# Clinical and Genetic Characteristics of Pseudohypoparathyroidism Type 1A in Children Based on Single-center Cohort Study

Xuelian Zhou, Wei Wu, Guangping Dong, Ke Huang, Jinna Yuan, Xinyi Liang, Mingqiang Zhu, Junfen Fu

Corresponding Author: Junfen Fu, Email: fjf68@zju.edu.cn

*The Children’s Hospital, Zhejiang University School of Medicine, 3333 Binsheng Road, Hangzhou, 310052, China.*

## Abstract

**Background： Pseudohypoparathyroidism 1A (PHP1A) is a rare disease caused by mutations of GNAS gene, and characterized by Albright’s hereditary osteodystrophy (AHO) and resistance to multiple hormones. Infantile onset is often missing diagnosed due to atypical clinical manifestations. This study aims to summarize the clinical and genetic characteristics of child onset PHP1A patients.**

**Methods: 12 patients were diagnosed as PHP1A in our hospital from 2013 to 2019 based on the genetic and clinical characteristics. Sanger sequencing and methylation-specific multiple ligation-dependent probe amplification (MS-MLPA) were used for genetic diagnosis. Anthropological parameters, laboratory and imaging findings were collected for clinical diagnosis.**

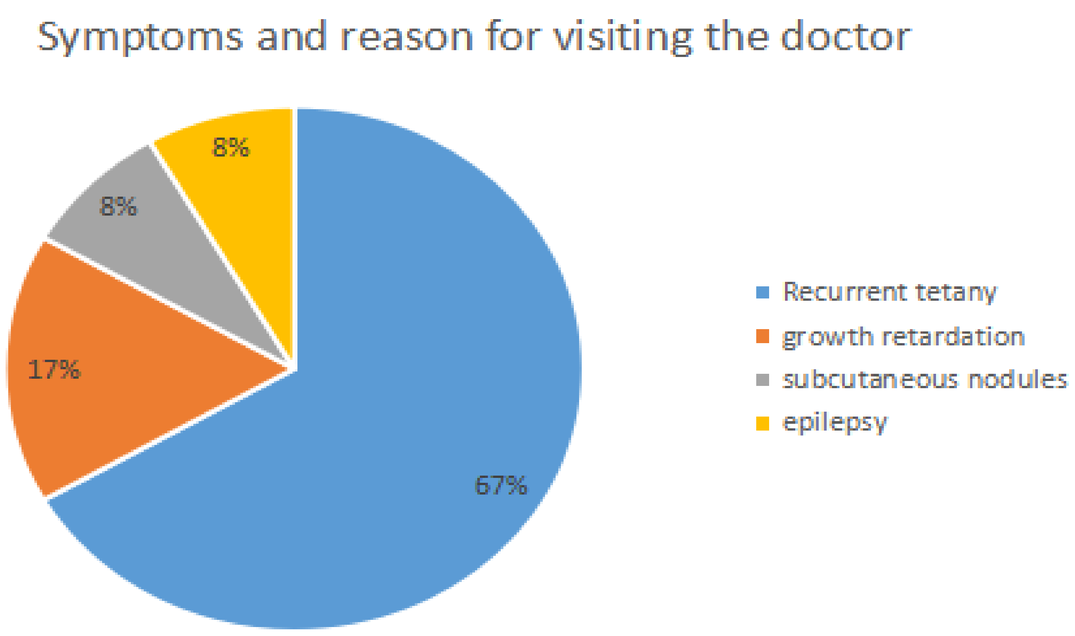


**Figure 1. First symptoms to visit the clinic**

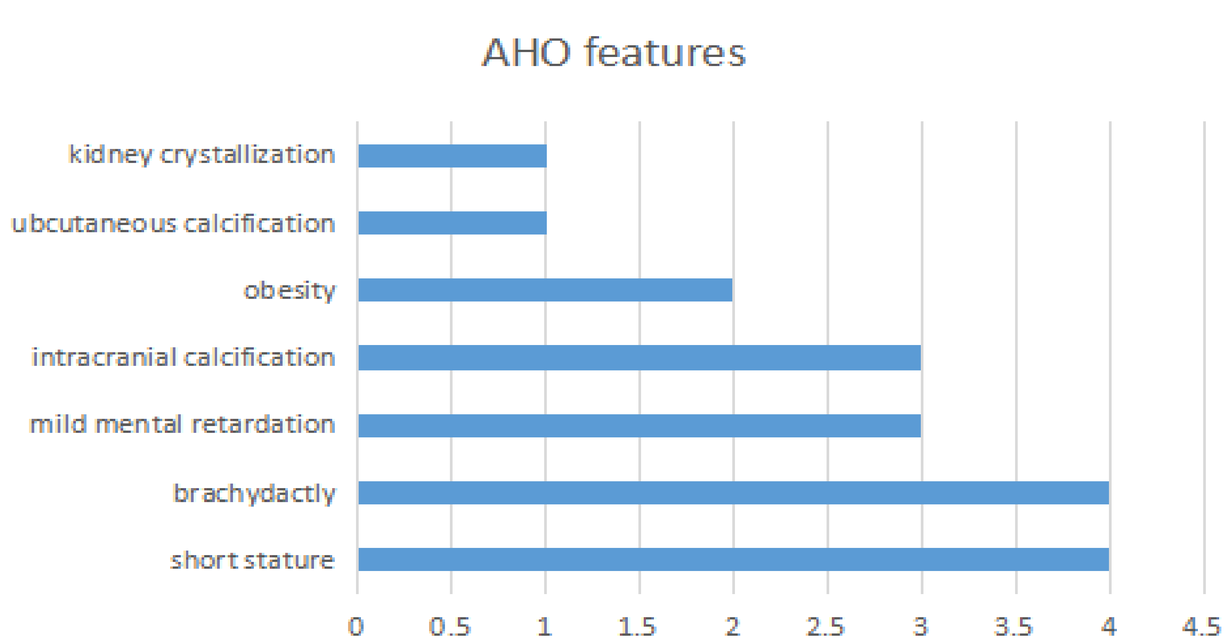


