Schaaf-Yang syndrome： Three cases report of *MAGEL2* variation and literature review

Xuefei Chen, Chaochun Zou
Department of Endocrinology, Children's Hospital of Zhejiang University School of Medicine, Hangzhou, China

Abstract

Objective: To highlight the clinical characteristics and early genetic diagnosis of Schaaf-Yang syndrome (SYS).

Methods: Three cases with truncating mutations in *MAGEL2* were identified and related literature were reviewed.

Results: Patient 1 and Patient 2, a newborn and a two-and-a-half-month-old infant, presented typical features of SYS with multiple facial dysmorphisms, tapering digits with camptodactyly of fingers, neonatal hypotonia, feeding difficulties and respiratory distress. Besides, patient 1 passed away at 19 days. By whole-exome sequencing, *de novo* heterozygous c.1996dupC pathogenic variants were detected in the two individuals. Patient 3 was a 30-month-old boy who showed dysmorphic facial features, delayed language development and cognitive deficits. A heterozygous c.1640-1641delTT mutation in *MAGEL2* was detected in the patient and his father. To our knowledge, the variant detected in patient 3 has not been described for other patients with SYS previously.

Conclusions: Our results indicated that testing for mutations in MAGEL2 should be considered in children with developmental delay, intellectual disability, neonatal hypotonia, feeding difficulties, joint contracture, and autism spectrum disorder. And we highly suggest that *MAGEL2* gene should be added to gene-panels or gene-filters in next-generation sequencing (NGS)-based diagnostics, which is of great significance for early diagnosis and early intervention of SYS patients.

Refereneces:

1. Schaaf CP, Gonzalez-Garay ML, Xia F, Potocki L, Gripp KW, Zhang B, et al. Truncating mutations of MAGEL2 cause Prader-Willi phenotypes and autism. Nat Genet 2013; 45: 1405-8.
2. Soden SE, Saunders CJ, Willig LK, Farrow EG, Smith LD, Petrikin JE, et al. Effectiveness of exome and genome sequencing guided by acuity of illness for diagnosis of neurodevelopmental disorders. Sci Transl Med 2014; 6: 265ra168.
3. Fountain MD, Aten E, Cho MT, Juusola J, Walkiewicz MA, Ray JW, et al. The phenotypic spectrum of Schaaf-Yang syndrome: 18 new affected individuals from 14 families. .Genet Med 2017; 19: 45-52.
4. McCarthy J, Lupo PJ, Kovar E, Rech M, Bostwick B, Scott D, et al. Schaaf-Yang syndrome overview: Report of 78 individuals. Am J Med Genet A 2018; 176: 2564-74.

Topic: Growth and syndromes