Original Article

Phenotypic Spectrum of 3 Pseudohypoparathyroidism type 1a, and 2 Pseudopseudohypoparathyroidism Chinese Patients with Novel GNAS Mutations

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Abstract

We present three cases (case 1-3) of Pseudohypoparathyroidism type 1a (PHP1a) with congenital hypothyroidism, Albright Hereditary Osteodystrophy (AHO) and mental retardation, and two cases (case 4-5) of Pseudopseudohypoparathyroidism (PPHP) with only features of AHO. A novel de novo heterozygous missense mutation c.152C>T in exon 2 was found in case 1, and a previously reported heterozygous missense mutation c.308T>C in exon 4 was found in case 2, a novel de novo heterozygous missense mutation c.719A>T in exon 10 was found in case 3, case 4 was the mother of case 2 and she also shared the heterozygous missense mutation c.308T>C in exon 4, and case 5 had a heterozygous nonsense mutation c.34C>T in exon 1; in the GNAS gene. The mother of case 2, who also carried the same missense mutation as her daughter, had only features of AHO; thus exhibiting the imprinting effect on GNAS gene, resulting in a PPHP phenotype. The authors discussed the phenotypic spectrum amongst the cases of PHP and PPHP; and emphasised the importance of early identification of female PPHP patients for genetic counselling.

Keyword : Albright Hereditary Osteodystrophy; Amenorrhoea; GNAS gene; Pseudohypoparathyroidism; Pseudopseudohypoparathyroidism