Movement Disorders
CLINICAL PRACTICE

CASE REPORT

Oculomotor Apraxia as an Early Presenting Sign of Juvenile-Onset Huntington's Disease

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Juvenile onset Huntington's disease (HD), defined as symptom onset before age 21 years accounts for 5–10% of all cases of HD.[1] HD is an autosomal dominant progressive neurodegenerative disorder caused by cytosine-adenine-guanine (CAG) trinucleotide repeat expansion in the huntingtin (*HTT*) gene. We report a case presenting with an early eye movement disorder with saccadic initiation delay (oculomotor apraxia).

Case Report

This 16-year-old Caucasian male presented for review at 14 years with prominent saccadic initiation delay (oculomotor apraxia). Neurological assessment identified a failure to initiate voluntary saccades and upward gaze palsy (Video 1, segment 1). In addition, he had mild cerebellar ataxia and dysarthric speech. Three months later, his assessment showed new findings of hypertonia with rigidity, bradykinesia with preserved strength and reflexes (Video 1, segment 2). Gait assessment identified dystonic posturing of trunk and limbs and difficulties turning (Video 1, segment 3). He was born at term to non-consanguineous parents, with normal birth and early developmental trajectory. From 13 years of age he experienced recurrent falls, regression in gross motor skills and co-ordination, which led to withdrawal from sports as he was not able to catch a basketball or swim a lap in his home pool. He was not able to complete fine motors tasks such as buttoning shirts and had a decline in school performance from an average to low average level with extra processing time required. His peers commented that he was not able to "move his eyes" rather he needed to turn his head to follow objects. Family history identified a maternal grandmother with Lewy-Body Dementia and following his diagnosis it transpired there was a paternal uncle with psychiatric symptoms.

Expanded urine metabolic screen, cerebrospinal fluid testing (including neurotransmitters), nerve conduction studies and electromyography were normal. Chromosomal microarray identified a duplication in 1p36.3 (VOUS), Fragile X testing and whole trio exome were negative. A review of his MRI brain, initially erroneously reported as normal from a referring rural hospital, identified bilateral neostriatal hyperintensity and atrophy with normal cerebellar and brainstem appearance (Fig. 1). This prompted Triplet repeat testing identifying CAG expansion in *HTT* of 74 consistent with Juvenile-onset HD. His parents, who remain asymptomatic aged 52 and 55 years have been counselled for testing including confirmation of paternity, however, have not proceeded at the time of finalizing this report. Over 2 years since the initial videos, his phenotype has progressed to complete ophthalmoplegia with impaired bulbar function, bradykinesia, rigidity, dystonia and spasticity with brisk reflexes. His gait is limited, and he predominantly mobilizes with a manual wheelchair.

Discussion

Juvenile HD cases have varied early symptomatology and typically present with a parkinsonian phenotype rather than the classical chorea or hypokinetic-rigid syndrome in adults.[2] Our case presented with an eye movement disorder with saccadic initiation delay (oculomotor apraxia), which is usually a late feature, being reported in ~20% of cases with juvenile HD.[2] In our case, the absence of a family history and late availability of neuroimaging led to consideration of wider differentials. Saccadic initiation delay in the presence of childhood onset parkinsonism and dystonia can be suggestive of disorders including ataxia telangiectasia

