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KLEEFSTRA SYNDROME — CASE SERIES OF A RARE NEURODEVELOPMENTAL DISORDER

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----- INTRODUCTION -----

Kleefstra syndrome (KS) is a **rare** AD neurodevelopmental disorder (100 cases) that includes:

- moderate-to-severe intellectual disability (ID), hypotonia and **characteristic** facial dysmorphisms;
- congenital heart, urogenital and CNS defects, psychiatric disorders and overweight;

Haploinsufficiency of **EHMT1** caused by either a microdeletion at **9q34.3** or intragenic mutations

----- CASES -----

♂ 9 years.
High risk pregnancy for nuchal translucency ↑ (karyotype XY), IUGR and fetal arrythmia
Birth at term. Hypotonia, brachycephaly and facial dysmorphias
Metabolic screening . . Cerebral MRI with enlarged subarachnoid space. Electroencephalogram (EEG):
Early GDD → evolution to intellectual disability with very rudimental language (Griffith's at 4y = 54).
Microdelection of 9q34.3

♂ 13 years
Caesarean at term due to fetal bradycardia
At birth: club foot, facial dysmorphias and hypospadias.
1 febrile seizure at 4Y and non-febrile at 13Y. EEG . Awaiting cerebral MRI
Intellectual disability but with extensive language (WISC at 10A = 51).
Microdelection 9q34.3

3 years
Normal pregnancy and birth besides facial dysmorphias.
NICU admission for 42 days due to **hypotonia**, cyanosis and feeding difficulties.
Pulmonary valve stenosis on the echocardiogram. Cerebral MRI with thin callous body. EEG
GDD without language (Griffith's at 2 = 54).
Microdelection of 9q34.3

♂ 15 years
High risk pregnancy for positive biochemical screening (karyotype XY). Caesarean at term for non-reassuring fetal status.
At birth, brachycephaly and facial dysmorphias *T21-like*
Cerebral MRI with T2 accentuation of the periventricular substance
Early GDD → evolution to intellectual disability with very rudimental language (Griffith's at 4y = 21).
ADHD and steryotype movement disorder

***Nonsense* variant in the EHMT1 gene** (exome)

----- CONCLUSIONS -----

No genotype-phenotype correlation was found.

One patient lacks significant expressive language impairment, a major feature described in the literature.

Early diagnosis and a targeted intervention, according to the child's neurodevelopmental and behavioral profile, are paramount on improving caregivers and patients' quality of life

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