Familial benign hypocalciuric hypercalcemia (FHH) and neonatal severe hyperparathyroidism (NSHPT) are associated with loss of CASR function. Homozygous or compound heterozygous mutations typically cause NSHPT, an autosomal-recessive disorder associated with life-threatening hypercalcemia and multiple fractures. We here report two cases with NSHPT together with their treatment and long-term follow-up.

**INTRODUCTION**

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**CASE REPORT**

**CASE 1:** A 12-day-old was referred to our hospital with hypercalcemia (Ca: 25 mg/dL; normal range [NR]: 8.8–10.8 mg/dL). On physical examination, he was conscious but restless. Ca, 19.4 mg/dL (NR 9–10.8 mg/dL); phosphate (P), 3.3 mg/dL (NR 4.5–6.7 mg/dL); alkaline phosphatase (ALP), 412 IU/L (NR 110–302 IU/L); PTH, 2,536 pg/mL (NR 11–67 pg/mL); urine Ca, 25.5 mg/dL; urine creatinine (Cr), <0.5 mg/dL; urine Ca/Cr, 51; 25-hydroxy vitamin D, 18.6 μg/dL (NR 10–80 μg/dL); and 1,25-dihydroxy vitamin D, 21.3 pg/mL (NR 16–65 pg/mL). A parathyroid technetium-99M sestamibi radionuclide scan was normal without evidence of parathyroid adenoma.

**CASE 2:** A 25-day-old female neonate born at term presented with severe hypotonia, listlessness, feeding difficulties, and failure to thrive. Ca, 17.2 mg/dL (NR 8.8–10.8 mg/dL); P, 2.8 mg/dL (NR 4.5–6.7 mg/dL); ALP, 314 IU/L (NR 110–302 IU/L); PTH, 2,330 pg/mL (NR 11–67 pg/mL); 25-hydroxy vitamin D, 15.6 μg/dL (NR 10–80 μg/dL); and Ca/Cr clearance ratio, 0.0004. Total parathyroidectomy and forearm implantation of a parathyroid gland were performed at 97 days of age. The patient was not able to make eye contact or hold her head upright for short periods of time during the neurological examination before parathyroidectomy, and there was mild developmental retardation. Serum levels of Ca decreased gradually until the 105th postnatal day, but subsequently increased again (Ca, 18.8 mg/dL; PTH, 133 pg/mL). The patient’s implanted parathyroid gland was removed at 124 days of age. A genetic analysis was revealed a point mutation (c.2045C>T; p.Pro682Leu) in the CASR gene, which was homozygous in both parents, resulting in a truncation at the extracellular N-terminal domain of the protein.

**DISCUSSION**

The medical management of NSHP cases is often difficult and complex. A prompt assessment of the type of mutation that affects the CASR protein is desirable to determine whether a calcimimetic treatment is suitable.