MEDWIN PUBLISHERS
Committed to create value for Researchers

Pediatrics & Neonatal Biology Open Access

Complex Neuropsychiatric Phenotypes in Children - A Matter

Peixoto I[1]*, Fernandes A[2], Santos C[1], Amorim M[5], Lopes P[6] Cano C[1], Ferreira AC[4], Dias M[7] and Duarte S[3]

[1]Hospital Dona Estefânia, Child and Adolescent Psychiatry, Portugal

[2]Centro Hospitalar Lisboa Central, Neurology, Portugal

[3]Hospital Dona Estefânia, Child Neurology, Portugal

[4]Hospital Dona Estefânia, Metabolic Diseases Unit, Portugal

[5]Hospital Dona Estefânia, Medical Genetics, Portugal

[6]Hospital Dona Estefânia, Developmental Paediatics Unit, Portugal

[7]Hospital Dona Estefânia, Nutrition Unit, Portugal

***Corresponding author:** Ivo Peixoto, Hospital Dona Estefânia, Child and Adolescent Psychiatry, Lisbon, Portugal, Email: ivopintopeixoto@gmail.com

Case Report

Volume 3 Issue 2

Received Date: May 03, 2018

Published Date: May 21, 2018

Abstract

Brunner syndrome is a rare disorder with recessive X-linked inheritance. It has been linked to various degrees of intellectual disability and antisocial behavior. There are only four families described in the literature so far. We present the clinical case of a young boy with a pervasive developmental disorder and irritability with explosive anger outbursts, together with a family history of male adults with similar early neuro developmental and behavioral problems and impulsive and violent behavior in adulthood. A disease-focused exome sequencing was performed and a diagnosis of Brunner syndrome was made with a newly identified mutation. This reinforces the need of a targeted and thorough investigation in the early developmental period in the presence of family clusters of aggression and intellectual disability phenotypes.

Keywords: Brunner syndrome; Recessive X-linked disorder; Monoamine oxidase A (MAOA); behavioral problems

Introduction

In the advent of neuropsychiatry, there has been a growing interest in the critical role of genetic and neurobiological factors in the ontogeny of impulsive aggressiveness and emotional regulation. In keeping with this, there is emerging evidence regarding the links between monoamine oxidase A (MAOA) activity and maladaptive manifestations of aggression. The total congenital deficiency of MAOA is called Brunner syndrome, a recessive X-linked disorder characterized by intellectual disability and prominent behavioral

abnormalities in affected males. Since the first description of the syndrome by Han Brunner [1] 20 years have elapsed with no additional cases reported. More recently, however, three more families with the syndrome have been identified [2,3] suggesting possible problems with ascertainment, rather than rarity of the phenotype.

Clinical Case

We present the clinical case of a 9-year-old boy presenting with pervasive developmental disorder, with intellectual disability, language and learning disorders, attention deficit and hyperactivity symptoms, socioemotional communication issues, sensory integration difficulties, irritability with explosive anger outbursts, sleep disturbance and epilepsy. Due to the complexity of the clinical picture, together with a family history of male adults with similar early neuro developmental and behavioral problems and impulsive and violent behavior in adulthood, the clinical suspicion of a recessive X-linked disorder was raised. Accordingly, a disease-focused exome sequencing was performed and a new MAOA mutation c.617G>A; p.Arg206Gln was identified in hemizigot in the clinical proband.

Discussion

This is, to our knowledge the first case of Brunner syndrome with the described genetic variant, the second clinical case described in children and, overall, this corresponds to the fifth family identified with this syndrome worldwide.

This study depicts the benefit of targeted biochemical and genetic screening of non-specific heterogenous conditions such as intelectual disability and autism spectrum disorders associated with behavioral issues, especially when these phenotypes run in the family. The future improvement of the diagnostic accuracy of these conditions in the early developmental period may further elucidate important aspects of the pathophysiology of aggression and its relationship with intellectual, social and emotional functioning. The emerging convergence of lines of evidence and the integration of preclinical and clinical research in this field will be crucial to the development of new targets for prevention and treatment.

References

1. Piton A, Poquet H, Redin C, Masurel A, Lauer J, et al. (2014) 20 ans après: a second mutation in MAOA identified by targeted high-throughput sequencing in a family with altered behavior and cognition. Eur J Hum Genet 22(6): 776-783.

2. Brunner H, Nelen M, Breakefield X, Ropers H, van Oost B (1993) Abnormal behavior associated with a point mutation in the structural gene for monoamine oxidase A. Science 262(5133): 578-580.

3. Palmer EE, Leffler M, Rogers C, Shaw M, Carroll R, et al. (2015) New insights into Brunner syndrome and potential for targeted therapy. Clinical Genetics 89(1): 120-127.