CASE REPORT J Pub Health Med Res 2015;3(1):63-65

Imaging Findings in A Rare Case of Padiatric Huntington's Disease – MRI Study

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(Received:05/12/2014, Revised: 01/02/2015, Accepted: 12/03/2015)

Abstract :
Huntington's Chorea is an autosomally transmitted neurodegenerative disorder that usually manifests in the adult age groups (mean age is 35-45 years). In 5-10 % cases, the disease may manifest before the age of twenty years in which case, it is labelled juvenile-onset Huntington's disease. CT and MRI studies are diagnostic of this condition and are crucial to making clinical decisions.

Keywords : Huntington's chorea, Juvenile-onset Huntington's disease, neurodegenerative disorder.

Introduction :

Huntington disease (HD) is a hereditary neurodegenerative disorder with a worldwide prevalence of 5 to 10 per 100 000 persons. Typically, patients with HD present during adulthood (30 to 40 years of age) with choreoathetoid movements ("Huntington chorea"), progressive dementia, and behavioral disturbance. However, 1% to 6% of HD patients will have childhood onset (1–3). Unlike adult HD, juvenile HD patients more commonly present with cerebellar symptoms, dyslalia, mental deterioration, seizures, "parkinsonlike" rigidity, and hypokinesis. Chorea, characteristic for adult HD, seldom is evident initially in the juvenile HD form, frequently making the clinical diagnosis of juvenile HD elusive until late in its course (1–3).

Case History and Imaging Findings

Our patient, an eight year old girl was referred for MRI study of the brain in order to evaluate the cause for her progressive spastic quadriparesis. Her antenatal and birth histories were non-contributory. No adverse events occurred in the first four years of life. Patient started showing signs of motor impairment in the fourth year of life, which progressed to the present clinical findings of spastic quadriparesis. No choreoathetoid movements were observed. No family history of neurological disease could be elicited from the patient's caretakers.

Non-enhanced MRI study of the brain was undertaken and the following findings were observed.

There was enlargement of the frontal horns of both lateral ventricles with a box-like configuration secondary to atrophy of the caudate nuclei heads(Fig 1,2). The intercaudate width was increased. The intercaudate width measured 2.05cm and the frontal horn width measured 3.2cm(Fig 3). There was also atrophy involving both lentiform nuclei.

Also, there was T2 and FLAIR hyperintensity of the caudate nuclei heads and both lentiform nuclei(1-4) with a small area of cystic change within the right lentiform nucleus.(Fig 4)

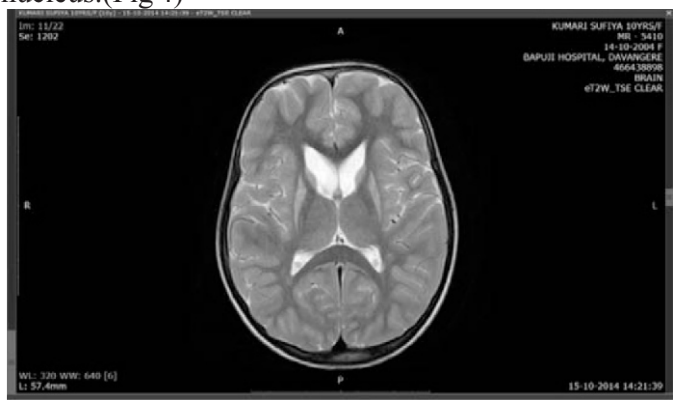

Fig 1 : T2W axial slice at the level of the basal ganglia shows the enlarged frontal horns of both lateral ventricles with shrunken hyperintense caudate heads and hyper intenselentiform nuclei.

