XXIV CONGRESO
INTERNACIONAL DE ACTUALIZACIÓN EN
TRASTORNOS DEL NEURODESARROLLO
Valencia, 4 y 5 de marzo de 2022

ALWADEI SYNDROME – A GENETIC CAUSE OF INTELLECTUAL DISABILITY

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BACKGROUND

- Intellectual disability (ID) is characterized by **deficits in intellectual functioning** associated with **alterations in the adaptive behaviour**, with onset in the developmental period.
- It affects 3% of the population, 10% of which have a genetic etiology.
- **Alwadei Syndrome** is an autosomal recessive neurodevelopmental disorder, with 3 cases described worldwide.
- It results from a homozygous nonsense mutation in *RUSC2* gene (found on chromosome 9p13.3) and is associated with **intellectual disability** and **dysmorphic facial features**.

CASE REPORT

Otherwise healthy 5 year-old-boy

Born to a healthy mother after a full-term uneventful pregnancy

Birthweight 50 – 75th percentile* | Head circumference 25th-50th percentile*

Family history: learning difficulties in the paternal brotherhood

Developmental history: first words at 2 years of age

referred to Neurodevelopmental consultation due to

Global developmental delay

Mild dysmorphic features: Long face | Dark infraorbital region | Low-set ears | Beaked nose | Retrognathism | High-arched palate

Joint hyperlaxity

Weight 25-50th percentile* | Height 90th percentile* | HC 10-25th percentile*

Wechsler Intelligence Scale for Children III full scale IQ: 61

Karyotype | Chromosomal microarray analysis | Fragile X molecular study

Normal

DNA sequencing

Mutation in the RUSC2 gene

* According to WHO child growth standards

CONCLUSION

- The etiological diagnosis of ID remains unknown in up to 80% of cases, creating uncertainty in children's families.
- The advances in DNA sequencing technologies have increased our knowledge about the genetic diseases involved, with the first cases of Alwadei syndrome being reported in 2016.
- The genetic diagnosis of ID allows family genetic counseling and enables the development of target therapeutic approaches.

References: 1- Alwadei AH, Benini R, Mahmoud A, Alasmari A, Kamsteeg EJ, et al. Loss-of-function mutation in RUSC2 causes intellectual disability and secondary microcephaly. Dev Med Child Neurol 2016; 58: 1317–22. 2- Abramowicz M. Microcephaly risk with RUSC2. Dev Med Child Neurol 2016; 58(12):1211-1212. 3 – Pereira C, Martins R, Bandeira de Lima C, Baptista M, Sousa A. Perturbação do Desenvolvimento Intelectual/Incapacidade Intelectual: Experiência de um Centro de Neurodesenvolvimento de um Hospital Nível III. Acta Pediatr Port 2017; 48:304-11.