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Case Report

MRI findings in juvenile Huntington's disease ☆,☆☆

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ABSTRACT

Juvenile Huntington's disease is a rare neurodegenerative disorder that first affects the basal ganglia. Presented here is a case of juvenile Huntington's disease in an 8-year-old male. Clinical features included epilepsy and developmental delay. Imaging findings showed severe atrophy of the caudate nuclei and putamina which prompted a genetic evaluation. The diagnosis was confirmed via molecular analysis which revealed the amplified CAG triplet characteristic of this disorder. This case report highlights the imaging features common in this rare cause of pediatric epilepsy.

Introduction

Huntington's disease (HD) is an autosomal dominant, progressive neurological disorder characterized by the degeneration of nerve cells within the striatum of the basal ganglia. It is known to present with motor, cognitive, and neuropsychiatric manifestations [1]. The genetic basis of HD involves a CAG trinucleotide repeat expansion of greater than 35-40 repeats on the huntingtin (HTT) gene on chromosome 4 [2]. The extent of CAG expansion has been discovered to correlate with disease severity, with a greater number of repeats hastening the age of onset [3]. The prevalence of HD varies among ethnic groups but tends to be higher in those of European ancestry, with reported rates as high as 10 to 15 cases per 100,000 people [4,5].

Juvenile Huntington's disease (JHD) is characterized by an earlier onset of disease, usually in childhood or adolescence, generally before age 20 [6]. The proportion of JHD cases in the Huntington's disease population is estimated to be approximately 5%-10% [7]. It is often reported that JHD is associated with greater than 60 CAG repeats on the HTT gene, although this value is sometimes contested [6]. Whereas adult-onset HD is traditionally characterized by chorea, JHD is more often

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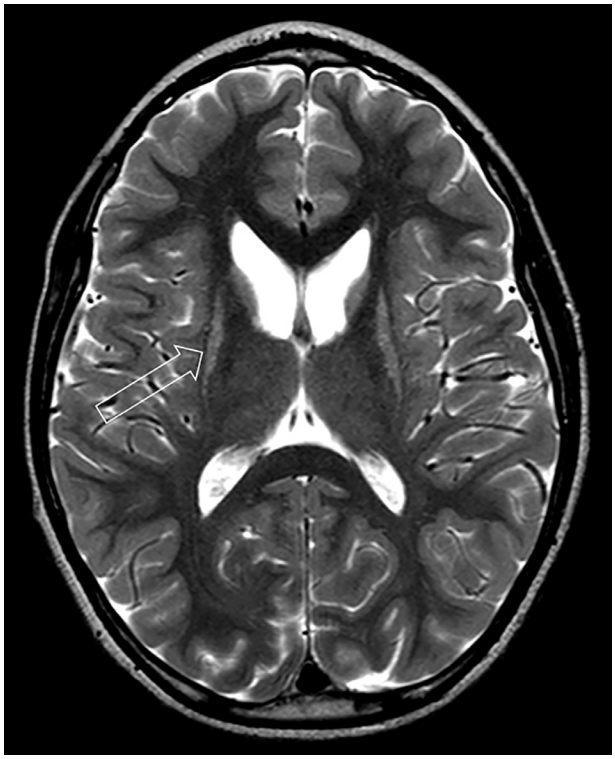

Fig. 1 – Axial T2-weighted image exhibits severe atrophy of the lentiform nuclei (arrow).

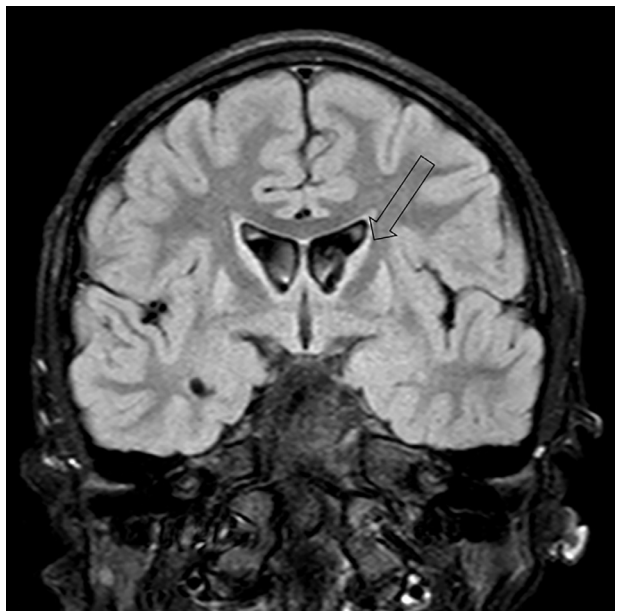

Fig. 2 – Coronal FLAIR reveals severe atrophy of the caudate heads (arrow).

