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Case Report

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Major neurocognitive disorder of rapid progression in Huntington's disease associated with triplet repeat CAG

Abstract

People with Huntington's disease have neuropsychologic disorders that may have a progressive impairment prognosis; in some unusual cases, this cognitive impairment is fastly progressive and generaly is associated with the repetition of the triplet cytosine-adenine-guanine (CAG). To establish with better precision the prognosis of the disease, may help to give a timely treatment and the person who suffers from it, can be as functional as possible and not limit it early in all spheres of the basic activities of daily life, an aspect that not only affects the individual, but also the caregivers. A woman diagnosed with Huntington's disease (42 CAG repetitions) was assessed with the Integrated Program for Neuropsychological Exploration "Barcelona Test", Rey-Osterreith Complex Figure, Artiola's Word List-learning and the Blessed Dementia Scale. The results support the presence of Moderate Cognitive Impairment (Major Neurocognitive Disorder, according to the DSM-V, 2014) multidomain rapidly progressive. The findings show consistent relationships with the literature in terms of repetition of the triplet CAG, it is observe d that the more the CAG triplet is repeated, the cognitive progress is faster. It is suggested that for future research, it should be taken into account that the association between the repetition of triplet CAG and the progression, may be more evident in a wider population if measured over a longer period of time and to ensure the hypothesis of substance abuse and its relationship to a form of progression, it could include a group that has this personal antecedent.

Volume 2 Issue 5 - 2017

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Received: September 25, 2017 | **Published:** November 22, 2017

Introduction

Huntington's disease (HD) is a rare neurodegenerative disorder of hereditary etiology, is considered a public health problem in several countries due to the clinical characteristics and complex evolution of its signs and symptoms. It is characterized by a clinical triad: motor alterations, psychiatric alterations and cognitive alterations, which are progressing to cognitive impairment and subsequently to dementia, making it impossible for the person who suffers it, to be functional and limiting it to all spheres of the basic activities of daily life.[1,2] Genetic posits that Huntington's Disease is produced by the expansion or repetition of the triplet cytosine-adenine-guanine (CAG) located on chromosome 4, the Huntington's Disease gene encodes a protein (huntingtin), the repeating of the CAG triplet causes an abnormal form of this protein in which the amino acid glutamine is repeated; is the presence of this abnormality and not the absence of the normal form which causes damage in the disease; the repeat CAG triplet does not correlate with the age of onset but in the way in which the disease progress.[3] The probability that the gene is inheritable transimissible is 50%.[4,5] We present the case of a person with Major Neurocognitive Disorder and Huntington's Disease with a rapid progression in the neuropsychological domains.

Case report

53-year-old woman with 9 years of schooling and a history of chronic alcohol and tobacco abuse, diagnosed with Huntington's disease through genetic testing (42 CAG repetitions) and clinical assessment with two and a half years of evolution. The assessment consists in the Integrated Program for Neuropsychological Exploration "Barcelona Test" (Peña-Casanova 1999), the Complex Figure (Rey-Osterreith, 1941), the Word List-learning of the Neuropsychological Assessment Battery in Spanish (Artiola, 1999) and the Dementia Scale (Blessed 1969). In the results it was found that there are difficulties in the sustained and selective attention; regarding executive functioning, problems were observed when starting tasks, difficulties in working memory, cognitive inflexibility, disorganization in behavior planning, poor self-monitoring and slow information process; in the process of memory and learning, verbal and visual mnesic deficits were observed in the three phases of memory (recording, storage and recall) which suggest difficulty in learning new information; and in the perceptual motor skills are evidenced of constructional and ideomotor apraxias. With regard to activities of daily living, basic activities are still preserved, however, instrumental activities are not; in the Demential Scale is scored 11, which means Moderate-Severe Deterioration. These findings support the presence of Moderate Cognitive Impairment (Major Neurocognitive Disorder, according to the DSM-V, 2014) rapidly progressive multidomain. Cognitive impairment is predicted to be rapidly progressive and at risk of developing dementia, based on the alterations that were evidenced and described in the course of the evaluation.

Discussion

In this case report, the results show consistent relation with the literature referring to the repetition of the triplet CAG, the more the CAG triplet is repeated, the cognitive progress is faster.[4–6] It is observed that the evaluated person has 42 repetitions of the triplet CAG, despite is not being considered as a subject with long repetitions, is considered significant because the symptoms just started two and a half years ago, and already has Major Cognitive Disorder, because in this period lost several cognitive skills and instrumental abilities

of daily life; this suggest that the CAG triplet was repeated rapidly, however, it would be necessary to evaluate at a given time, if the presented Major Neurocognitive Disorder has progressed and relate it to another genetic analysis, to see if the CAG triplet increased in repetitions. It is emphasized that this case is remarkable because the Major Neurocognitive Disorder presented in the HD, although it is common that it has a progression, it is unusual a fast progression; the typical progression occurs in a period between 10 to 20 years[6] and in this case it was given in two and a half years. In the literature, it has been described that neuropsychiatric comorbidities are present in the HD, among these comorbidities is substance abuse [7,8] it should be noted that the person in this clinical case had chronic consume of alcohol and tobacco; to date, the relationship between chronic substance abuse, and the occurence and progression of cognitive symptoms has not been described, however, it has been investigated the relationship between substance use and the onset of motor symptoms and rapid progress. In an investigation[7] it is reported that there is a strong relationship between the chronicity of substance abuse and the increase in motor symptoms, especially in women, this because the affected structures include basal ganglia and cortico-subcortical decrease; in other investigation[8] it is described that lifetime alcohol abuse and lifetime tobacco abuse is associated with earlier age of HD onset for women. While there is no information on the relationship of substance use to cognition in the HD, it can be assumed that there could be a relationship, and that it could cause, as well as motor symptoms, a rapid progression cognitive symptoms since it is known that the structures that alcohol damages, are also related to cognition.[7,9] This finding contributes to the generation of knowledge about this disease and may highlight the importance of relating the repetition of the CAG triplet so that it can later be established with greater precision a prediction in the prognosis of the disease and to know the reasons for which in some people can find rapid progressions. It is suggested that for future research it should be taken into account that the association between the triplet CAG repeat and the progression, may be more evident in a wider population if measured over a longer period of time and to ensure the hypothesis of substance consume and its relationship to a form of progression, it could be include a group that has this personal antecedent.

Acknowledgements

We acknowledge the "Programa de Maestría y Doctorado en Psicología" of the Universidad Autónoma de México and to the Consejo Nacional de Ciencia y Teconología (CONACYT) for the scholarship support with number: 606371.

Conflict of interest

Authors declare that there are no conflicts of interest.

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