CASE REPORT

Huntington's disease with comorbid myasthenia gravis: a case report

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Abstract

Background: In the literature, several reports are describing the coexistence of Huntington's disease (HD) or myasthenia gravis (MG) with other neurodegenerative and autoimmune disorders. Herein, we report a rare case of HD in a 66-year-old male with MG.

Description of the case: The diagnosis of MG was established by acetylcholine receptor antibodies testing and compatible clinical presentation. The diagnosis of HD was based on clinical features, family history, and DNA testing. Several immunologic mechanisms have been proposed regarding the pathogenesis of HD and MG, respectively. Sharing a common autoimmune aspect could be an uncertain but potential association between the two disorders.

Conclusion: The probability of HD and MG occurring in the same patient is extremely small. While a number of neurological and autoimmune disorders have been reported with HD and MG, this is the first described coexistence of these two entities. HIPPOKRATIA 2019, 23(1): 28-29.

Keywords: Huntington's disease, myasthenia gravis, coexistence, management complexities

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Introduction

MG is an autoimmune disease with a postsynaptic defect of neuromuscular transmission. The diagnosis is based on the combination of clinical symptoms and presence of specific antibodies. Pathophysiological classification is according to age (early/late), disease phenotype (ocular/generalized), pathology of thymus, and antibody specificity[1]. HD is an autosomal dominant neurodegenerative disorder caused by the expansion of the cytosine-adenine-guanine (CAG) repeats in the HD gene; *HTT* gene. Clinically, HD is characterized by motor features (mainly chorea, dystonia, Parkinsonism), behavioral symptoms, and cognitive impairment[2]. To our knowledge, this is the first described patient with HD coexisting with MG.

Description of case

A 66-year-old man was admitted to the Neurology department for evaluation of hyperkinetic movement disorder, presented as involuntary movements of the upper limbs that progressively spread to the whole body and face. According to his relatives, he had also shown social withdrawal, depression, and cognitive problems. The symptoms had started about 30 years ago, and the psychiatric manifestations had preceded the involuntary movements.

Concerning past medical history, the patient had been diagnosed with MG at the age of 58 years. At that time, he had episodes of reduced muscle strength after mild exercise. He also had episodes with swallowing difficulty and inability to maintain straight head posture with intermittent head drops. No thymus pathology was found on the magnetic resonance imaging (MRI) of the chest, and acetylcholine-receptor antibodies were found positive. No known family history was reported.

On neurological examination, the patient was alert. He had slow horizontal saccades, normal muscle strength in the upper and lower extremities, brisk tendon reflexes, and diffuse muscle atrophy. Prominent choreic movements of the face, trunk, and limbs were present, with impaired ability to walk, sit, and eat. Cognitive status was also impaired as assessed by neuropsychometric tests. Psychiatric symptoms of apathy and social withdrawal were also present.

Routine laboratory screening tests were within normal ranges. Testing for acanthocytes in the blood smear was negative. The 24-hour urine copper levels and ceruloplasmin blood levels were normal. Brain MRI revealed mild enlargement of the lateral ventricles. Finally, DNA testing showed 43 and 17 CAG repeats for each of the two alleles of the *HTT* gene, confirming the diagnosis of HD.

A thorough family history reevaluation revealed that also other family members had a movement disorder. His mother had choreic movements that started at the age of 60 years and died 15 years later without a definite diagnosis. Additionally, his sister presented cognitive decline and mild chorea when she was 60 years old. Subsequent genetic testing for HD was performed and found positive.

Discussion

Herein, we report a rare case of a patient with coexistence of MG and HD. In the literature, MG has been described coinciding with several neurological diseases such as amyotrophic lateral sclerosis (ALS)[3], chronic inflammatory demyelinating polyneuropathy[4], neuromyotonia[5], and Parkinson's disease[6]. Similarly, there are cases of HD with comorbid multiple sclerosis[7], Wilson's disease[8], ALS[9], and hereditary spastic paraplegia[10]. Based on current knowledge on HD and MG, no known pathogenic mechanism links these two rare diseases, and their co-occurrence may be incidental. Interestingly, a common feature of both is that most frequent and more significant cases of comorbidity concern ALS, raising a possibility that all these clinical entities may share a common pathophysiological pathway, unknown for the moment[11-12]. A possible shared mechanism could be the involvement of matrix metalloproteinases (MMPs), a group of proteolytic enzymes of the central and peripheral nervous system. In particular, it has been shown that the gelatinase MMP-9 is implicated in the pathogenesis of ALS, MG, and HD[13-14]. Moreover, a three-generation pedigree was created, but no family member was identified with ALS or other neurodegenerative diseases. Of note, the fact of the longer than anticipated time of disease duration and initial denial or failure of the patient and his family members to recognize the mild presenting symptoms had led to a delayed diagnosis of HD, almost 30 years later. It is likely that, in the presented case, the disease had a longer "prodromal" period, manifesting mainly psychiatric symptoms, which in general cannot be properly evaluated in individuals without a known family history. Large cohort studies have shown that the severity of prodromal HD symptoms may be associated with CAG repeat length and closeness to disease onset[15-16].

The coexistence of two rare clinical entities that affect the nervous system, such as HD and MG, is a challenge for the neurologist, and additional data are needed to clarify if a common underlying neuropathophysiological mechanism is present. Another point of concern, highlighted by this case, is the resultant complexities of management of multiple, chronic neurological conditions in one patient. Multidisciplinary support is essential, as different aspects of the diseases must be dealt with by different professions, medical specialties, and genetic counseling.

Conflict of interest

The authors have no conflict of interest to disclosure

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