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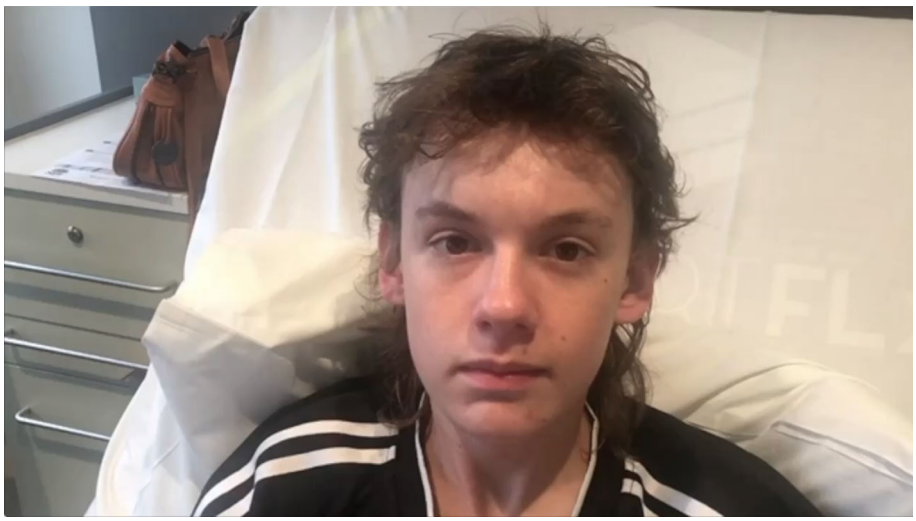

Video 1. Segment one demonstrates slow saccadic initiation with severe impairment. The patient blinks or head thrusts to try to help initiate saccades. There is limitation of upwards gaze with relatively preserved downgaze. Segment two shows bradykinetic movements when the patient is asked to copy the examiner in fractionated finger movements, alternating hand movements and finger nose test. Segment three shows the patient walking with dystonic posturing of the limbs, a stiff trunk, difficulties turning and a narrow based gait. Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13775

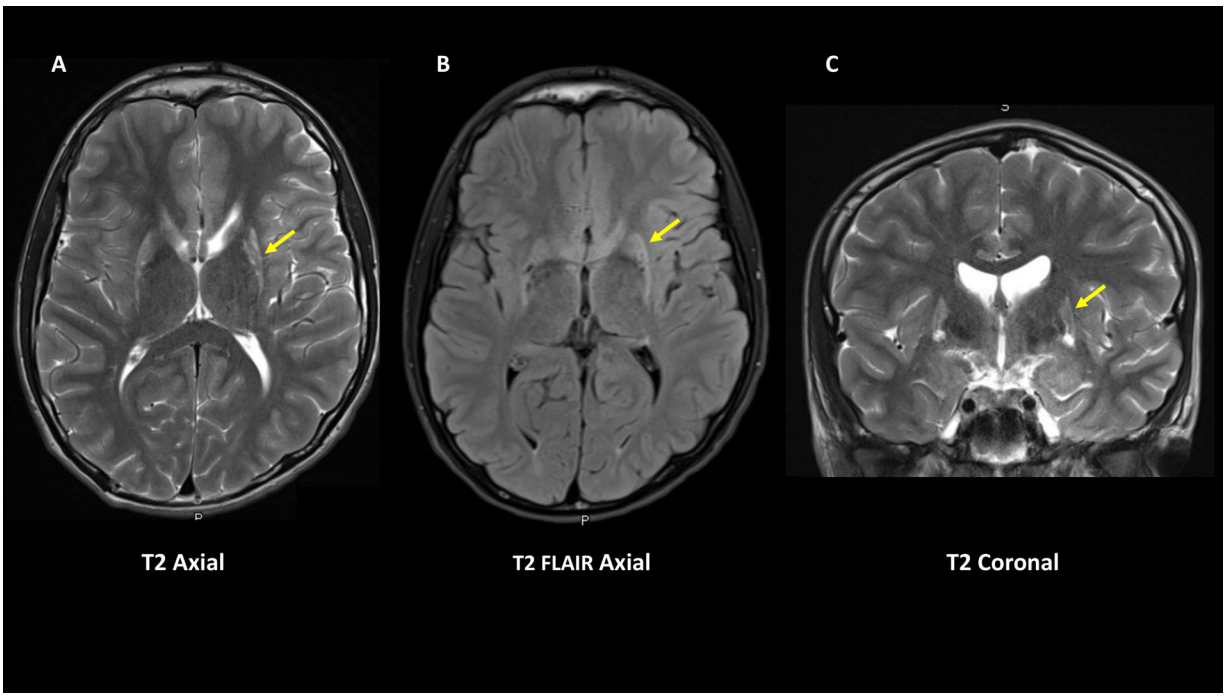

Figure 1. MRI brain (T2 axial, T2 FLAIR axial, T2 coronal) at age 14 years demonstrating bilateral neostriatal hyperintensities and atrophy.

