

Dear Editors and Reviewers:

We sincerely thank the editors and all reviewers for their valuable feedback. Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments

Reviewer #1:

1 Response to comment: *There were some language errors in the manuscript that need to be revised as a native speaker.*

Response: Thanks for your suggestion. We have tried our best to polish the language in the revised manuscript. We had invited native speakers of English to help correct the language errors in the manuscript, and obtained the language editing certificate. The language quality of the manuscript reaches A.

2 Response to comment: *How to distinguish whether the boy's height increase is due to physiology or rhGH treatment? Maybe it can be analyzed according to the performances of his father and grandfather in the family.*

Response: We sincerely appreciate the valuable comments. Our assessment of the boy's height increase was due to the effect of rhGH treatment based on the following two points:

(1) In the first year of treatment, the annual growth rate was 9.0 cm/year, and the height increased from -3.64 SDS to -2.88 SDS, an increase of 0.76 SDS. According to Cohen P *et al*^[18] "Successful first-year response to GH treatment includes an increase in height SDS of more than 0.3–0.5." Suggesting that rhGH therapy was effective.

(2) In the patient's family, the height of the father was 140 cm (< -5 SDS) tall and the grandfather was 147 cm (< -4 SDS) tall. In the first 5 years of treatment, the growth rate of the patient remained at 5.3 cm/year, and the

height increased from -3.64 SDS to -3.09 SDS. It seems that the treatment had some effect, and the first year was the most significant. However, whether it would have a positive effect on the final height remains unclear, and long-term follow-up observation is needed.

3 Response to comment: *The pathogenicity criteria of the mutation had better be offered to the manuscript according to American College of Medical Genetics and Genomics (ACMGG).*

Response: Thanks for your suggestion. We have added pathogenicity criteria of the mutation to the manuscript. According to American College of Medical Genetics and Genomics (ACMGG), the pathogenicity criteria of the mutation was **Likely Pathogenic** [7].

4 Response to comment: *In the title "Acromicric dysplasia caused by a mutation of Fibrillin1 in a family: A case report", "Fibrillin1" should be written separately.*

Response: We have written separately "**fibrillin 1**" in the title "**Acromicric dysplasia caused by a mutation of fibrillin 1 in a family: A case report**".

5 Response to comment: *In the part of background, did this sentence "which is easy to be confused with idiopathic short stature." describe appropriately?*

Response: Thanks for your suggestion. We have recognized the inappropriateness of this statement and have removed "which is easy to be confused with idiopathic short stature." Also add the sentence "**Extensive endocrine examination has not revealed a potential cause.**"

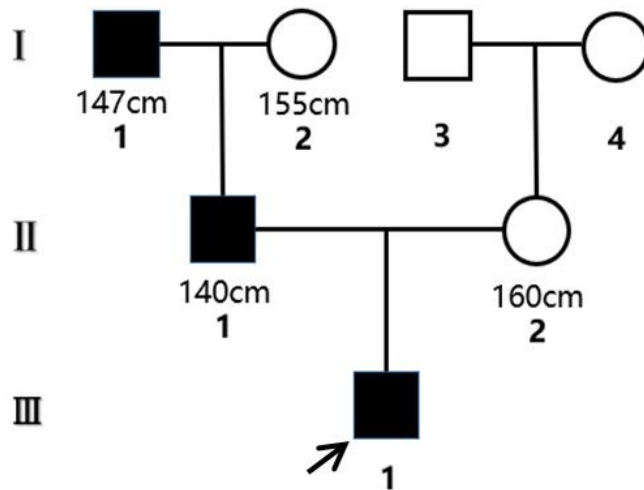
6 Response to comment: *It's recommended that a general description of previously reported cases should be included in the manuscript to adequately describe the background, present status and significance of the study.*

Response: We sincerely appreciate the valuable comments. We have added three previously reported cases of AD in the manuscript. We reviewed three previously reported AD cases associated with mutation of *FBN1* (OMIM 102370) gene c.5183C>T (p.Ala1728Val). A Brazilian boy developed severe dwarfism at the age of 10 years and 2 mo (-3.9 SDS). He was born with

normal birth length, his mother was short (131 cm, -5 SDS), while his two brothers and father were of normal height. The proportion of hands and fingers in physical examination was small, the third finger was 6.4 cm (3%) short, the hand was 14.4 cm ($< 3\%$) short, and the palm was 8 cm ($< 3\%$) short. He had a slightly broad nasal bridge, a bulbous nose with a prominent philtrum and thick lips, and he had obvious genu varus, but his gait was normal. No abnormality was found in endocrine examination. He was empirically started on rhGH treatment (50–66 $\mu\text{g/kg/d}$) for a diagnosis of idiopathic disproportionate short stature, with poor overall response^[15]. An African-American girl born in the USA was 107.5 cm (-4 SDS) tall at the age of 7 years. She had been born small for gestational age with a birth length of 43 cm (-2.3 SDS) and a birth weight of 2580 g (-0.9 SDS) at a gestational age of 37 wk. Familial stature was within the normal range with a maternal height of 160 cm (-0.5 SDS) and a paternal height of 188 cm ($+1.6$ SDS). The physical examination found that the bridge of the nose was broad, and she had slight osteoporosis, thick lips, small hands and feet, but no other abnormalities. Endocrine examination was normal, and bone age was delayed by about 2 years. At the age of 8 years and 9 mo, recombinant IGF-1 was administered according to experience, and reached a maximum dose of 90 $\mu\text{g/kg/d}$. The growth rate increased significantly. However, this growth acceleration was confused with the onset of early puberty (Tanner 2–3 breast development) at the age of 9 years and 1 mo. After the start of leuporelin treatment, the growth rate decreased to 4–5 cm/year before treatment. Treatment with recombinant IGF-1 was stopped at the age of 9 years and 4 mo^[15]. A 5 years and 7 mo old Chinese boy was 100.3 cm tall (< -3 SDS). The birth length was 49 cm. His father was 148.0 cm tall (< -4 SDS). His mother was 160 cm tall. Physical examination showed that the hands were wide and short, but there was no joint stiffness, and there were no abnormality in cardiovascular, abdominal or endocrine examination. The radiological examination revealed shortened tubular bones in the hands and a beak-like femur head^[13].

7 Response to comment: *There should be a proband mark in the pedigree map of the family.*

Response: Thanks for your suggestion. We have added a proband mark to the pedigree map of the family.



Patient (III.1) , the paternal line is affected. The black means heterozygous, white means normal.

We tried our best to improve the manuscript. We appreciate for Editors/Reviewers' warm work earnestly, and hope the correction will meet with approval. Once again, thank you very much for your comments and suggestions.

Yours Sincerely,
Shan-Pu Yang