Obsessive-compulsive disorder in a patient with SCA type 1

Transtorno obsessivo compulsivo em um paciente com SCA tipo 1

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ABSTRACT
For many years, the cerebellum was thought to be only responsible for balance, movement, planning and execution. Nowadays, it is well accepted that most cerebellar connections are involved in non-motor functions. Herein, we provide a case report in which a 27-year-old Brazilian male, diagnosed with Obsessive-Compulsive Disorder (OCD), has demonstrated cerebellar features that could be connected to Spinocerebellar ataxia type 1 (SCA-1), an autosomal dominant polyglutamine neurodegenerative disorder that had been previously ruled out. Since obsessive compulsive symptoms (OCS) are known to correlate with alterations in the cortico-striato-thalamo-cortical circuitry, we propose a possible association between OCS and SCA onset.

Key words: Spinocerebellar Ataxias, Obsessive-Compulsive Disorder, Cerebellar Disorders.

RESUMO
Durante muitos anos, o cerebelo foi considerado responsável exclusivamente pelo controle das funções de equilíbrio, movimento, planejamento e execução. Atualmente, já está consagrada a participação das conexões cerebelares em funções não-motoras. Apresentamos um relato de caso de um paciente de 27 anos de idade, diagnosticado com Transtorno Obsessivo-Compulsivo (TOC). O paciente apresentava sintomas cerebelares compatíveis com o diagnóstico de ataxia espinocerebelar tipo 1 (SCA-1), um distúrbio da poliglutamina, autossômico dominante neurodegenerativo, que havia sido previamente descartado. Como os sintomas obsessivos compulsivos (SOC) são conhecidos por correlacionar-se com alterações nos circuitos cortico-estriato-tálamo-cortical, propomos uma possível associação entre o SOC e o início da SCA.

Palavras-chave: Ataxias espinocerebelares, Transtorno obsessivo-compulsivo, Doenças cerebelares

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INTRODUCTION

Spinocerebellar ataxia type 1 (SCA-1), an autosomal neurodegenerative disorder, is characterized by ataxia, dysarthria, dysphagia, oculomotor disfunctions, pyramidal signs, visual impairments and cognitive deficits. SCA-1 patients have been shown to score higher on depression scales\(^1\) and depressive traits and these symptoms can occur 10 years after the onset of this condition.\(^2\) Other disorders, like Obsessive-Compulsive Disorder (OCD), were not association with SCA-1. In general population, the onset of OCD occurs typically in people aged less than 30 years and has a lifetime prevalence of 1 to 3% with no differences in gender for adults, but tend to initiate symptoms earlier in boys.\(^3\) Its world’s prevalence tends to enhance with latitude.

SCA-1 is part of the narrow group of polyglutamine diseases, which cause mutations in specific genes. The genetic product generated is a protein (ataxin-1) with multiple glutamine sequences (polyQ), that accumulate in cerebellar cells ultimately causing neurodegeneration by interacting with other proteins in a disfunctional manner.\(^4\)

The cerebellum’s role in non-motor processes is well-established nowadays, with its damaged functions being descriptive of a Cerebellar Cognitive Affective Syndrome (CCAS). Clinical manifestation of this syndrome consists of impairments in executive functions, language disorders, visual–spatial disorganization.\(^5\) In addition to CCAS, several other psychiatric conditions have been reported to be present.\(^6\)

Herein, we report a case of a 27-year-old male patient with OCD presenting simultaneously with early SCA-1 neurological manifestations. The patient signed informed consent.

CASE REPORT

A 27-year-old Brazilian male patient, previously diagnosed with OCD, was referred by a psychologist to a psychiatric appointment in an outpatients university clinic. He had been treated with Cognitive Behavioral Therapy (CBT) for three years and showed interest in being started on drug therapy to improve treatment results. On his first appointment, he presented recurrent and persistent intrusive thoughts of sexual content, that were relieved with repetitive behaviors. The family history investigation reveals that he had two aunts and his father diagnosed with SCA-1 and no other neuropsychiatric disorders had been reported in those family members. Interestingly, the patient had already been submitted to a neurologic investigation since his relatives were positive for SCA-1. A brain MRI was performed and was compatible with mild cerebellar atrophy. On that occasion, despite this finding, SCA-1 diagnosis was ruled out because he didn’t have any motor symptoms.

