Multiple Sclerosis and Comorbid Huntington’s Disease: A Case Report

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Abstract

We report a case of Huntington’s disease (HD) presenting in a 51-year-old man with a 22-year history of multiple sclerosis (MS). The diagnosis of MS was supported by history, neurological examination, cerebral spinal fluid (CSF) analysis and magnetic resonance imaging (MRI). The diagnosis of HD was established by DNA testing and family history. There are several reports of comorbid neurologic and autoimmune diseases with MS. There are no reports associating MS and HD. This case report documents the unique association of MS and HD and provides an account of the clinical and paradoxical aspects of both diseases.

Introduction

MS is a chronic, progressive, neurodegenerative disease of the central nervous system. While the cause of MS is unknown, the current hypothesis is that genetic susceptibility and environmental agents or agents initiate immune dysregulation resulting in progressive neurological morbidity. Most MS is sporadic and is considered to be a complex genetic disease. Familial MS, generally defined as two or more cases of MS within a family, constitutes up to 20% of all cases.1 HD is a rare neuropsychiatric, autosomal dominant disorder caused by 36 or more trinucleotide repeats of CAG in the huntingtin gene. HD carries 90% genetic susceptibility. HD is progressive in nature, and characterized by involuntary movements, depression, anxiety, irritability, and apathy, and cognitive decline progressing to dementia. In this report we review a case with both MS and HD. The coexistence of MS and HD has not been reported.

Pedigree

![Pedigree Diagram]

Case Report

A 51-year-old, white male retired US Army artillery officer experienced double vision and headache in 1991. A history of intermittent motor and sensory symptoms evolved over time and a diagnosis of definite relapsing-remitting MS was made in 1997. Paraneoplastic support for a diagnosis of MS came from positive oligoclonal bands in the cerebrospinal fluid and typical brain and cervical MRI lesions that met the standard diagnostic criteria for MS.3 The patient retired from the Army in 2005 and took a full-time job as a government contractor. The patient retired in 2010 from employment as a government contractor due to cognitive difficulties. Major neurological symptoms included: spastic paraparesis, 3- limb ataxia, neurogenic bowel and bladder, fatigue, and poor attention and short-term memory. Cognitive testing in late 2010 revealed average to superior performance in most domains. However, low average testing was seen in mental and psychomotor processing speed and verbal fluency. Over the past year, the subject reports an increase in anxiety and depression but denies suicidal ideation. The patient started using a cane in 2012 and his current Kurtzke Expanded Disability Status Score (EDSS) is 6.5, indicating need for unilateral assist to walk up to 20 meters with aid.

A diagnosis of HD was confirmed in December 2010 following positive DNA CAG testing. This testing was motivated by the diagnosis of HD in his mother in 2006 (Fig. 1). The patient’s mother was 72-years-old at diagnosis and symptoms included subcortical dementia with apathy and motor claususes. She has significant chorea-like movements controlled by medicine. Psychiatric symptoms have not been reported to date in either mother or index patient. The subject’s aunt was diagnosed with HD in 2007 at age 71 by DNA testing and remains asymptomatic (Fig. 1). The patient has two brothers and a sister. One brother tested HD negative and one has not been tested to be. The sister was diagnosed with Turner’s syndrome and died at the age of 46 years of unknown cause.

Discussion

HD classically has motor, cognitive and psychiatric manifestations.4 The motor features involve both involuntary (e.g. chorea) and voluntary (e.g. rigidity) impairments. Cognitive and psychiatric features include frontal lobe dysfunction, irritability, depression and obsessive-compulsive symptoms. Many of these symptoms can be present in patients with MS. Like MS, HD progresses over 1-2 decades. Motor symptoms shared by MS and HD in our patient include ataxia, limb and mild dysphasia. He does not have chorea or rigidity. His depression, irritability and mild cognitive deficits are concerning and we question if these symptoms herald early HD. Our subject has lost 20 pounds over the past year which may be related to depression, dysphagia or an early sign of HD.

Turning to neuroimaging, the patient’s brain MRI shows white matter disease and atrophy typical of MS (Figs. 3, 6). The PET scan is normal (Fig. 4). Based on the PET signal intensity throughout the brain, there is no alteration in the fluorodeoxyglucose (FDG) uptake within the basal ganglia or other subcortical structures. The finding of concomitant MS and HD is novel. The literature on comorbid neurodegenerative disease and motor is sparse. There are a few reports of coexisting MS and amyotrophic lateral sclerosis (ALS) and Parkinson’s disease (PD).1, 2, 4, 5, 6 More commonly, autoimmune disorders have been associated with MS.7 Some reviews argue that these findings are chance associations but others suggest a common environmental exposure.4, 5 or implicate shared genes.6, 8 This case highlights a patient with sporadic secondary progressive MS and possible early HD symptoms. His neurologic and psychiatric progression may be accelerated by HD and its concomitant neurodegenerative diseases but, thus far his course is typical for patients with MS. For example, he progressed to an EDSS of 6 by 22 years from first symptom onset which is within the normal range for males with MS based on a recent Canadian cohort study.3 Because early cognitive and psychiatric manifestations of HD are similar to MS, it is difficult to know the exact clinical onset of HD. The patient and his HD affected relation were diagnosed later in life and have fewer CAG repeats indicating the possibility of delayed symptom onset.

Conclusions

• This case illustrates the importance of taking a thorough family history during the clinical encounter.
• Vigilant monitoring for new neurological symptoms and imaging findings is important in MS cases with a comorbid neurodegenerative disease. We will continue follow this patient closely.
• Genetic testing has implications for patients and families. Following established guidelines and proper genetic counseling before and after HD testing is critical.

References: