A case of Wiedemann–Steiner syndrome with central precocious puberty

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Introduction

✓ Wiedemann–Steiner syndrome (WSS) is a rare autosomal dominant disorder characterized with hypertrichosis cubiti, dysmorphic facial appearance (hypertelorism, thick eyebrows, and narrow palpebral fissures), psychomotor delay, and short stature. WSS is caused by a mutation in the *KMT2A* gene. The timing of secondary sexual characteristics in patients with WSS is not well known.

Objective

✓ To present a case of the patient with WSS presenting CPP considered as a rare complication.

Case presentation

✓ A female patient was born at 39 weeks of gestation with a weight, height, and head circumference at birth of 2712 g (+0.15 SD), 47.5 cm (-0.69 SD), and 29.0 cm (-3.06 SD), respectively. She has had hypertrichosis on her arms and legs since birth.

✓ She showed hypertelorism, narrow palpebral fissures, and arched and thick eyebrows. Her psychomotor development was delayed with head support obtained at 7 months, and she was able to sit stably at 10 months, walk independently at 3 years, and speak her first words at 5 years.

✓ She was referred to our endocrinology outpatient clinic at 9.3 years of age with a history of pubic and axillary hair development over several months. Her breast pubertal status was Tanner stage 3 or 4, and her bone age was advanced more than 2 years at the first visit. Her levels of luteinizing hormone and follicle-stimulating hormone were elevated at 0.7 and 3.3 mIU/mL, respectively. Menarche occurred at 9.6 years of age, and the diagnosis of CPP was made. She had no family history of CPP. Her head MRI showed no brain tumor. She did not receive luteinizing hormone-releasing hormone analogue treatment at the time. Her adult height was 126.0 cm (-6.1 SD) at 17 years of age.

✓ We identified a novel, de novo splicing mutation (c.4012+1G>C) in the *KMT2A* gene by trio whole-exome sequencing, thus confirming the diagnosis of WSS.