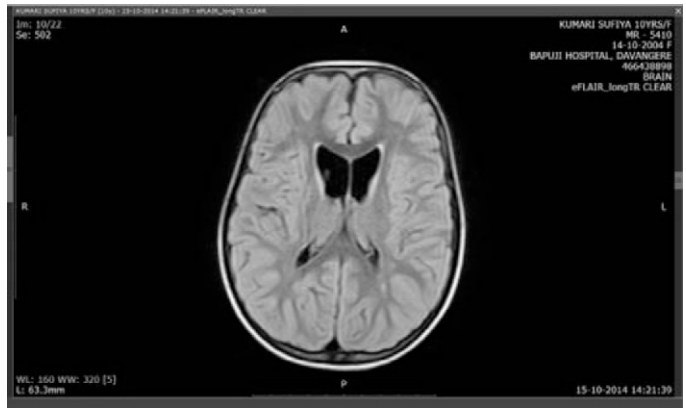

Fig 2 : Axial FLAIR section at the level of the lateral ventricles shows the box-like configuration of the frontal horns of the ventricles.

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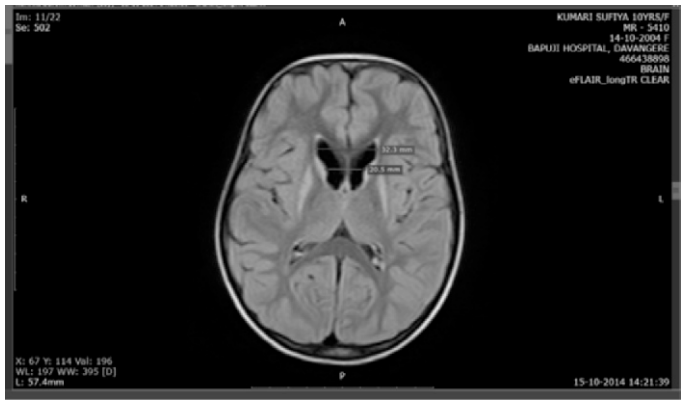

Fig 3 : FLAIR axial section shows the frontal horn width and the intercaudate distance.

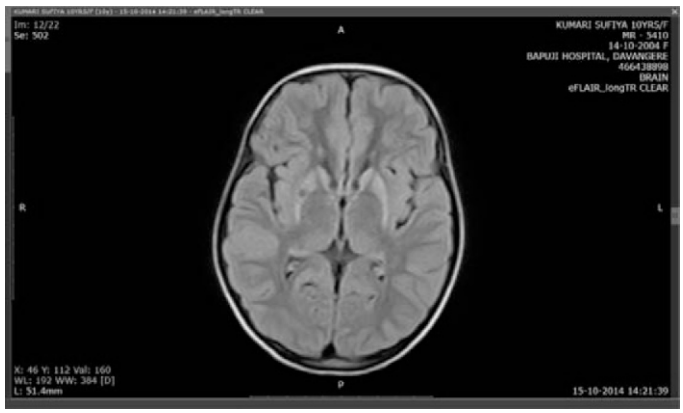

Fig 4 : FLAIR Axial section of the brain shows a small cystic change within the right lentiform nucleus.

Discussion :

HD is an autosomal dominant neurodegenerative disorder that typically presents during adulthood but occasionally may manifest during childhood[2,4,5]. HD has a wide variation in its age of onset even within a single family. Although there is no clear sexual predilection for HD, there appears to be a sex-related factor that affects the age of presentation. Bird et al, in their review of 291 parent-child pairings, found a much earlier onset and faster progression of HD in the children of male patients when compared with those of female parents[5]. Reports of monozygotic Huntington twins, even separated at birth, who experienced clinical onset of HD at the same age[4] further support this notion of a sex-related factor affecting disease onset

Genetically, HD has been linked to a locus within the terminal subband of the short arm of chromosome 4[1]. The HD gene contains an expanded and unstable DNA segment made up of repeating patterns of a polymorphic trinucleotide, CAG. Normally, there are 10 to 30 copies of this triplet at this locus; however, in HD patients, this segment is typically unstable and expanded to greater than 36 copies.

