Excessive body hair, short stature and advanced bone age in a girl: Hypertrichosis versus adrenarche ?

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Case presentation

- A 6-year-old girl presented with hypertrichosis allover the body. She was born at term with birth weight 2 kg. She had paralytic squint with excess body hair since birth.

- She had delayed developmental milestones. She had HTSDS = -1.3, BMI SDS = 0.66. Her Mid-parental HtSDS = 0.
- She had no other signs of puberty. (breast Tanner 1).
- She had slow learning abilities attending a regular school.
- She had normal cardiac function by Echocardiography.

Test	value
FSH	1.5 IU/L
LH	0.5 IU/L
Testosterone	0.63 nmol/L
DHEAS	3.3 Umol/L
Estradiol	43 pmol/L
IGF1	200 ug/L
TSH	1.66 mIU/L
FT4	14 pmol/L

Table 1: Hormonal work up at 6 years of age

At the age of 12 years, she continued to have learning difficulties, hypertrichosis, with hairy elbow, ptosis and squint (underwent corrective surgery).
She had gastritis and digestion complexities. Her HtSDS = -1.3 (normal growth rate) BMI = 1.5).
She started menstruation at the age of 11.5 years. She had normal renal and hepatic functions and normal hemogram.
Her bone age = 14.5 years (advanced). Her predicted adult height was = 150 cm.
CT of the head revealed normal optic chiasm, normal pituitary and para-sellar structures. Visualized brain and the ventricles are unremarkable.

Test	Value
FSH	7.8 IU/L
LH	9.3 IU/L
Estradiol	147.0 pmol/L
17OHP	4.7 nmol/L
DHEAS	4.5 pmol/L
IGF1	479.0 ug/L
Testosterone	1.76 nmol/L
TSH	1.96 mIU/L
FT4	16.2 pmol/L

Table 2: Hormonal work up at 12years of age

Whole Exome sequencing plus mito (WES+) revealed that she is heterozygous for a De Novo Pathogenic Variant in KMT2A gene associated with Autosomal Dominant Wiedemann-Steiner Syndrome which is consistent with her reported clinical features.
As both parents tested negative for the variant, it is suggested that it arose de novo in the child.

Discussion

- Pathogenic variants in the KMT2A gene have been identified in multiple individuals with Wiedemann-Steiner syndrome, a clinically variable autosomal dominant disorder characterized by hypertrichosis cubiti (excessive growth of hair on upper forearms or elbows), intellectual disability, short stature, and characteristic facial features.
- Additional features may include cardiac, renal, and skeletal anomalies, behavioral problems, hypotonia, gastrointestinal dysfunction, and delayed or advanced bone age.

Conclusion

This girl with Wiedemann–Steiner syndrome had significant hypertrichosis, short stature (compared to her mid-parental height), with normal IGF1 level and advanced bone age.
She had normal pubertal tempo and hormones and normal menarche. She continued to have mild developmental delay.

Wiedemann–Steiner syndrome shall be considered in children with hypertrichosis and short stature with mild developmental delay.