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REVIEW ARTICLE

Psychiatric manifestations of 22q11.2 deletion syndrome: A literature review☆

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KEYWORDS
22q11.2 deletion syndrome;
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Abstract
Introduction: The 22q11.2 deletion syndrome is a genetic disorder with variable clinical manifestations. It affects one out of 5950 neonates and has an autosomal dominant inheritance pattern. The aim of this article is to review its psychiatric manifestations and any underlying genetic alterations.
Methods: We reviewed the scientific literature available as of October 2014 in the LILACS and Medline databases.
Results: Sixty per cent of these patients fulfilled diagnostic criteria for a mental disorder at some point in their lives, referring to psychotic disorders, attention deficit hyperactivity disorder, mood disorders, anxiety disorders, and autism spectrum disorders. Specific genes, such as *COMT* and *PRODH*, have been linked to these psychiatric manifestations.
Conclusions: It is necessary to raise awareness among all health care professionals so that they understand the relevance of these manifestations, are able to anticipate them, and can provide appropriate information to patients and family members.

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PALABRAS CLAVE
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Manifestaciones psiquiátricas del síndrome de deleción 22q11.2: una revisión de la literatura

Resumen
Introducción: El síndrome de deleción 22q11.2 es un trastorno genético con manifestaciones clínicas variables. Afecta a 1 de cada 5.950 recién nacidos y tiene un patrón de herencia autosómico dominante. El objetivo de este artículo es realizar una revisión de las manifestaciones psiquiátricas y de las bases genéticas asociadas.
Métodos: Se realizó revisión bibliográfica de la literatura científica disponible hasta octubre de 2014 en bases de datos LILACS y Medline.
Resultados: El 60% de estos pacientes en algún momento de la vida cumple criterios diagnósticos de psicopatología, incluyendo trastornos psicóticos, trastorno por déficit atencional con hiperactividad, trastornos del ánimo, trastornos de ansiedad y trastornos del espectro autista. Se han identificado genes, como COMT y PRODH, que estarían relacionados con las manifestaciones psiquiátricas del síndrome.
Conclusiones: La sensibilización de los equipos de salud acerca de estas manifestaciones, permitiría su búsqueda dirigida y la información adecuada para el paciente y su familia.

Introduction

The 22q11.2 deletion syndrome (22q11.2DS) is a genetic disorder with highly variable clinical manifestations. Due to its phenotypic heterogeneity, the syndrome was initially known by different names, including DiGeorge syndrome, velocardiofacial syndrome, CHARGE syndrome, and conotruncal anomaly face syndrome, depending on the clinical manifestation. It is now known that the vast majority of these patients present the same deletion on the long arm of chromosome 22; they are therefore grouped under a single entity, named for the genetic alteration.[1]

This condition has an estimated incidence of 1 case per 5950 live births and is more frequent in Hispanic populations.[2] The most frequent clinical manifestations include heart disease; hypocalcaemia; velopharyngeal abnormalities; thymic hypoplasia associated with immunodeficiency; and renal, ophthalmological, and dental alterations.[1]

Diagnosis is performed by fluorescence in situ hybridisation (FISH). Although de novo presentation accounts for the majority of cases, the disease has an autosomal dominant inheritance pattern, meaning that 50% of the offspring of affected individuals will inherit the mutation.

This article reviews the psychiatric symptoms affecting patients with 22q11.2DS, and the genetic basis of these manifestations.

Methods

We conducted a literature review in the LILACS and Medline databases using the MeSH term ''22q11 deletion syndrome'' to gather all articles written in either English or Spanish and published until October 2014. Our search yielded a total of 1108 articles. The articles in our final sample ($n = 76$) included at least one of the following keywords in the title: psychiatric, neuropsychiatric, psychosis, schizophrenia, ADHD, bipolar, depression, anxiety, or autism.

Psychiatric manifestations of 22q11.2 deletion syndrome

Although schizophrenia is the neuropsychiatric phenotype most frequently associated with the 22q11.2DS, around 60% of patients with the syndrome are estimated to meet diagnostic criteria at some point in their lives for some type of psychiatric disorder, including psychotic disorders, attention-deficit/hyperactivity disorder (ADHD), mood disorders, anxiety, and autism spectrum disorders (ASD), among others.[3] Furthermore, 50% of these patients have some level of cognitive impairment, with mean IQ scores ranging from 71 to 73.[4,5]

Despite the high frequency of psychiatric manifestations in patients with 22q11.2DS, geneticists in the United States and Canada provide families with much less information on these manifestations than on any other symptom of the disease, especially in the case of preschool and school-age children.[6] This results in a majority of parents receiving more information on psychiatric manifestations from the Internet than through their healthcare providers.[7,8]

Psychotic disorders

The first description of psychotic disorders in adolescents and adults with 22q11.2DS was made by Shprintzen et al.[9] in 1992, nearly 15 years after the same research group described velocardiofacial syndrome. Since then, there has been a growing body of scientific evidence on the association between psychotic symptoms and this syndrome. Today,