XXIV Congreso Internacional de actualización em TRANSTORNOS DEL NEURODESARROLLO

NEURODEVELOPMENT IN KBG SYNDROME: A PORTUGUESE CLINICAL SERIES

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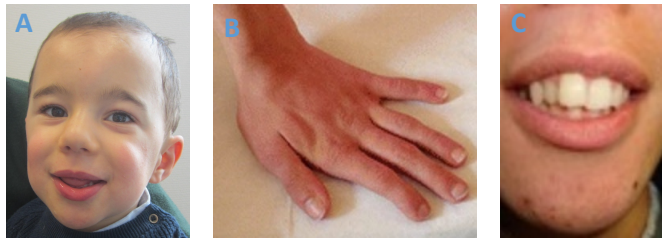
INTRODUCTION

KBG Syndrome is a **genetic disorder** of AD transmission, characterized by **global development delay/intellectual disability (GDD/ID)** (99% of all cases). This Syndrome may also include:

- Specific craniofacial, dental (characteristically macrodontia) and skeletal anomalies, as well as short stature.
- Cryptorchidism, congenital cardiac and renal malformation.
- Epilepsy and autism spectrum disorder (ASD).

It is caused by a pathogenic variant in or a deletion including the ***ANKRD11*** **at 16q24.3 locus.**



Figures: A. Craniofacial dysmorphisms; B. Clinodactyly; C. Dental alterations

DESCRIPTION

♂, 13 years old. Ano-rectal malformation (ARM). Fabry disease.
Older brother with similar phenotype (except ARM), congenital cataracts and Fabry disease.
Phenotype → Short stature, facial dysmorphisms, synophrys, brachydactyly, fifth finger clinodactyly and bilateral single palmar crease.
GDD → ID. Attention Deficit Hyperactivity Disorder (ADHD). Global Developmental quotient (GDQ) 56.5. WPPSI-R: Q.I.G 56.
Speech-language, occupational and psychological therapies, and inclusive education. Able to read and write, more difficulties in maths.
Diagnostic at **10 years old.** Pathogenic variant **c.7535G>A (p.Arg2512Gln) – exon 11.**

♂, 5 years old. Premature at 33 weeks.
Older brother with ano-retal and pulmonary malformations.
Phenotype → frontal bossing, hypertelorism, large central incisors, micro and retrognathia, low implantation ears, pectus escavum and inverted nipples.
GDD. GDQ 81.1. Speech-language and occupational therapies, and inclusive education.
Diagnosis at **2 years old**. Array CGH: **arr(hg19) 16q.24.3 (89,394,003_89,561,269)x1 – haploinsufficiency.**

♂, 13 years old. **Cryptorchidism and interventricular communication.** Benign myoclonic epilepsy from 2 to 4 years.
Older brother with similar phenotype, myoclonic epilepsy and ADHD.
Phenotype → horizontal eyebrows and synophrys, dysthychiasis, stall upper lip, low front hair implementation and brachydactyly.
Mild GGD → mild ID. Language disorder and **ADHD.** GDQ 93. WPPSI-R: Q.I.G 68. Speech-language therapy and inclusive education. Able to read, more difficulties in write and maths.
Diagnostic at **11 years old.** Pathogenic variant **c.4961A>G (p.(Tyr1654Cys)) – exon 5.**

♂, 3 years old. Bilateral **cryptorchidism** and left **congenital hip dysplasia**. **Epilepsy** since 9 months.
Father with similar phenotype (craniofacial and single palmar crease),
Phenotype → plagiocephaly, low front hair implementation, hypertelorism, brachydactyly, bilateral single palmar crease and sacrococcygeal malformation.
GDD, mainly **motor**. GDQ 83.1. Occupational therapy and inclusive education.
Initial suspicion of bone dysplasia → Skeletal dysplasia (531 gene WES-based NGS panel)
Diagnostic at **3 years old.** Pathogenic variant in heterozygosity **c.866dup p.(Tyr289) – exon 8.**

CONCLUSION

KBG Syndrome is a **rare genetic disorder**, with only 150 cases described worldwise → It seems to be **underdiagnosed**, a fact explaned by the great phenotypic variability, even between affected members of the same family. In our unit 4 cases of KBG Syndrome are followed, supporting the hypothesis that it is na underdiagnosed situation.

Although ASD expected to occur in 20% of patients, **none of our patients** is affected. Meanwhile, ADHD, described in 10% of these children, affects **2 of our patients**.

Early diagnosis and intervention, according to the patient's neurodevelopmental and behavioral profile, are of paramount importance to the aim of **improving** both patients and family's **quality of life,** allowing also **genetic counselling.**