However, his neurological examination showed dysarthria, ataxic gait, and “bulging eyes” at the moment of our evaluation. These findings prompted our medical team to consider other differential diagnosis. On his first appointment, for the treatment of OC symptoms, fluoxetine was initiated.

On his second appointment, the patient scored 13 on the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), and his neurological exam revealed impairment in balance and gait. Our patient was submitted to molecular genetic testing for SCA-1, and results revealed 29 and 59 CAG repeat expansion of the ataxin-1 gene, confirming SCA-1 diagnosis.

The authors present the Patient’s Consent to Publication.

DISCUSSION

Here, we reported a case in which the presence of a psychiatric feature preceded motor-related symptoms in a SCA-1 patient. SCA-1 gene is located on the short arm of chromosome 6 and, in healthy individuals, the triplet CAG is repeated 6 to 36 times while, in mutant SCA-1 alleles, the number of repeats can range from 39 to 82. The length of the expanded allele is known to be inversely associated with the age of ataxia onset as well as symptoms severity. As a consequence, the mutant protein, ataxin-1, tends to aggregate into insoluble intranuclear neuronal inclusion bodies (NI) inside the brain of affected SCA-1 patients.\(^7\) A small number of studies has documented anatomopathological findings associated with SCA-1. For example, in addition to loss of cerebellar nerve cells, mainly among the Purkinje cell layer, other features have been reported as findings in serial brain tissues sections of clinically diagnosed and genetically confirmed SCA-1 patients, such as atrophy of frontal, temporal and parietal brain lobes. Damage to the brain could also be associated with the motor cerebellothalamicortical and basal ganglia-thalamocortical circuits.\(^1\)

For many years, the cerebellum was thought to be only responsible for balance, movement planning and execution. With the development of new characterization me-
thods, based on neuroimaging techniques, that old concept has changed completely. These approaches have allowed the mapping of cerebellar topographic regions according to its corresponding area in the brain. In fact, nowadays, it is well accepted that the majority of cerebellar connections are involved in non-motor functions. More specifically, the cerebellum connects with the brain cortex through two main circuits: an input, from brain cortex to ipsilateral pons, then to contralateral cerebellar hemisphere; and an output, which projects to the deep cerebellar nuclei, contralateral thalamus and finally to the brain cortex. These networks allow the cerebellum to influence information processing in brain cortex correlated to emotional and cognitive functions.

Our case highlights a possible connection between OCS and SCA-1 presentation. Although there are many hypotheses to understand OCD physiopathology, there is no consensus about its specific etiology. However, it is commonly accepted that OCD is related to alterations in the cortico-striato-thalamo-cortical circuitry. Furthermore, there is increasing evidence suggesting that disruption of the neurotransmitter glutamate pathway and its receptors is an important factor for OCD pathophysiology.

Huntington’s disease (HD), another neurodegenerative disorder caused by an expanded CAG repeat, present similar pathological mechanisms in comparison to SCA-1 such as abnormal protein processing, aggregation and toxic cellular effects. However, the affected gene in HD is located at the short arm of chromosome 4. Cerebral impairment in HD exhibits a relative striatal selectivity that could be associated with the expression of Rhes protein, which undertakes preferentially in the striatum. Most individuals affected by HD develop cognitive and/or behavioral issues such as OCS before motor features, could be present even prior to diagnosis.

In conclusion, we propose a possible association between OCS and SCA-1 onset in our patient, taking in account several interconnection features: the non-motor cerebellar role; brain circuits and brain regions affected in SCAs; the fact that HD and SCA1 share similar etiopathogenesis as well as HD patients presenting important psychiatric manifestations including OCD.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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REFERENCES