**Figure 2. AHO features of the patients**

**Results： The average onset and diagnose age was 6.4y (0.2-12.1y) and 8.1y (0.2-12.2y), respectively. GNAS mutation was detected in 3 of the 12 patients including c.568_571delGACT, c.521_524delACTG and c.939delT, and patient B with a family history of PHP. 6 of the remaining 9 mutation negative were confirmed with methylation abnormalities, and the other 3 patients refused to do MS-MLPA analysis. Recurrent tetany is the most common symptoms and reason for visiting the doctor (8/12, 66.7%), following with growth retardation (2/12, 16.7%)， subcutaneous nodules (1/12, 8.3%), epilepsy(1/12, 8.3%). All the patients present with different kinds of AHO features, 4 short stature, 4 brachydactly, 3 mild mental retardation, 3 intracranial calcification, 2 obesity, 1 subcutaneous calcification, 1 kidney crystallization.10 of them present with hypocalcaemia, hyperphosphatemia and PTH resistance, 3 patients with TSH resistance, 1 patient with GH deficiency. Routine calcium was prescript to all the patients. Calcitriol were also supplemented except the 2 patients with normal serum calcium, phosphorus, and PTH , who are diagnosed before 1 years old. Levothyrocine was supplemented in the patients with TSH resistance, and 1 patient also received antiepileptic therapy.**

**Conclusions: This study summarizes the clinical and genetic features of the child onset PHP1A. Clinical characteristics of early onset PHP1A patients, especially infants were atypical, close following up combined with gene sequencing and/or MS-MLPA analysis can help early diagnosis of PHP1A.**

## Acknowledgement

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