Further delineation of neuropsychiatric findings in Tatton-Brown-Rahman syndrome due to disease-causing variants in DNMT3A: seven new patients

Por: Tenorio, J (Tenorio, Jair)[1,2]; Alarcon, P (Alarcon, Pablo)[3]; Arias, P (Arias, Pedro)[1,2]; Dapia, I (Dapia, Irene)[1,2]; Garcia-Minaur, S (Garcia-Minaur, Sixto)[1,2]; Bralo, MP (Bralo, Maria Palomares)[1,2]; Campistol, J (Campistol, Jaume)[4]; Climent, S (Climent, Salvador)[5]; Valenzuela, I (Valenzuela, Irene)[6,7]; Ramos, S (Ramos, Sergio)[1,2] ...Más

Autoría conjunta: SOGRI Consortium

Ver número de ResearcherID y ORCID de Web of Science

EUROPEAN JOURNAL OF HUMAN GENETICS
Volumen: 28
Número: 4
Páginas: 469-479
DOI: 10.1038/s41431-019-0485-3
Fecha de publicación: APR 2020
Tipo de documento: Article

Ver impacto de la revista

Abstract

Tatton-Brown-Rahman (TBRS) syndrome is a recently described overgrowth syndrome caused by loss of function variants in the DNMT3A gene. This gene encodes for a DNA methyltransferase 3 alpha, which is involved in epigenetic regulation, especially during embryonic development. Somatic variants in DNMT3A have been widely studied in different types of tumors, including acute myeloid leukemia, hematopoietic, and lymphoid cancers. Germline gain-of-function variants in this gene have been recently implicated in microcephalic dwarfism. Common clinical features of patients with TBRS include tall stature, macrocephaly, intellectual disability (ID), and a distinctive facial appearance. Differential diagnosis of TBRS comprises Sotos, Weaver, and Malan Syndromes. The majority of these disorders present other clinical features with a high clinical overlap, making necessary a molecular confirmation of the clinical diagnosis. We here describe seven new patients with variants in DNMT3A, four of them with neuropsychiatric disorders, including schizophrenia and psychotic behavior. In addition, one of the patients has developed a brain tumor in adulthood. This patient has also cerebral atrophy, aggressive behavior, ID, and abnormal facial features. Clinical evaluation of this group of patients should include a complete neuropsychiatric assessment together with psychological support in order to detect and manage abnormal behaviors such as aggressiveness, impulsivity, and attention deficit-hyperactivity disorder. TBRS should be suspected in patients with overgrowth, ID, tall stature, and macrocephaly, who also have some neuropsychiatric disorders without any genetic defects in the commonest overgrowth disorders. Molecular confirmation in these patients is mandatory.

Palabras clave

KeyWords Plus:DOMINANT CEREBELLAR-ATAXIA; PREFRONTAL CORTEX; MUTATIONS; OVERGROWTH; EXPRESSION; DEAFNESS; TOOLKIT; GENES

Información del autor

Dirección para petición de copias: Lapunzina, P (autor para petición de copias)

Hosp Univ La Paz UAM, Inst Genet Med & Mol INGEMM IdiPAZ, Paseo La Castellana 261, Madrid 28046, Spain.

Dirección para petición de copias: Lapunzina, P (autor para petición de copias)

ISCIII, Ctr Invest Biomed Red Enfermedades Raras, CIBERER, Calle Melchor Fernandez Almagro 3, Madrid 28029, Spain.

Direcciones:

[1] Hosp Univ La Paz UAM, Inst Genet Med & Mol INGEMM IdiPAZ, Paseo La Castellana 261, Madrid 28046, Spain

[2] ISCIII, Ctr Invest Biomed Red Enfermedades Raras, CIBERER, Calle Melchor Fernandez Almagro 3, Madrid 28029, Spain

[3] Hosp Clin Univ Chile, Secc Genet, Santos Dumont 999, Santiago, Chile

[4] Hosp Univ St Joan de Deu, Dept Neurol, Barcelona, Spain

[5] Hosp Gen Ontinyent, Dept Pediat, Valencia, Spain

[6] Univ Autonoma Barcelona, CIBER CV, Hosp Univ Vall dHebron, Dept Cardiol, Barcelona, Spain

[7] Pso Vall Hebron, Hosp Valle Hebron, Mol & Clin Dept, Barcelona 119129, Spain

[8] Hosp St Joan de Deu, Dept Genet & Mol Med, Barcelona, Spain

[9] Hosp St Joan de Deu, Rare Dis Paediat Unit, Barcelona, Spain

[10] NIMGENETICS, 7 Parque Cientifico Madrid, Madrid 2804, Spain

[11] Quiron Hosp, Dept Pediat Neurol, Madrid, Spain

[12] Hosp Univ La Paz UAM, Dept Psychiat, Paseo La Castellana 261, Madrid 28046, Spain

[13] UAM, CSIC, Inst Invest Biomed Madrid, Arturo Duperier 4, Madrid 28029, Spain

Direcciones de correo electrónico:pablo.lapunzina@salud.madrid.org

Financiación

Entidad financiadora	Número de concesión
ISCII, FEDER funds	FIS-PI15/01481

Ver texto de financiación

Editorial

NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND

Información de la revista

- **Impact Factor:** Journal Citation Reports

Categorías / Clasificación

Áreas de investigación: Biochemistry & Molecular Biology; Genetics & Heredity
Categorías de Web of Science: Biochemistry & Molecular Biology; Genetics & Heredity

Información del documento

Idioma: English
Número de acceso: WOS:000520639600009
ID de PubMed: 31685998
ISSN: 1018-4813
eISSN: 1476-5438