Clinics in Diagnostic Imaging (47)

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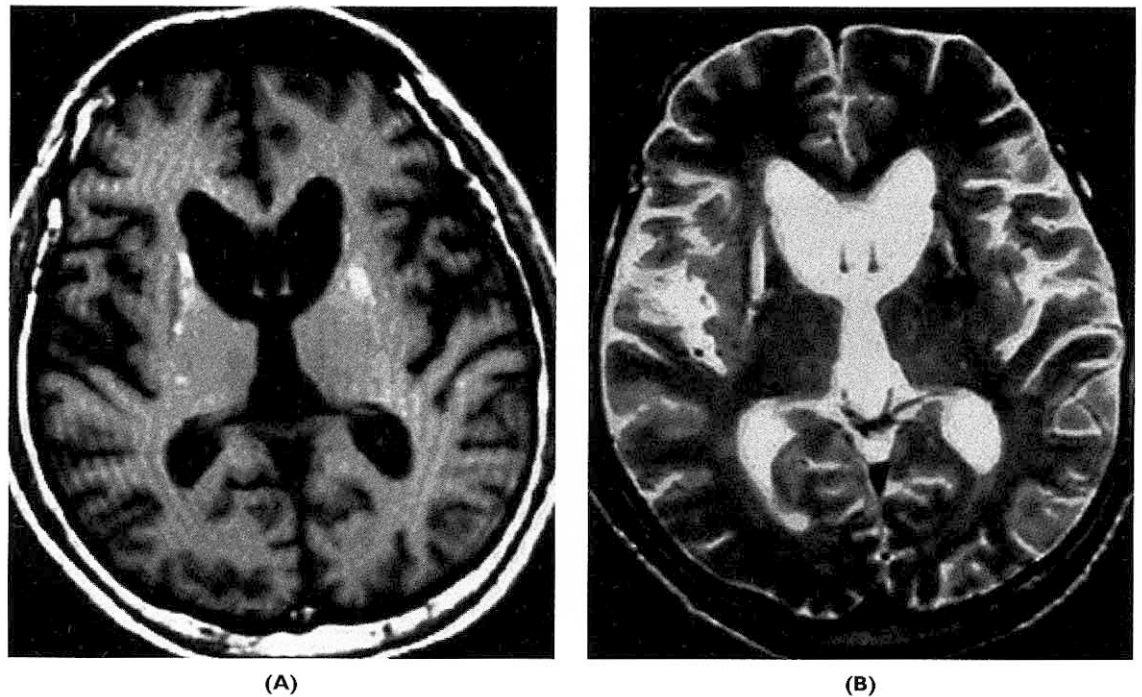

(A)   (B)

Fig 1 – Axial (A) T1- and (B) T2-weighted MR images of the brain.

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CASE PRESENTATION

A 38-year-old man first presented with choreoathetosis four years before his present admission. He had progressively increasing choreoathetosis. Oral-facial dyskinesia, dysarthria and behavioural changes were observed recently. The patient had a past history of diabetes mellitus, which was diagnosed during the initial presentation in 1994. There was no family history of choreoathetosis. On examination, he was found to have generalised involuntary movements, which were present at rest and were accentuated by activity. The patient had an unsteady gait and diminished jerk reflexes affecting both upper and lower extremities. Facial grimacing and uncoordinated tongue movements were also present. There was no detectable sensory loss. What do the magnetic resonance (MR) images of the brain show (Fig 1A-B)? What is the diagnosis?

