COFFIN SIRIS SYNDROME: A RARE DISORDER WITH NEURODEVELOPMENTAL IMPACT

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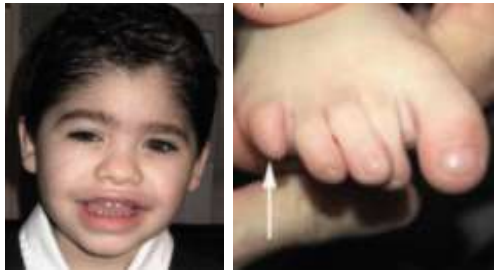
INTRODUCTION

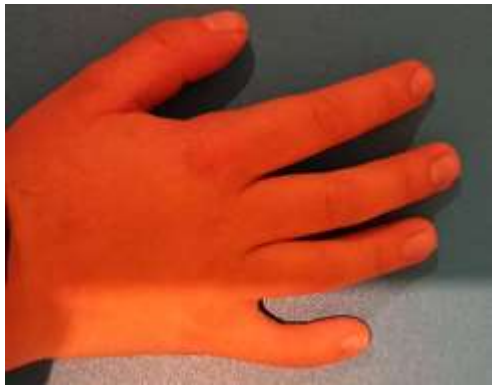
The evolution of genetic techniques enables a better diagnostic yield of global developmental delay (GDD) and intellectual disability (ID) along with the identification and better characterization of new syndromes. Coffin Siris syndrome (CSS) is a rare, multisystem AD-transmitted disease that can be caused by mutations in different genes (most commonly in *ARID1B - 6q25.3*), which in addition to GDD/ID can include:

- Micro/macrocephaly, wide nose, macroglossia, thick eyebrows and eyelashes, hypertrichosis/hirsutism, short stature, syndactyly and/or hypoplasia of the 5th finger, anonychia, cardiac and reno-vesical malformations
- Hypotonia, feeding difficulties, frequent respiratory infections, hearing loss, epilepsy

CASES

♂, 3 YEARS (DIAGNOSIS AT 2Y)	♀, 5 YEARS (DIAGNOSIS AT 2Y)	♂, 8 YEARS (DIAGNOSIS AT 7Y)	♀, 9 YEARS (DIAGNOSIS AT 5Y)	♀, 16 YEARS (DIAGNOSIS AT 12Y)	♀, 17 YEARS (DIAGNOSIS AT 17Y)
Term pregnancy without complications Facial dysmorphisms Bilateral nail hypoplasia of D5 Hirsutism Recurrent respiratory infections Hypotonia with sucking problems – Failure to thrive **GDD** - Head control: 8M - Sit: 12M - Walking: 20M - 1st words: 18M - Does not build sentences Griffith´s: GQ 65,3 Gene: *ARID1B*	Term pregnancy without complications Facial dysmorphisms Bilateral nail hypoplasia of D5 Nystagmus Recurrent respiratory infections Hypotonia with sucking problems - Failure to thrive **GDD** - Head control: 6M - Sit: 14M - Walk: 20M - 1st words: 18M - Sentences: >24M Griffith´s: GQ 51 Gene: *ARID1B*	Term pregnancy Facial dysmorphisms Surgical interventions: Congenital glaucoma, tracheostomy (6M to 3Y) for laryngomalacia, orchidopexy and inguinal herniorrhaphy Recurrent respiratory infections Hypotonia with sucking problems - Failure to thrive (needed PEG) **GDD** - Head control: >4M - Sit: >12M - Walk: 30M - 1st words: >4A ; - Sentences: 5A **ID** Gene: *DPF2 - 11q13.1*	Term pregnancy (ventriculomegaly; 46,XX | cesarean by acute fetal distress) Facial dysmorphisms Corpus callosum hypogenesis Surgical interventions: atrial septal defect closure at 5Y Recurrent respiratory infections Hypotonia with sucking problems - Failure to thrive **GDD** - Head control: 7M - Sit: 15M - Walk: 24M - 1st words: 24M - Sentences: 36M **ID** **ADHD** Gene: *ARID1B*	Term pregnancy (cesarean by acute fetal distress) Facial dysmorphisms Recurrent respiratory infections Hypotonia with sucking problems - Failure to thrive **GDD** - Head control: 6M - Sit: 10M - Walk: 18M - 1st words: 12M - Sentences: 24M **ID** (WISC-III: FSIQ 45) **ADHD** Gene: *ARID1B*	Term pregnancy without complications Facial dysmorphisms Recurrent respiratory infections Hypotonia with sucking problems - Failure to thrive **GDD** - Head control: 1,5M - Sit: 10M - Walk: 24M - 1st words: 18M - Sentences: >24M **ID** (WISC-III: FSIQ 55) **ADHD** Gene: *ARID1A - 1p36.11*





DISCUSSION

- CSS is a very rare genetic disorder, slightly more frequent in females, caused by mutations in multiple genes. The most common is *ARID1B*, as occurred in our sample
- The identification of D5 nail hypoplasia associated with facial dysmorphia and hypotonia, with feeding difficulties, should evoke the syndrome
- There is no specific treatment. Medical follow-up and stimulation through multidisciplinary therapies is needed to improve the outcome

References: 1. Genetics Home Reference. Coffin-Siris syndrome [Internet]. MedlinePlus. Aug 30, 2021. https://medlineplus.gov/genetics/condition/coffin-siris-syndrome/. Accessed 04/01/2022, 2, Vergano SS, Santen G, Wieczorek D, Wollnik B, Matsumoto N, Deardorff MA. Coffin-Siris Syndrome. GeneReviews. July 11, 2013. http://www.ncbi.nlm.nih.gov/books/NBK131811/. Accessed 04/01/2022