Chapter 9

Neuropsychiatry in Late Onset Tay–Sachs Disease:
Key Features and Possible Etiology of Psychosis

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ABSTRACT

The neuropsychiatric adult onset Tay-Sachs disease is relatively unknown. Although clinical features and mode of presentation are variable, there are common symptoms and signs of, for example, spinocerebellar atrophy, motor neuron disease, psychiatric disorder, and neuroimaging features of cerebellar atrophy. This chapter reviews the neuropsychiatric features of Late Onset Tay-Sachs disease, discussing possible interconnections between psychosis and the cerebellum in this disease. Understanding this interlink offers some important insights into the rarity of the disease that together with the diverse clinical onset and manifestations are responsible for a marked delay in diagnosis and even misdiagnosis. Genetic testing for the activity of Hexosaminidase A, prompted by the presence of cerebellar atrophy will establish the diagnosis. In all, the combination of cerebellar degeneration together with atypical psychiatric features is in line with the ongoing assumption that the cerebellum and its thalamo-cortical outflow are responsible for psychosis, and in particular, schizophrenia.

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INTRODUCTION

Rare genetic diseases present a diagnostic challenge since the clinical manifestations are complex (Maddalena, Bale, Das, Grody, & Richards, 2005; Zelnik et al., 2000) and variable due to slow progression of the disease as the patients get older, heterogeneity of the genetic defects responsible for a particular syndrome and or variable deficiency of a specific enzyme (Hechtman, & Kaplan, 1993).

A diagnosis of rare yet “undiagnosed” diseases is very often reached retrospectively, after “accidently” reading a case report describing identical clinical features to those of a particular “undiagnosed or misdiagnosed” patient (Kielgman, Bordini, Basel, & Nocton, 2017; Ramoni et al., 2017).

Late Onset Tay-Sachs (LOTS) disease fits perfectly into this framework. It is very rare, with a progressive complex and variable clinical course which appears as the patients are getting older and the presence of heterogeneous mutations which are responsible for different degrees of enzyme deficiency (Neudofer et al., 2005; Rucker et al., 2004). While the neurological characteristics of LOTS may resemble motor neuron disease (Amyotrophic Lateral Sclerosis [ALS] - like, Spinal muscular atrophy [SMA] - like) (MacQueen, Rosebush, & Mazurek, 1998), they can also include psychiatric, cognitive and movement disorders. Thus, familiarity with the complex clinical pictures of LOTS is essential for the early diagnosis, avoiding unnecessary, time consuming and frequently costly tests.

The combination of early onset psychosis and cerebellar atrophy is present in the majority of the patients (Streifler, Golomb, & Gadoth, 1989). Brain imaging in late-onset GM2 gangliosidosis is intriguing since the cerebellum and its thalamo-cortical pathways are implicated in the etiology of psychosis, and in particular, in schizophrenia.

In this chapter, the neuropsychiatric features of LOTS are reviewed and the possible link between psychosis and the cerebellum as manifested in this disease are discussed. The review carried out provides an example in which different knowledge basis are necessary to dialogue within the scientific community to advance on different aspects of a rare disease.

TOWARDS THE RARE NEURONOPATHY

GM2 GLANGLIOSIDOSIS

GM2 gangliosidosis is a rare neurometabolic lysosomal storage disease. The lysosomes are cytoplasmic membrane bound organelles that contain a variety of enzymes (hydrolases) necessary for breaking down complex macromolecules. A deficiency of a single lysosomal enzyme will cause storage of a macromolecule
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(2020). *Translation and Communication in the Promotion of Business Tourism: Emerging Research and Opportunities* (pp. 159-167).
www.igi-global.com/chapter/practical-cases/234203?camid=4v1a