There is informed consent on showing clinical data and images


Figure1

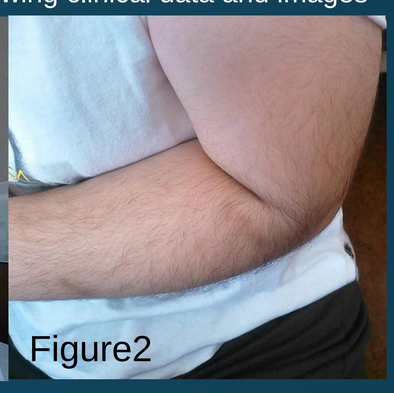
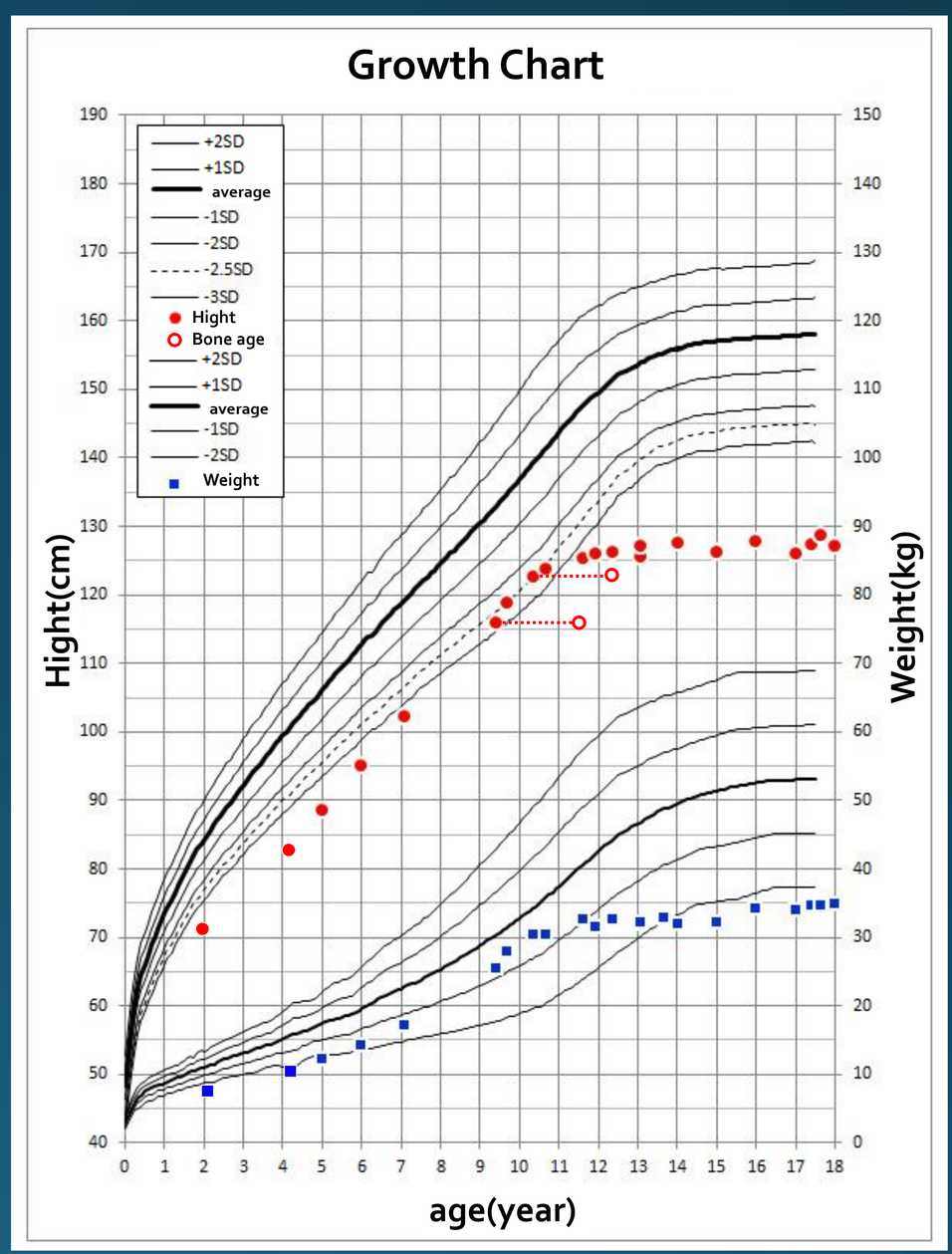


Figure2

Figure1: showed hypertelorism, narrow palpebral fissures, and arched and thick eyebrows

Figure2: hypertrichosis on her arms



Discussion

✓ To our knowledge, two patients (one boy and one girl) with WSS have been reported to have had central precocious puberty (CPP) [1, 2].

✓ There are several reports that patients with WSS showed advanced bone age [3,4].

✓ It has been reported that 20–47% of patients with WSS showed advanced bone age[2,5]; however, signs of secondary sexual characteristics in these cases are not almost described. Therefore, some of the cases with advanced bone age in these reports might have had CPP.

Conclusions

✓ CPP should be considered as a rare complication of WSS, resulting in extremely short stature.

References

1. *Hum Genet. 2017 Mar;136(3):307-320. Mutations in chromatin regulators functionally link Cornelia de Lange syndrome and clinically overlapping phenotypes.*
2. *Orphanet J Rare Dis. 2018 Oct 11;13(1):178. Description of the molecular and phenotypic spectrum of Wiedemann-Steiner syndrome in Chinese patients.*
3. *Am J Med Genet A. 2010 Sep;152A(9):2372-5. Advanced Bone Age in a Girl With Wiedemann–Steiner Syndrome and An Exonic Deletion in KMT2A (MLL)*
4. *Am J Med Genet A. 2014 Aug;164A(8):2079-83. Wiedemann-Steiner syndrome: three further cases.*
5. *Clin Genet. 2018 Jul;94(1):141-152. Wiedemann-Steiner syndrome as a major cause of syndromic intellectual disability: A study of 33 French cases.*

There is no conflict of interest

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Growth and syndromes (to include Turner syndrome)

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