Partial trisomy 21: report of a rare Down syndrome case

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INTRODUCTION

Down syndrome (DS; OMIM #190685) is characterized by multisystem involvement and clinical variability, often associated with intellectual disability, characteristic facial features, and congenital anomalies affecting the cardiovascular, endocrine, gastrointestinal, and nervous systems. It is caused by an extra copy of chromosome 21, either complete or partial. The prevalence is estimated at 1:1,000. Partial trisomy of chromosome 21 is a rare form of DS, accounting for approximately 1% to 5% of reported cases.

CASE REPORT

Female patient, 16 years old (yo), was referred to the Genetics Outpatient Clinic of Hospital Universitário Júlio Müller (HUJM, Cuiabá-MT, Brazil) for evaluation. She was born at term, after an uneventful pregnancy and delivery, with no significant findings during prenatal care. At birth, the presence of facial dysmorphisms raised the clinical suspicion of trisomy 21. Complete atrioventricular septal defect was subsequently identified. Developmental milestones were met within the expected timeframe. Conventional karyotyping did not show numerical or structural chromosomal abnormalities. At 15 yo, the patient returned to resume the investigation and reach a diagnosis. Upon physical examination, phenotype was consistent with DS, presenting brachycephaly, downward slanting palpebral fissures, flat nasal bridge, macroglossia, short neck, low-set ears, and single transverse palmar crease. A new karyotype was requested and, again, no abnormalities were detected. Given strong clinical suspicion, a single nucleotide polymorphism (SNP) microarray analysis was requested. It identified a 1.3 Mb heterozygous duplication of uncertain significance: arr[GRCh38] 12p13.33(126796_1432868)x3; and a pathogenic 8.1 Mb heterozygous duplication: arr[GRCh38]21q22.11q22.2(32532881_40661152)x3.

DISCUSSION

A 34 Kb segment in chr21q22.13 (HR-DSCR) is crucial in determining DS phenotype in individuals with partial trisomy of chromosome 21. In the present case, the duplication identified by SNP-array involves HR-DSCR, spanning approximately 8.1 Mb and affecting 134 genes. Among these, *DYRK1A* gene stands out for its well-established association with cognitive impairment and facial dysmorphisms characteristic of DS. More recently, a role for this gene in the pathogenesis of congenital heart disease has been proposed.

CONCLUSION

This is a confirmed case of a rare DS form. The investigation was long and definitive diagnosis was only reached after identification of a duplication involving HR-DSCR through array. It highlights the importance of complementary genetic testing in patients with a suggestive DS phenotype and normal conventional karyotype. The patient is currently under regular follow-up in both primary and specialized care settings for developmental monitoring and management.

Pictures 1 and 2: brachycephaly, downward slanting palpebral fissures, flat nasal bridge, and short neck are shown.

ADDITIONAL INFORMATION

Our patient is an artist. A documentary about her, her unique drawing technique, and art work are available here: