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Research Article

HUNTINGTON'S DISEASE WITH NO CHOREA-WESTPHAL VARIANT

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A B S T R A C T

Huntington's disease (HD) is a rare hereditary neurodegenerative disorder which is autosomal dominant and is characterized in over 90% of cases, by chorea as the presenting motor symptom along with dementia and neuropsychiatric manifestations in adults. Juvenile Huntington disease (JHD) known as Westphal variant (WV) presents itself with significantly different signs characterized mainly by rigidity and myoclonus, therefore causing diagnostic difficulties. In this paper, we present WV in a 13 year old girl.

INTRODUCTION

HD is an autosomal dominantly inherited neurodegenerative disease caused by an elongated CAG repeat on the short arm of chromosome 4p16.3 in the Huntingtin (HTT) gene.Midlife onset (35-50 years) of dementia, personality disorders and chorea are characteristic aspects of HD with dystonia and parkinsonism usually appearing later over the course of the disease. But *Westphal, 1883*[1]described a rigid and akinetic syndrome in a small proportion of patients at the time of HD onset. *Milunsky and Milunsky*[2], observed an inverse relation of the number of CAG repeats with the age of onset of HD and a correlation between the expansion of the trinucleotide sequence with the anticipation phenomenon in affected families. JHD as defined by *Levy, Nobre et al*[3]occurs in approximately 10% of HD's patients and 80 to 90% of these, inherit the disease from their fathers. Unlike HD, WV has parkinsonian features, cerebellar involvement, presence of seizures (in more than 80% of JHD cases)[4] and absence of chorea.

Case Report

Our patient, a 13 year old girl born of non-consanguineous marriage was apparently normal till the age of 9 years when she started having behavioural disturbances. As per the family she started having loss of interest, decreased sleep, slowing of movements with poor performance at school.

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She could not cope up with her peers and she had to leave school after one and half years, when she started experiencing tremors at rest and increased stiffness of body; developed myoclonic jerks and over the course of time started developing seizures. Two weeks prior to admission she started having multiple generalised seizures followed by loss of consciousness and postictal confusion. Her father had onset of chorea at 30 years with progression to dementia and leading to death at 43 years. One out of his five siblings, his younger sister had developed chorea movements as well. Patient's paternal grandmother had three siblings, all of them had onset of involuntary movements at 40 years and succumbed to the disease after 10-15 years except one sister who committed suicide attributable to the disease. However the patient neither had chorea during her course of illness nor her siblings were symptomatic *(Figure 1)*. She is thin built with normal higher mental functions but with parkinsonian features (resting tremors, hypomimia, decreased blink rate, bradykinesia, dystonia, cogwheel rigidity, slow speech) and cerebellar signs. Deep tendon reflexes were exaggerated with extensor plantar response and ill sustained clonus.

Ophthalmic examination was normal. EEG had evidence of generalised polyspikes and wave discharges. MRI reported bilateral shrunken caudate nucleus, causing enlargement of frontal horns with atrophied globuspallidus and thinned hyperintense bilateral putamen. DNA polymerase chain showed expanded 83 CAG repeats. She was started on valproate and clonazepam following which her myoclonic

jerks improved and seizures were totally controlled. On genetic testing, her father had 46(+/-3) CAG repeats with onset at 30 years. All her siblings are healthy and pre-symptomatic genetic examination disclosed that the repeat sequence of the elder sister was expanded with repeat length 58 and those of others were normal.

DISCUSSION

HD, which was first described by George Huntington in 1872, is a progressive neurodegenerative disorder with choreoform movements, psychological changes and dementia. Mean age of HD's onset is 35-42 years while JHD has an onset at below 21years in around 5%(1-15%) of HD cases.1.3% of all cases are in childhood (0-10 years) and 4.4 % in adolescent (11-20 years).[5-8]

In JHD there is a subset which presents with more prominent parkinsonian feature - the hypokinetic and rigid characteristics ofWV. It can be Primary Westphal or Secondary Westphal. While in primary it starts with parkinsonian features, whereas in secondary it begins with choreoform movements and then progresses to generalised rigidity, hypokinesia, hypomimia. In children typically less than 10 years in age, even cerebellar features like intention tremors postural instability, titubation and dysarthria have been observed. They have associated behavioural disturbances like learning difficulties, cognitive dysfunction, developmental delay, depression, OCD, phobia, autism, ADHD, tics, suicidal tendencies and other neuropsychiatric disorders.[5-9]

JHD classically develops with more than 60 CAG repeats (in more than 50% cases), childhood onset with usually more than 80 repeats.[9] As *Levy, Nobre et al*[3] noted, earlyonset of JHD is also related to paternal inheritance due to high instability of CAG repeats during spermatogenesis. Likewise, this patient revealed paternal transmission with 83 CAG repeats, with all the atypical features mentioned above. MRI findings include changes in the volume ofthe striate and other cerebral regions such as the thalamus, hippocampus, amygdala, hypothalamus, cerebellum, frontal andinsular cortex as well as atrophy of the caudate and putamen. [10] The patient had bilaterally symmetricalhy perintensity in the caudate and putamen with volume lossand mild atrophy *(Figure 2)*. PET scans are more sensitive and specific of JHD; EEG does not have much of significance but helps to rule out other differential diagnosis common in this age group and shows paroxysmal features. [4] Treatment still remains symptomatic with psychosocial support. Sodium valproate, levetiracetam, and topiramate for seizures, baclofen for muscle relaxation, tetrabenazine if chorea is present.

We report this rare entity with characteristic clinical, laboratory and radiological findings of JHD in a 13yearold girl with all the atypical features beginning with psychosocial symptoms then with parkinsonian and cerebellar features and then developing myoclonus and seizures. The diagnosis was confirmed by PCR-based genetic analysis. The diagnosis is a clinical challenge especially when the disease manifests in children with heterogeneous and overlapping features, where a myriad of other possibilities are present, leading to delayed diagnosis, unnecessary investigations and delayed targeted treatment. Therefore, we clinicians need to understand that in this age group the manifestation of HD is atypical and varied, present with variable clinical phenotypes, which are different from adult-onset HD.

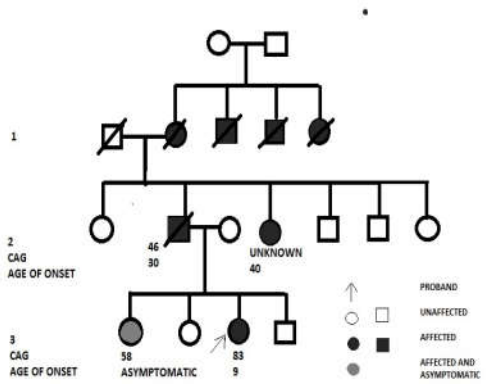

Figure 1 Pedigree of the patient.

1 - All had history of involuntary movement and deceased at 50-55 years of age.

2 – II and III progeny in this generation had similar kindof abnormal movement and had onset at 30 years and 40 years of age respectively and ii (patients father) died at 35 years of age. But genetic test of HD was not performed for iii but has chorea.

3 - I progeny was diagnosed at 17 years of age by presymptomatic test while the child iii in line had onset at 9 year of age with Westphal variant of HD.

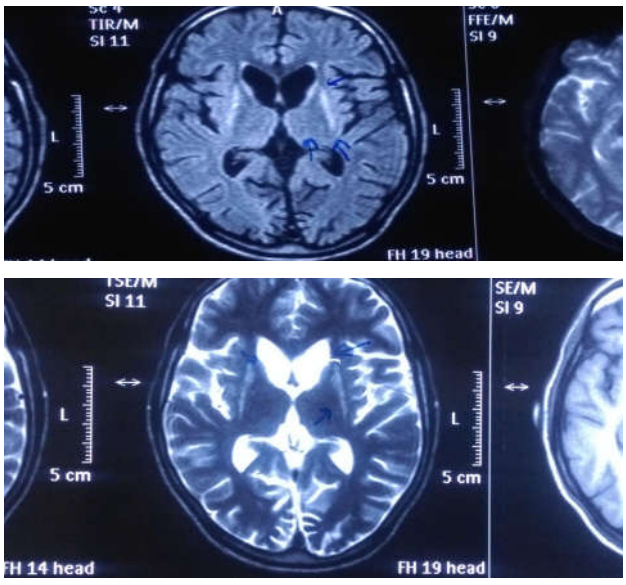

Figure 2 MRI of the patient T2W / FLAIR (TOP) and T2 (BELOW) - MRI BRAIN shows bilateral putamen T2/FLAIR hyperintensity. Bilateral caudate nuclei shows atrophy with mild prominence of adjoining part of the frontal horns of bilateral lateral ventricles. T2 bilateral globus pallidi appear atrophic with caudate atrophy.

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