associated with tremor, bradykinesia, and dystonia. Cerebellar signs, myoclonus, epilepsy, and spasticity may also occur in the juvenile form. Similar to adult-onset HD, JHD can present with psychiatric and cognitive manifestations [6,8].

Case report

An 8-year-1-month-old African-American male presented for to the pediatric neurology service for imaging to evaluate progressive developmental regression and seizures. His birth history was unremarkable, and his developmental regression began at approximately age 5. By age 6, myoclonus and seizures had begun. The patient had mixed focal and generalized epilepsy characterized by generalized tonic-clonic seizures, myoclonic seizures, and staring spells. There was no family history of a heritable neurologic disorder, though the father's medical history was unknown.

An MRI was obtained. The images revealed severe atrophy and increased T2 signal within the bilateral lentiform nuclei (Fig. 1). The caudate nuclei were also atrophic with increased FLAIR signal (Fig. 2). The frontal horns of the lateral ventricles were prominent due to the regional volume loss. Given the strikingly abnormal findings that were ostensibly limited to the corpus striatum at the time of imaging, a provisional diagnosis of JHD was suggested. The patient was shown to have 100 CAG repeats in the HTT gene thus confirming the diagnosis. The patient passed away at age 9 years, 2 months.

Discussion

Huntington's disease is caused by a trinucleotide expansion of CAG repeats on chromosome 4, with the juvenile variant of the disease usually presenting with greater than 60 repeats. Analysis of this patient's HTT gene showed 100 CAG repeats. Greater numbers of CAG repeats have been associated with earlier age of onset; however, no reliable association has been found between number of CAG repeats and progression of disease [6].

Many studies have attempted to ascertain the life expectancy of HD after diagnosis. Due to the variable course of both HD and JHD, no exact ranges have been agreed upon by the scientific community. However, on average, life expectancy of adult-onset Huntington's disease seems to be roughly 15-20 years after onset of symptoms [8]. JHD is thought to have a shorter duration of disease due to more rapid progression [9]. The patient in this case report progressed quickly and had a relatively high number of CAG repeats.

The course of JHD has been noted to be more progressive in younger children and has been described in 3 phases. Initial signs include behavioral challenges, learning difficulties, and gait disturbances. The next phase is marked by mental deterioration, rigidity, speech disturbances, and seizures. During the final phase, seizures become more frequent and refractory, and bed confinement is increasingly seen [9]. The patient in this case exhibited features of these 3 phases, though speech disturbances were seen earlier in his course. He had developmental regression, speech disturbance, and

abnormal gait at age 5. Myoclonus and seizures began to manifest at age 6 which is when he sought medical attention, so it is likely that he was already in the second stage. He later suffered mental deterioration, loss of coordination, and abnormal eye movements which were observed at age 8. His epilepsy worsened and became refractory to therapy by age 9.

Imaging findings of JHD have been found to include atrophy of the caudate nucleus and increased signal intensity on T2-weighted imaging in the basal ganglia and thalamus [9,10]. Ventriculomegaly as a result of parenchymal atrophy is also thought to be a later sign of disease [9]. At presentation, the patient in this case had MRI findings of increased T2 signal throughout the caudate heads and lentiform nuclei with mild ventriculomegaly.

The diagnosis of JHD is often made after a clinical suspicion arises, usually due to a family history of HD, as well as the early manifestations described above. MRI showing characteristic features of HD, including caudate atrophy, can aid in the diagnostic process, and the final diagnosis can be made with the discovery of excessive CAG repeats on the HTT gene. Although at this time, HD is not a curable disease, early diagnosis can allow for more thorough monitoring and interventions for quality of life improvement. It may also guide genetic counseling for potentially affected family members.

Consent statement

Informed consent was obtained for publication of the findings related to this patient's diagnosis.

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