CASE PRESENTATION

The T1-(Fig 1A) and T2-weighted MR images (Fig 1B) show gross atrophy of the heads of both caudate nuclei. This was seen as dilatation of the frontal horns of the lateral ventricles with loss of concavity or flattening of the lateral aspect of frontal horns. Atrophy of the putamina was also noted. The putamina were T1-hypointense (Fig 2A), and were relatively hyperintense on T2-(Fig 2B) and proton density-weighted images (Fig 2C). The globus pallidi were T1-hyperintense (Fig 2A) and T2-hypointense (Fig 2B). OnT2*-weighted images (Fig 2D), the globus pallidi were very hypointense, probably due to a combination of iron deposition and calcification. Capacious cisternal spaces and cerebral sulci were observed, indicating cerebral atrophy (Fig 1,2). A cavum septi pellucidi et verge, a normal variant, was incidentally noted.
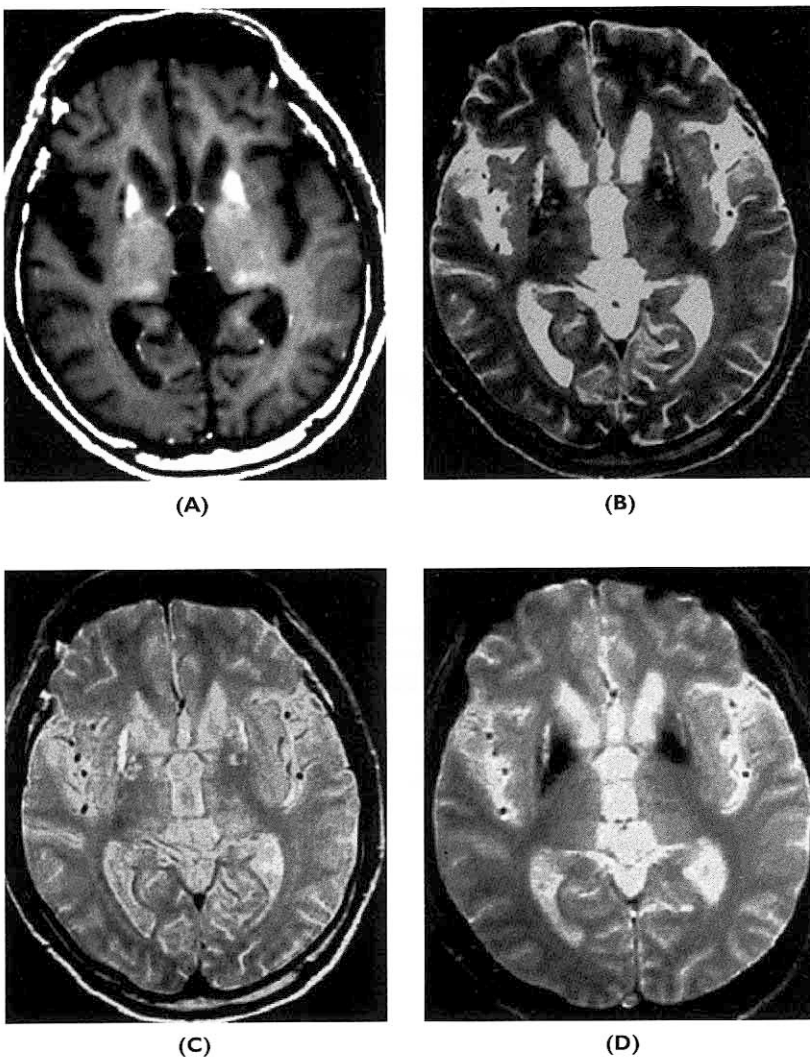

(A)　　　　(B)

(C)　　　　(D)

Fig 2 – Axial (A) T1-, (B) T2-, (C) proton density and (D) T2*-weighted images of the brain show abnormal signal changes in the putamina and globus pallidi bilaterally. The changes in the globus pallidus were highly suggestive of iron deposition and calcification.

DIAGNOSIS

Huntington's disease.

CLINICAL COURSE

Initial and subsequent serum biochemical studies were unremarkable. Serum copper, ceruloplasmin, lead and pyruvate levels were all within normal limits. Cerebrospinal fluid analysis for oligoclonal bands was negative. Electroencephalography (EEG) did not reveal any abnormal focus of activity. A computed tomography (CT) scan of the brain four years before revealed only mildly dilated ventricles and bilateral basal ganglia calcifications. The cranial MR scan on admission showed generalised cerebral and bilateral focal caudate nuclei atrophy.

The patient subsequently developed behavioural abnormalities and was diagnosed to have a violent organic personality and mood disorder. A progressive deterioration of the choreoathetosis with involvement of both upper and lower limbs rendered the patient to be wheel-chair bound.

DISCUSSION

Huntington's disease (HD) is an inheritable progressive neurodegenerative disorder. It is transmitted genetically as an autosomal dominant disorder with complete penetrance. The terminal subband of the short arm of chromosome 4 has been identified as the site responsible for the disease[1]. There is no clear sexual predilection although sex-related factors probably affect the age of presentation[2]. The world-wide prevalence of HD is about 5 – 10/100,000 of the population[3]. However, an incidence as high as 7000/100,000 in Western Scotland and Venezuela has been reported by Shoulson[4].

