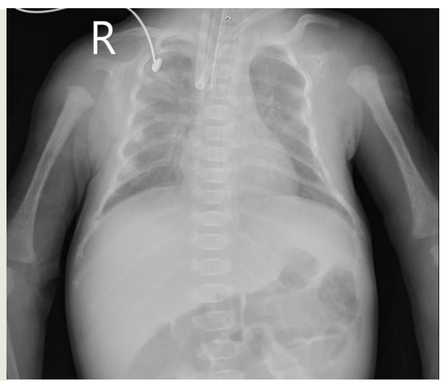
INTRODUCTION

Neonatal severe primary hyperparathyroidism (NSHPT) is characterized by having markedly elevated serum calcium (Ca), inappropriately raised plasma intact parathyroid hormone (iPTH) and decreased fractional excretion of urinary Ca (FECa) during the neonatal period. It is caused by inactivating mutation in *CASR* gene, which encodes Ca-sensing receptor.

CASE REPORT

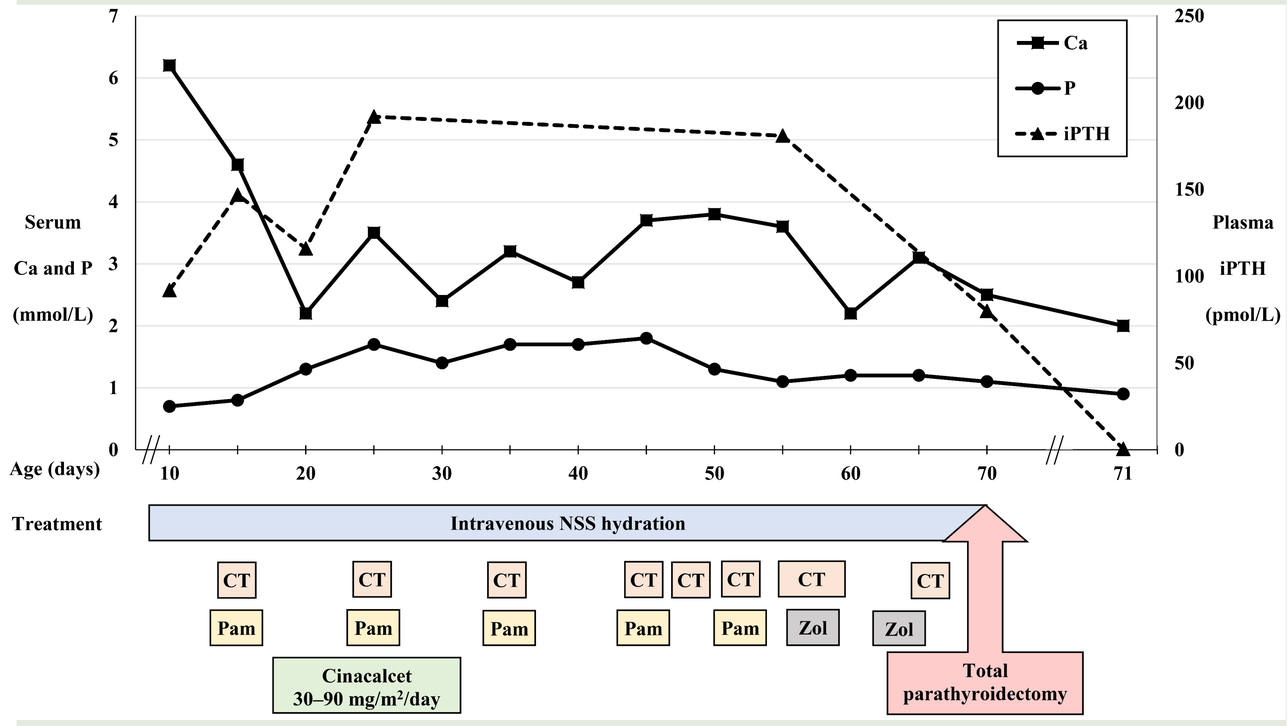
A 10-day-old female term neonate who was born uneventfully to consanguineous parents with a birth weight of 2,490 g presented with lethargy and respiratory failure. Physical examination revealed lethargy with body weight of 2.3 kg (-3 SDS), length of 49 cm (-0.4 SDS) and head circumference of 32 cm (-1.6 SDS). Heart, lungs and abdominal examinations were unremarkable. Multiple rib fractures and generalized osteopenia were found on the chest radiograph (Figure 1).

Figure 1 Chest radiograph showed bell-shaped thoracic cage, fractures of 4th-7th ribs of both sides and generalized osteopenia



Blood chemistries showed markedly elevated serum Ca at 6.2 mmol/L (N, 2.3–2.8), phosphorus (P) 0.7 mmol/L (N, 1.3–2.1) and iPTH 93 pmol/L (N, 1.1–6.9). The FECa was 2.6%. Severe hypercalcemia with elevated plasma iPTH and relative hypocalciuria led to the diagnosis of NSHPT. Subsequent *CASR* sequencing analysis identified a homozygous nonsense mutation, c.1660C>T (p.Arg554*) in exon 6 which confirmed the diagnosis. Standard treatments for severe hypercalcemia including intravenous saline hydration, loop diuretics and anti-resorptive agents, as well as cinacalcet were administered but hypercalcemia still persisted. Therefore, total parathyroidectomy was undertaken at 70 days of age (Figure 2).

Figure 2 Clinical course of the patient



CT, salmon calcitonin; Pam, pamidronate; Zol, zoledronic acid

Owing to the difficulty in performing parathyroidectomy in a small infant, intraoperative plasma iPTH levels were monitored to ensure complete removal of the parathyroid glands. The plasma iPTH levels fell from the preoperative level of 80 to 3.8 and 2.8 pmol/L at 15 and 20 minutes, respectively after removing all 4 parathyroid glands. Hypoparathyroidism was documented 10 days after the operation with serum Ca of 1.8, P of 2.3 mmol/L and undetectable plasma iPTH level. Ca carbonate and calcitriol concomitant with low phosphate formula were administered. The serum Ca and P levels were later normalized.

Blood chemistries of the parents showed mild hypercalcemia with inappropriately raised plasma iPTH levels and low FECa. The parents had no symptoms of hypercalcemia. Thus, both of them are likely to have the heterozygous mutation of *CASR* gene. However, the familial mutation analysis has not been performed.

CONCLUSIONS

A homozygous nonsense mutation (p.Arg554*) in the *CASR* gene was the cause of NSHPT. The patient with this mutation did not respond to the medications including cinacalcet. Intraoperative iPTH monitoring was helpful in successful parathyroidectomy.

Written informed consent was obtained from the legal guardian.