Juvenile HD has a different clinical presentation from that of its adult counterpart[1–3]. Chorea, a distinctive early feature of adult HD, usually is a late manifestation in younger patients that eventually will be manifest in up to 66% to 90% of patients. In children with HD, cerebellar symptoms, dyslalia, mental deterioration, and rigidity are the dominant protean initial features. Pediatric patients also may demonstrate seizure activity, which typically is not encountered in the adult form.

The clinical course of HD in children, furthermore, often is more progressive. The average survival of juvenile patients is 7 to 8 years after onset versus 14 to 15 years as seen in adult patients [2,5].

Pathologically, HD is characterized by diffuse cerebral atrophy, which is most dramatic in the caudate nuclei and, to a lesser extent, the putamina[1,2,6]. There is 2½ times more destruction of the basal ganglia than of the remainder of the brain in HD[6]. In pediatric HD patients, the globus pallidus and the cerebellum, areas not typically involved in adult patients, may be involved[2]. These regions of additional destruction may account for the rigidity and balance difficulties seen in juvenile HD but not in the adult form.

The primary CT and MR feature of HD is caudate atrophy, which is best identified by separation of the horizontally apposed heads of the caudate nuclei (increased CC distance). A widened CC, however, is not specific for HD and also can be seen with hydrocephalus or other forms of diffuse atrophy. Because there is preferential caudate atrophy in HD, ratios comparing the intercaudate distance (CC) with internal standards have been used to differentiate HD from other disorders [7–9].

Recently, Aylward et al have shown by MR that both the FH/CC and bicaudate (CC/IT) ratios correlate well with caudate volume in patients with Huntington disease. In any case, established criteria for HD are based primarily on adult data (normal meanFH/CC, 2.2 to 2.6; normal mean CC/IT, 0.09 to 0.12). Because the FH/CC ratio decreases with normal aging, presumably because ventricular size increases with age, the use of adult standards especially for the FH/CC would serve as conservative standards in children.

Mirowitz et al, in their series of 65 pediatric patients with neurodegenerative disease, also had reported bilateral symmetric basal ganglia T2 hyperintensity in two patients with HD. Increased T2 signal has yet to be described in adult HD, to our knowledge. Symmetric involvement of the basal ganglia, of course, is not limited to juvenile HD and may be found in a host of other conditions, many of which are metabolic in nature. The

differential considerations include chronic disorders such as Leigh disease and Wilson disease.

Acute hypoxia, carbon monoxide, hypoglycemia, and near drowning also may manifest bilateral basal ganglia lesions; however, with the clinical history of chronic symptoms, these causes should be easily discounted. The differentiation of juvenile HD from Leigh and Wilson diseases may be more difficult. Leigh and Wilson diseases may have additional focal involvement of white matter, thalamus, brainstem, and cerebellum, whereas HD typically would not. Biochemically, patients with Leigh disease will have elevated lactate/pyruvate ratios and lactic acidosis; patients with Wilson disease, decreased serum ceruloplasmin and elevated urinary copper. Because these disorders are typically hereditary, a family history also would be helpful.

MR can potentially identify abnormalities not readily apparent with CT within the caudate nuclei and putamina in juvenile HD. The added use of the FH/CC and bicaudateratios can help differentiate HD from other neurodegenerative disorders, such as Leigh and Wilson diseases, which also may manifest bilateral basal ganglia abnormalities.

The presence of abnormal high signal intensity in atrophic caudate nuclei and putamina on proton density– and T2-weighted images in a child should suggest the diagnosis of Huntington disease.

Conclusion :

Due to the atypical clinical presentation of the disease in the paediatric age group, imaging plays a very crucial role in the diagnosis of Huntington's disease and in the clinical management of the same. MRI offers imaging details that are not provided by Computed Tomgraphy therefore effectively ruling out many close imaging differentials.

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How to Cite this article :
Vats AK, Hegde K, G R Rohith. G.R, G Rashmi, Imaging Findings in A Rare Case of Padiatric Huntington's Disease – MRI Study. J Pub Health Med Res, 2015;3(1):63-65

Funding: Declared none
Conflict of interest: Declared none