

Two Chinese Children with FBN1-Related Acromelic Dysplasia

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Objectives:

Geleophysic dysplasia (GD) and acromelic dysplasia (AD) are rare skeletal dysplasias belonging to the group of acromelic dysplasias and are both characterized by severe short stature, short hands and feet, stiff joints, facial anomalies and some radiological manifestations, including delayed bone age, shortened long tubular bones and ovoid vertebral bodies. Patients with GD clinically present the characteristic “happy” facial features, cardiac valvular abnormality, progressive hepatomegaly and tracheal stenosis. The clinical features of AD are usually similar to GD but without cardiac valvular abnormality. This study reported two Chinese children with acromelic dysplasia due to FBN1 gene mutations.

Methods:

The clinical and genetic characteristics of two Chinese children from unrelated families with acromelic dysplasia were analyzed retrospectively, including one case each of GD and AD. The microfibrillar structure and the level of TGFβ in GD individual are also studied simultaneously.

Results:

(1) Patient 1 was a 7-year and 1-month-old boy with GD. He presented severe short stature without intellectual disability, full cheeks, flat nose, thick lips, short neck, short limbs and both of his hands were stubby with claw deformity and limited extension of fingers. He had mild pulmonary stenosis and his bone age was 4-year old. A heterozygous missense mutation c.5284G>A (p.Gly1762Ser) of FBN1 gene was detected by next-generation sequencing (NGS), which had been reported previously. The microfibrillar structure was no significant difference from controls, while the level of TGFβ was significantly higher than controls. (2) Patient 2 was a 2-year and 6-month-old girl with AD. She presented severe short stature with normal intellectual function. She had a round face, narrow palpebral fissure, flat nose, thick lips, short neck, short limbs, small hands, small feet and thickened skin but without limitation of joint range of motion. Her fingers were short with claw deformity and palm hypertrophy, and her bone age was nearly 2-year old. A heterozygous missense mutation c.5159G>A (p.Cys1720Ser) of FBN1 gene was detected by NGS, which had never been reported.

Conclusions:

Both GD and AD can be caused by mutations of FBN1 gene. The mutation c.5284G>A (p.Gly1762Ser) of FBN1 gene presents pleiotropic nature, and enhanced TGFβ signaling plays an important pathophysiologic role. A novel missense mutation c.5159G>A (p.Cys1720Ser) of FBN1 gene is identified in our study. Further research is required to understand the mechanism of FBN1-related acromelic dysplasia.

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