There is wide variation with regard to the age of clinical onset of the disease. The typical age of presentation is between 30 and 40 years. Five percent of cases have the juvenile form of HD, with disease onset at or before the age of 19 years[5]. Adult patients with HD commonly present with choreoathetoid movements, progressive dementia and behavioral disturbances[2]. On the other hand, juvenile HD patients usually present with cerebellar symptoms, dyslalia, mental deterioration, seizures, Parkinson-like rigidity and hypokinesis. Furthermore, rapid progression of the disease with more severe emotional and intellectual deterioration is encountered[6], while choreoathetoid movements are a late presentation in this younger age group[2].

Pathologically, three forms of HD have been identified[6], namely akinetic-rigid variant, classic hyperkinetic form, and juvenile form. All forms show diffuse cerebral atrophy with marked neuronal loss within the caudate nuclei and putamina. The globus pallidi are affected to a lesser degree[7]. In the akinetic-rigid form, there is greater atrophy of the putamen and loss of the striatal neurons that project to the medial and lateral segments of the pallidum[7]. However, the projections to the lateral aspect of the globus pallidus are primarily lost in the classic

hyperkinetic form[7]. In the juvenile form, on the other hand, greater cell loss and atrophy in the stratum is observed[7].

The characteristic radiological features of HD are atrophy of the caudate nuclei and putamina, as well as generalised cerebral atrophy. In the early stages of the disease, frontal lobe atrophy is more prominent. This advances posteriorly toward the parietooccipital regions in the later phases[8]. Neuroimaging of HD is relatively insensitive in the early stages. Clinical symptoms commonly predate the CT findings[2]. However, evidence of caudate nuclei atrophy may be demonstrated on CT with the clinical appearance of the first motor signs[3]. The sensitivity of CT in diagnosing clinically evident HD has been shown to be 87.5% by Sharma et al[9]. MR is more sensitive than CT, and is capable of depicting subtle changes of tissue loss in the caudate nuclei and putamina[2]. Caudate atrophy, which is characteristic but not specific of HD, was first demonstrated on pneumoencephalography by Blinderman et al in 1964[10]. The radiological features of caudate atrophy are enlargement of the frontal horns of the lateral ventricles with loss of concavity or flattening of the lateral aspect of the frontal horn. Normally the caudate nucleus bulges into the lateral aspect of the frontal horn resulting in its concave lateral margin. Quantitation of caudate volume has been reported to be useful and to correlate well with the severity of the clinical disease[2,6,11]. In addition, there is a decrease in frontal horn/bicaudate ratio (normal 0.089 – 0.095)[6]. However, normal ageing and hydrocephalus may have a similar appearance[2]. In another published study, volumetric measurements of the putamina were claimed to be a more sensitive indicator in early disease[12].

Besides atrophy of the basal ganglia, signal intensity changes of basal ganglia have been reported as well. The majority of akinetic-rigid variant and juvenile HD cases demonstrate an increase in MR signal intensity of the neostriatum on intermediate and long TR images, whereas in the greater proportion of the classic form of HD, no signal changes were identified[2,6,7,13]. This signal change was assumed to be due to the greater striatal damage as seen in the akinetic-rigid variant and juvenile forms of HD, which similarly reflect the greater motor and cognitive compromise in these patients[13]. A child presenting with atrophic caudate nuclei and putamina, as well as abnormal MR high signal intensity changes on intermediate and T2-weighted images, suggest the diagnosis of HD[2].

Bilateral symmetrical basal ganglia involvement is not exclusive or diagnostic of HD. Other causes of bilateral basal ganglia involvement include Leigh disease, Wilson disease and acute hypoxia. Carbon monoxide poisoning, hypoglycaemia and near drowning can give rise to bilateral basal ganglia abnormalities. However, these aetiologies can usually be excluded by the clinical history. Hypoxia results in bilateral basal ganglia atrophy and MR signal changes, but other parts of the brain are involved as well. In Leigh disease and Wilson disease, selective atrophy of neostriatal tissue is not a prominent feature[6]. Leigh disease usually involves the globus pallidus, while involvement of the putamen is a feature of Wilson disease. In addition, MR signal changes or involvement of the thalamus, brain stem and subcortical white matter may be seen in such cases[14]. For example, an increased long TR signal in the periaqueductal region may be visualised in Wilson disease[14]. Biochemically, increases in the lactate/pyruvate ratio and lactic acidosis are features of Leigh disease. Wilson disease, on the other hand, tends to have an increased urinary copper and a decreased serum ceruloplasmin level.

