A Rare GCMB Gene Mutation in an Isolated Hypoparathyroidism Case

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Familial isolated hypoparathyroidism is mostly caused by the calcium sensing receptor (*CaSR*) gene, the parathyroid hormone (*PTH*) gene, and the glial cells missing (*GCMB*) gene mutations. Inheritance can be autosomal dominant or autosomal recessive. Here, we are presenting an autosomal recessive hypoparathyroidism case with a new mutation on the *GCMB* gene.

A 22-year-old male patient has been referred for genetic consultation to our clinic with mental retardation and a convulsion history. Patient's hormonal and neurologic physical examination and biochemical examinations were done. A coding and intron/exon adhesion site sequence analysis of *CaSR* and *GCMB* genes was carried out as well.

There was no consanguineous marriage between the parents. There was no other family member with similar findings. He was first admitted to a hospital at age 3 with hypocalcaemia and hypomagnesaemia. In his physical examination, shortness, motor and mental development retardation, and chronic tetany were described. His brain MRI revealed calcifications at basal ganglions. A bilateral cataract was found in ophthalmologic examination. Cranial computed tomography showed diffuse cerebral atrophy. He had a chronic hypoparathyroidism with hypocalcaemia and hyperphosphatemia. Thyroid function tests were normal. There was not any mutation detected on CaSR coding and intron/exon cohesive site sequence analysis. On sequence analysis of GCMB coding and intron/exon cohesive site, we found a new homozygous mutation (c.90+1 G>A) that activates the first intron's universally preserved 5' end cohesive site.

We came to the conclusion that "c.90+1 G>A" mutations that we detected on the *GCMB* gene with modeling programs causes the disease. Same mutation was found as heterozygote in the unaffected sister and brother. In molecular investigation, the parents were found to have the same mutation in heterozygote form. Further studies are needed in order to understand the exact mechanism; however, it is possible that the homozygous mutation causes abnormal transcript expression and non-sense mediated mRNA slicing or a nonfunctional protein expression. Thus, regarding the complete loss of functional GCMB protein as well, we thought that this case is an autosomal recessive hypoparathyroidism.

Key words: Isolated hypoparathyroidism, *GCMB*, hypocalcaemia, CaSR, glial cells, parathormone