(AT), ataxia with oculomotor apraxia 2 (AOA2), Niemann Pick Type C, Kufor-Rakeb disease and *PLA2G6* or *GNB1* associated movement disorders and other conditions.[2] Ataxic disorders such as AT and AOA2 can present with dystonia but not parkinsonism. HD and autosomal dominant spinocerebellar ataxias are usually inherited however, rare sporadic cases of HD have been described before.[3] In our case, segregation analysis of the family is still pending.

Markham and Knox first described "oculomotor apraxia" in patients with HD in 1965.[4] The earliest eye movement abnormalities are difficulty initiating voluntary saccades and slow saccadic velocity.[5–7] To initiate eye movements patients will blink or head thrust and were thus felt to have an "oculomotor apraxia." Smooth pursuit is initially preserved.[6,7] As the disease progresses, saccades become slow and hypometric and can result in gaze palsies and ophthalmoplegia as in our case. Gaze fixation is also affected due to an inability to inhibit saccades towards a stimulus.[5–7] In our case, oculomotor apraxia was a striking feature seen early in the disease course of Juvenile HD compared to the motor manifestations which were subtle and later progressed. Earlier onset of eye abnormalities can be seen in those with a higher CAG repeat[7] yet this would generally occur later in the disease course following onset of motor signs.

There is ambiguity of the phrase "oculomotor apraxia" in HD given this is not a disorder of motor planning rather a loss of voluntary control of saccades, pursuit and vergence.[6,7] Reflexive eye movements (vestibulo-ocular reflex) were previously reported to remain intact,[6,7] however, this was challenged by Grabska et al[8] who reported prolonged latency and reduced velocity of reflexive and volitional saccades 10 years after the onset of Juvenile-HD. It is proposed there is dysfunction of the pathway involving the descending inputs from frontal and parietal eye fields/cortex to the basal ganglia, superior colliculus, brainstem and then cerebellum.[6] Further, there is a head-eye incoordination, likely reflective of cerebellum dysfunction as initiation of eye movements are impaired independent of head movements; there is a greater latency of eye movements compared to the head movement component of combined gaze shift.[6,7] Given Juvenile HD can present with ataxia and neuro-psychiatric symptoms, examination of eye movements is important to help distinguish "cerebellar" eye movement abnormalities present in differential diagnoses including spinocerebellar ataxias and Friedrich's ataxia.

Typical neuroimaging findings in HD are neostriatal hyperintensities followed by atrophy, with caudate involvement seen more frequently than the putamen.[1] Cases are described with cerebellar atrophy, increased pallidal susceptibility with or without early caudate involvement.[9] Neostriatal volume loss is more severe in Juvenile HD and also has a linear correlation with size of the CAG expansion.[1] Currently there is no definitive treatments for HD, as such management is supportive, targeting seizures, dystonia and spasticity.

In summary, oculomotor apraxia with parkinsonian features in a teenager should alert the clinician to considering Juvenile HD as a differential. Trinucleotide repeat testing is a key investigation, as repeat expansions are not evaluated on microarray or whole exome-based testing, though whole genome sequencing has shown high sensitivity and specificity in identifying them in neurological disorders.[10]

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Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Manuscript Preparation: A. Writing of the first draft, B. Review and Critique.

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Disclosures

Ethical Compliance Statement: The use of diagnostic and clinical information in this report was complied with the requirements of the clinical ethics committee of the Sydney Children's Hospital, Randwick. Verbal and written informed consent for use of information and videos was gained from the patient. All authors confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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