

Westphal Variant of Huntington's Disease

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Abstract

Keywords

- ▶ juvenile Huntington's disease
- ▶ *HTT* gene
- ▶ CAG repeat expansion

A Westphal variant of Huntington's disease (HD) is an infrequent presentation of this inherited neurodegenerative disorder. Here, we describe a 14-year-old girl who developed symptoms at the age of 7, with molecular evidence of abnormally expanded Cytosine-Adenine-Guanine (CAG) repeats in exon 1 of the Huntingtin gene. We briefly review the classical features of this variant highlighting the importance of suspecting HD in a child with parkinsonism and a family history of movement disorder or dementia.

Introduction

Huntington disease (HD) is an autosomal dominant progressive disease caused by a Cytosine-Adenine-Guanine (CAG) repeat expansion in the huntingtin (*HTT*) gene, characterized by the triad of choreic abnormal movements, cognitive decline, and psychiatric disturbances such as depression.¹ The juvenile variant of HD (JHD), with onset \leq 20 years, accounts from 4.81 to 9.95% of all cases of HD and only approximately 20% of JHD have childhood-onset HD with onset of symptoms before 10 years of age (Westphal variant, W-HD).² This clinical triad is also observed in JHD but with a different clinical presentation, with bradykinesia, dystonia, and parkinsonian features being predominant over chorea, associated to neuropsychiatric manifestations and myoclonus and epilepsy in nearly half of patients with JHD.³

Case Report

A 14-year-old girl was referred to our neuropediatric clinic because of a 7-year history of frequent falls by progressive postural instability. During the past 2 years, she developed clumsiness, limb stiffness, dysarthria, hearing impairment,

marked emotional lability with periods of agitation and anxiety, and rapidly declining school performance.

Her early developmental milestones and cognitive function were normal. Her father suffered from a progressive neurological disorder, characterized by chorea and dementia at the age of 45, and her paternal grandmother, uncles, aunts, and a cousin presented a similar clinical picture (▶ **Fig. 1**).

General examination was otherwise normal. Neurologic examination showed slurred speech, abstraction, and calculation impairment; assessment of cranial nerves was unremarkable. We found generalized hyperreflexia and hypertonia, cogwheel rigidity, marked left hemibody dystonic posture with gait limitation and bradykinesia. Sensory examination was unremarkable. No ataxia was observed.

Brain magnetic resonance imaging (MRI) showed bilaterally caudate and putamen atrophy (▶ **Fig. 2**). Routine blood tests were normal. Molecular analysis of *HTT* showed an abnormally expanded 79 CAG repeats allele in exon 1 consistent with a molecular diagnosis of HD.

Tetrabenazine was started at 12.5 mg/d and increased up to 100 mg/d with a slight improvement of abnormal dystonic

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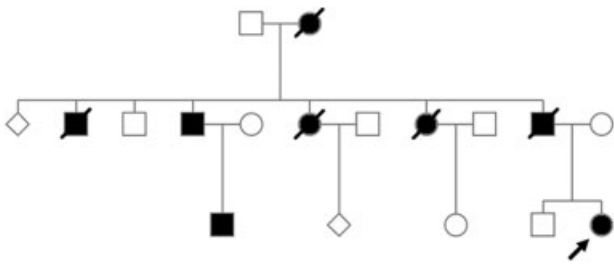


Fig. 1 Family pedigree. Filled boxes indicate symptomatic participants. Arrow points to the proband object of this report.

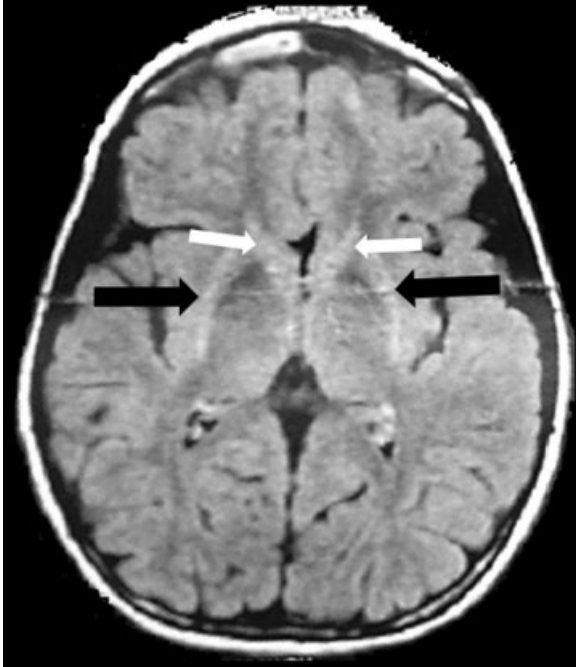


Fig. 2 Axial T2-weighted FLAIR image showing bilateral putaminal hyperintensities (black arrows) and atrophy of the head of caudate nuclei (white arrows). FLAIR, fluid attenuation inversion recovery.

posture and dysarthria. Genetic counseling was given to the family for prenatal guidance.

Discussion

The described patient had dystonia, gait impairment, rigidity, and neuropsychiatric symptoms that started at the age of 7 years, which is characteristic of the W-HD. This form differs from that in adults, as it has prominent parkinsonism features.⁴ It is proposed that these clinical manifestations are the result of a degeneration of the direct inhibitory striatopallidal projection, which results in increased inhibition of the ventrolateral thalamus.⁵ In the largest study to date, only seven children (1.92%) had onset of symptoms before the age of 10 years.¹

Molecular analysis in our patient showed an abnormally expanded 79 CAG repeats in HTT. Patients with early age onset carry large CAG expansions on the HD gene⁶ and most of them, as well as other CAG expansion diseases, show

anticipation when the disease is inherited from their father.⁷ An inverse correlation has been described between the number of CAG repeats and the age of onset of HD,⁸ with patients with JHD carrying usually over 60 repeats. There is also a direct correlation between the CAG repeats and the rate of motor and cognitive progression.⁹ Thus, W-HD shows more similarities with an advanced form of adult-onset HD, although other modifier genes might alter the phenotype.¹⁰

As a predictive test, genetic testing should not be done if the child presents neuropsychiatric symptoms suggestive of HD and the responsible health professional is concerned about the information being harmful to the patient.¹¹ Pre-symptomatic testing is not indicated in children unless there is a clinical intervention appropriate in childhood; thus, parents should defer knowing their child's genotype.¹² In HD, an early diagnosis or detection will not give a cure nor will it improve the prognosis. Furthermore, testing positive for HD can generate social stigma, insurance discrimination, and affect patients' development.¹³

Treatment is essentially supportive. Tetrabenazine has been approved by the United States Food and Drug Administration for chorea, but its effect in W-HD is limited. Haloperidol or risperidone have been helpful for behavioral problems, and antidepressants or mood stabilizing medications have been used for neuropsychiatric manifestations. Physical, speech, and occupational therapies are important for maximizing functionality, particularly as the disease progresses.^{4,5}

Even though infrequent, W-HD should be suspected when parkinsonism and cognitive decline present in a child with family history of movement disorder and dementia.

Conflict of Interest

None declared.

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