Positron emission scanning is capable of depicting a decrease in striatal metabolism in cases of HD, which is characteristically present before any demonstrable atrophy on CT or MR imaging. Again, this is a sensitive but non-specific finding, but may be of value in the monitoring of appropriate therapies in HD[15]. The value of MR spectroscopy (MRS) in HD is yet to be determined. Thus far, a decrease in N-acetylaspartate and creatinine, and an increase in choline and myoinositol have been demonstrated in patients with HD[16].

In conclusion, the diagnosis of HD is mainly a clinical one. Neuroimaging demonstrating characteristic features is supportive, but lacks specificity. MR is more sensitive than CT scans and may be able to depict subtle changes within the basal ganglia in early cases.

REFERENCES

1. Gusella JF, Wexler NS, Conneally PM, et al. A polymorphic DNA marker genetically linked to Huntington's disease. Nature 1983; 306:234-8.
2. Ho VB, Chuang HS, Rovira MJ, Koo B. Juvenile Huntington Disease: CT and MR features. AJNR 1995; 16:1405-12.
3. Simmons JT, Pastakia B, Chase TN, Shults CW. Magnetic resonance imaging in Huntington disease. AJNR 1986; 7:25-8.
4. Shoulson T. Huntington's disease. Neurol Clin 1984; 2:515-26.
5. Myers RH, Goldman D, Bird ED, et al. Maternal transmission in Huntington's disease. Lancet 1983; 1:208-10.
6. Comunale JP, Heier LA, Chutorian AM. Juvenile form of Huntington's disease: MR imaging appearance. AJR 1995; 165:414-5.
7. Savoiardo M, Strada L, Oliva D, Girotti F, D'Incrsti L. Abnormal MRI signal in the rigid form of Huntington's disease. J Neurol Neurosurg Psychiatry 1991; 54:888-91.
8. Sax DS, O'Donnell B, Butters N, Menzer L, Montgomery K, Kayne HL. CT, neurologic and neuropsychological correlates of Huntington's disease. Int J Neurosci 1983; 18:21-36.
9. Sharma P, Savy L, Britton J, Taylor R, Howick A, Patton M. Huntington's disease: a molecular genetic and CT comparison. J Neurol Neurosurg Psychiatry 1996; 60:206-8.
10. Blinderman EE, Weidner W, Markham CH. The pneumoencephalogram in Huntington's chorea. Neurology 1964; 14:601-7.
11. Aylward EH, Schwartz J, Machlin S, Pearlson G. Bicaudate ratio as a measure of caudate volume on MR images. AJNR 1991; 12:1217-22.

12. Harris GJ, Pearlson GD, Peyser CE, Aylward EH, Roberts J, Barta PE, Chase GA, Folstein SE. Putamen volume reduction on magnetic resonance imaging exceeds caudate changes in mild Huntington's disease. Ann Neurol 1992; 31:69-75.

13. Oliva D, Carella F, Savoiardo M, Strada L, Giovannini P, Testa D, Filippini G, Caraceni T. Clinical and magnetic resonance features of the classic and akinetic-rigid variants of Huntington's disease. Arch Neurol 1993; 50:17-9.

14. Ho VB, Fitz CR, Chuang SH, Geyer CA. Bilateral basal ganglia lesions: pediatric differential considerations. Radiographics 1993; 13:269-92.

15. Kuhl DE, Phelps ME, Markham CH, Metter EJ, Riege WH, Winter J. Cerebral metabolism and atrophy in Huntington's disease determined by 18 FDG and CT scan. Ann Neurol 1982; 12:425-34

16. Hoang TQ, Bluml S, Dubowitz DJ, Moats R, Kopyov O, Jacques D, Ross BD. Quantitative proton-decoupled 31P MRS and 1H MRS in the evaluation of Huntington's and Parkinson's diseases. Neurology 1998; 50:1033-40.

ABSTRACT

A 38-year-old man presented with progressive worsening of choreiform movements. Serum biochemistry analysis did not reveal any abnormality.

Magnetic resonance imaging demonstrated symmetrical caudate nucleus atrophy and generalised cerebral strophy. Huntington's disease was diagnosed in view of the clinical presentation and the characteristic imaging findings. The clinical, pathological and imaging features of this disease process are discussed.

Keywords: Huntington's disease, caudate nucleus atrophy, magnetic resonance imaging, choreoathetosis