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Late Onset Familial Hallervorden-Spatz Disease: MR Findings in Two Sisters

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Summary: Two sisters affected by late onset Hallervorden-Spatz disease are described. In both patients, MR showed rings of decreased signal intensity surrounding hyperintense areas that gave a target-like appearance to the globi pallidi, a finding that corresponds with the known pathologic lesions in the disease. MR reflects the metabolic and anatomic evaluation of this disease.

Index terms: Degenerative brain disease; Hallervorden-Spatz disease; Iron, brain

Hallervorden-Spatz disease (HaSpD) is an autosomal recessive hereditary disorder, presumably of metabolic origin (1). Although ferrokinetic studies demonstrate iron storage in the basal ganglia in patients affected by the disease (2), the diagnosis rests on the demonstration of typical clinical and pathologic findings. The main clinical features are represented by both progressive pyramidal and extrapyramidal signs, predominantly in the lower limbs, dysarthric speech, and mental deterioration. The characteristic neuropathologic findings are represented by deposition of iron-staining pigments in both globi pallidi, substantia nigra, and red nuclei associated with pallidal demyelination, and focal axonal swelling distributed in the pallidonigral system.

Since magnetic resonance imaging (MR) is able to demonstrate iron deposits (3) its usefulness for the *in vivo* diagnosis of HaSpD has been evaluated (4–7).

We describe two sisters in whom the clinical picture, the ferrokinetic studies, and MR findings suggested the diagnosis of HaSpD.

Case Reports

Case 1

This 56-year-old woman presented with motor and speech difficulties. She was in good health until age 32,

when she was first admitted to the Hospital because of unsteady gait. Two years later, progressive generalized motor difficulty associated with dysarthric speech appeared. A series of clinical investigations, including serum copper and urinary copper excretion and liver biopsy, were normal. Computed tomography (CT) at age 45 revealed no abnormalities.

On admission, neurologic examination revealed an expressionless woman with marked diffuse rigidity, both pyramidal and extrapyramidal, mainly in the lower limbs. Diffuse torsion dystonia was present, more marked in the inferior limbs. Speech was almost incomprehensible and she was barely able to walk. Deep tendon reflexes were all brisk and Babinski sign was positive bilaterally. Ferrokinetic studies showed an increased uptake of ⁵⁹Fe in the basal ganglia.

MR (Philips Gyroscan 0.5 T) revealed rings of decreased signal intensity surrounding hyperintense areas, giving a target-like appearance to the globi pallidi (Fig. 1).

Case 2

This 53-year-old woman was the sister of the patient in case 1. She was in good health until age 30, when she began to show abnormal gait with a tendency to rotate the feet internally. She suffered frequent falls and in the following years the gait worsened and slurred speech appeared. A series of laboratory investigations, including serum copper and urinary copper excretion, were normal. A CT scan performed at the age of 43 revealed mild cortical and subcortical atrophy.

On admission, neurologic examination revealed a "stiff faced" woman with opisthotonic posturing and marked dystonia of the neck and inferior limbs. Pyramidal and extrapyramidal rigidity were present in the inferior limbs. Dystonic movements were present in the inferior extremities. Deep tendon reflexes were all brisk with bilateral Babinski signs. Speech was severely dysarthric and she was unable to walk. Mild dementia was present and ferrokinetic studies revealed a marked increased uptake of ⁵⁹Fe in the basal ganglia. MR was identical to that of the sister (Fig. 1), revealing a target-like lesion with rings of

