BAOJ Pediatrics

Margarida Silva Fonseca, et al., BAOJ Pediatrics 2018, 4: 3
4: 061

Case Report

# Array-Based Comparative Genomic Hybridization Sheds Light into a Family History

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## Abstract

Array-based comparative genomic hybridization (aCGH) has been increasingly recognized as a primary tool for the evaluation of intellectual developmental disorders and autism spectrum disorders. We describe a case of an adolescence girl with an autism spectrum disorder recently diagnosed with 22q11.2 microduplication syndrome by aCGH, whose mother, with cardiac health problems, was later diagnosed with same mutation. This genetic syndrome has a variable phenotype, ranging from mild to severe clinical manifestations. These two cases reveal the high importance of the aCGH testing for a timely surveillance of associated medical conditions of this syndrome and an adequate genetic counselling.

**Keywords:** Autism Spectrum Disorders; Array Comparative Genomic Hybridization; Chromosome 22q11.2 Duplication Syndrome: Genetic Counseling; Intellectual Development Disorders

## Introduction

Array-based comparative genomic hybridization (aCGH) is an essential tool for the evaluation of intellectual developmental disorders (IDD) and autism spectrum disorders (ASD). The 22q11.2 microduplication syndrome (dup22q11 syndrome), is a disease associated with a highly variable phenotype, ranging from normal, to patients with heart defects, urogenital abnormalities, velopharyngeal insufficiency and intellectual disability, with some overlapping features with DiGeorge syndrome [1-3]. Dup22q11 syndrome occurs by an autosomal dominant inheritance or as a de novo condition; mostly it is inherited from a parent and has a penetrance of about 21.9% [4-6]. We describe a case which highlights the importance of aCGH genetic testing for the better understanding of this particular syndrome, with two distinct interfamilial presentations.

## Case report

We describe an interesting case of a girl with ASD with moderate IDD, associated with dup22q11 syndrome. She was referred to Neurodevelopmental Pediatric Consultation at 5-year-old for behavior and social adaptation problems. She had no previous health conditions. Her mother had an IDD and a congenital heart disease (subaortic stenosis) with a prosthetic mechanic valve.

Physical examination revealed no dysmorphisms, normal cardiopulmonary and neurologic exam. Psychomotor development evaluation assessed by Ruth Griffiths scale at 64 months of age, showed a general developmental quotient of 64%, indicating a moderate IDD. Her behavior profile met the DSM-IV diagnostic criteria for ASD: deficits in social-emotional reciprocity (failure to initiate or respond to a social interaction, lack of a back-and-forth conversation, reduced sharing of affect and comfort); deficits in nonverbal communicative behaviors for social interaction (lack of eye contact, facial expressions and gestures to communicate); deficits in developing, maintaining, and understanding relationships, no interest in peers , no shared imaginative play; the presence of repetitive patterns of behavior (deferred echolalia) and persistent unusual sensory interests.

Initial etiologic investigation for ASD/IDD was performed according to the institutional guidelines at that time, which included: auditory evaluation, metabolic screen, cranial magnetic resonance imaging with spectroscopy and cytogenetic studies (karyotype, multiplex ligation-dependent probe amplification for subtelomeric rearrangements, Southern blotting for fragile X syndrome). All tests had a normal result.

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**Sub Date**: April 17th 2018, **Acc Date**: April 24th 2018, **Pub Date**: April 25th 2018.

**Citation**: Margarida Silva Fonseca, Sérgio Alves, Armanda Passas, Helena Santos and Ana Flores Lopes (2018) Array-Based Comparative Genomic Hybridization Sheds Light into a Family History. BAOJ Pediat 4: 061.

Recently, the inclusion of aCGH in evaluation guidelines for ASD/IDD allowed an etiologic clarification, with the genetic diagnosis (GD) of dup22q11 syndrome (figure 1). Considering the GD, she performed renal and cardiologic echography, which was normal. This result was reported to the mother´s cardiologist, who requested the aCGH and confirmed the same genetic alteration.

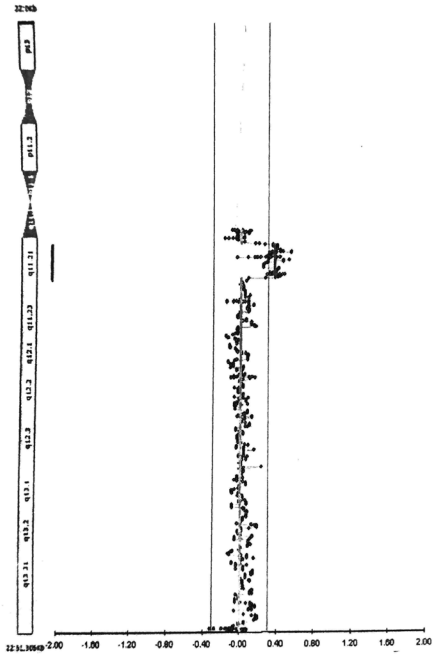
## Discussion

Our case shows the interfamilial phenotype variability and the most common inheritance pattern (about 70%) of the 22q11.2 syndrome, confirming that previously described in literature [2,6,7]. These two family members had varied widely in their clinical features: mother had severe cardiac manifestations and daughter had ASD, although both shared intellectual disability. In addition, our patient inherited the duplication from a parent – her mother.

**The variable expressivity of 22q11.2 syndrome was revealed in these two family members.**

We emphasize the importance of aCGH in the investigation of idiopathic IDD and/or ASD, as it can contribute to a better understating of disease progression, timely surveillance of associated medical conditions, and adequate genetic counseling. Currently, our patient is 12-years-old and she is autonomous in her self-care activities, has verbal communicative skills and is well-integrated in her special education school context, although presenting serious limitations in academic skills´ acquisition.

**Figure 1:** Detail of the molecular karyotype showing the duplication at 22q11.21.

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