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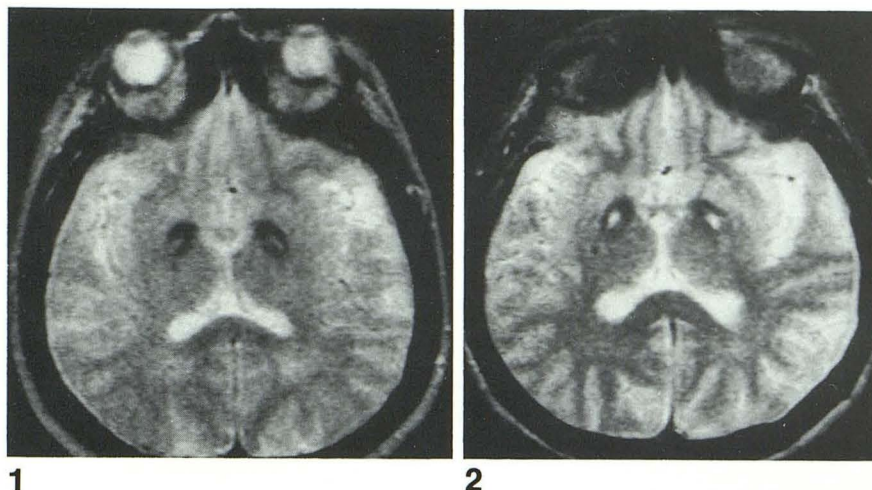


Fig. 1. MR of case 1 (spin echo 2000/100/2) showing rings of decreased signal intensity surrounding hyperintense areas that give a target-like appearance to the globi pallidi.

Fig. 2. MR of case 2 (spin echo 2000/100/2) showing rings of decreased signal intensity surrounding hyperintense areas that give a target-like appearance to the globi pallidi.

decreased signal intensity surrounding hyperintense areas in the globi pallidi (Fig. 2).

Discussion

HaSpD is a rare hereditary disorder (1). Onset is usually in late childhood or early adolescence, but autopsy-documented cases beginning at age 20 or later have been reported (8–16). Typical clinical findings consist of relentlessly progressive dementia, bradykinesia, rigidity, spasticity, and dystonia, as well as choreoathetosis and other hyperkinesias; however, the clinical diagnosis should be supported by the characteristic pathologic findings. These are represented by bilateral destruction of the globus pallidus and pars reticulata of the substantia nigra, loss of myelinated fibers, variable amounts of gliosis, iron deposits, and swollen axonal “spheroids.”

Laboratory investigations have not been definitely helpful in the diagnosis of HaSpD. As much as twice the normal uptake of ^{59}Fe in the basal ganglia has been reported, but this finding has not been consistent enough to have clinical utility (2). Recently, MR first offered the possibility of detecting iron deposit abnormalities in the brain (3), and its usefulness for the *in vivo* diagnosis of HaSpD has been emphasized (4–7). MR can map the distribution of macromolecular complexes of Fe(III) in the brain in long TR/long TE images (3). This is accomplished through contrast created by a local inhomogeneity in the magnetic field that dephases spins and produces loss of signal (3). Therefore, iron deposits in the brains of patients affected by HaSpD appear as hypointense areas.

The typical pathologic features of HaSpD, such as demyelination, neuronal loss, gliosis, and focal axonal swelling are lesions known to increase

signal intensity in T2-weighted images of the brain. Therefore, both hypo- and hyperintense lesions should be expected in the MR study of patients affected by HaSpD. Different MR findings have been reported in the disease, including hypointensity (5, 7), hyperintensity, and the coexistence of both hypo- and hyperintensity with a target-like appearance of the globi pallidi (4, 6). In the case reported by Gallucci et al, all these findings were present in the same patient, and the authors suggested that they represented different pathologic manifestations of the disease during its evolution (4). This evolution of the MR findings from hyperintense to the target-like lesions in the globi pallidi seems to be confirmed by pathologic specimens, in which neuroaxonal degeneration and consequent spheroid production are observed even in the early stages of the disease (17).

Pallidonigral pigmentation is only a later phenomenon, deriving from autooxidation of lipopigments at an increasing rate (17). Deposition of physiologic pigments, particularly iron, in the globus pallidus and substantia nigra is not specific for HaSpD and has been reported in encephalitis, Wilson disease, idiopathic hemochromatosis, myoclonic epilepsy, radiation exposure, storage disorders, and even normal-aged brain (16). Thus, both very early MR study of patients suspected of having HaSpD and periodic follow-up studies reveal a typical evolution of MR findings in the globus pallidus, reflecting metabolic as well as anatomic characteristics of the disease.

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