## NEUROIMAGING

# Multiparametric 3T MRI evaluation of hereditary spastic paraplegia: A case report

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#### Abstract

Hereditary spastic paraplegia (HSP) is a rare heterogeneous group of familial neurodegenerative disorders characterized by degeneration of the corticospinal tracts and posterior column of the spinal cord. Previously described radiological findings included nonspecific brain abnormalities such as brain atrophy and white matter lesions, as well as atrophy of the corpus callosum and spinal cord. Magnetic resonance spectroscopy may reveal reduced concentrations of normal brain metabolites and elevated levels of myoinositol. Diffusion tensor imaging shows increased mean diffusivity and reduced fractional anisotropy in the periventricular white matter, which is compatible with damaged myelinated axons. We present here two cases of HSP in a single family with typical imaging findings.

Key words: Corpus callosum atrophy; hereditary; MRI; spastic paraplegia

## Introduction

Hereditary spastic paraplegia (HSP) is a heterogeneous group of familial neurodegenerative disorders characterized by progressive lower limb spasticity. Clinically, they are classified as "pure" and "complicated" when other major clinical features are present.<sup>[1]</sup> Genetically autosomal dominant, autosomal recessive, and X-linked recessive forms of inheritance are seen. Diagnosis is principally done by the clinical criteria proposed by Harding in 1984.<sup>[1]</sup> Genetic analysis serves as the confirmatory test. Magnetic resonance imaging (MRI) of the neuraxis can help in early diagnosis and to exclude secondary causes of spastic paraplegia. We present here two cases of HSP in a single family with typical imaging findings.

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## **Case History**

#### Case 1

A 22-year-old male born out of nonconsanguineous parentage with normal developmental history presented with history of progressive spastic gait disturbance for the past 8 years. It initially started in the left lower limb, and 6 months later the right limb was involved. His bladder and bowel functions were normal. Similar history was noted in his elder sister who is currently non-ambulatory (Case 2). No history of similar symptoms in either of the parents or other first and second degree relatives was present. General physical examination was normal except for limping of gait. Speech was dysarthric. He had normal

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muscle bulk with spasticity of lower limbs. The power in lower limbs was grade IV in all groups of muscles. All the deep tendon reflexes in both the lower limbs were symmetrically brisk and plantar response was bilaterally extensor. Sensory system examination was normal and the gait was spastic.

Hematological investigations were normal. Cerebrospinal fluid analysis was mildly positive for oligoclonal band. Electromyography and nerve conduction studies were normal. MRI brain and spinal cord was done using a 3 T machine, which revealed a thin anterior part of body and genu of corpus callosum (CC) with mild brain atrophy [Figure 1A]. Abnormal high signal intensities were noted in periventricular white matter and centrum semiovale on fluid-attenuated inversion recovery (FLAIR) images [Figure 1B]. MRspectroscopy (MRS) did not show significant alterations in normal metabolites [Figure 1C]. Diffusion tensor imaging (DTI) with voxel-based analysis of fractional anisotrophy (FA) and mean diffusivity (MD) revealed reduced FA and increased MD predominantly in the anterior CC [Figures 1D and E]. FA values in the genu and splenium of CC were 0.41 and 0.78, respectively; MD

values were 1.42 and  $0.83 \times 10^{-6}$  mm<sup>2</sup>/s. Mild atrophy was noted in the dorsal cord. Abnormal high signal intensity was seen in the dorsal column of thoracic cord at the level of D3-D4 [Figure 1F].

#### Case 2

A 35-year-old, nondiabetic, nonhypertensive female, who is the elder sister (first degree relative) of the patient described in Case 1, presented with insidious onset progressive gait disturbances and frequent falls for the last 10 years.

Physical examination was unremarkable except for bilateral pes cavus. Neurological examination showed dysarthria. There was no evidence of muscle wasting. Power in both the lower limbs was grade III in all groups of muscles. Deep tendon reflexes in both upper and lower limbs were symmetrically brisk and plantar response was bilaterally extensor. MRI brain revealed diffuse atrophy and long repetition time (TR) hyperintensities in periventricular white matter and centrum semiovale [Figure 2A]. CC appeared unremarkable morphologically. Significant changeswith increased MD and FA reduction were found in the visible lesions and CC (FA in genu and splenium were 0.61 and



Figure 1 (A-F): (A) MRI brain sagittal T2-weighted image showing thin anterior corpus callosum (white arrow) with mild atrophy. (B) MRI brainaxial T2 FLAIR showing periventricular frontal (ears of lynx appearance) white matter hyperintensity (white open arrow) and thin genu of corpus callosum (white solid arrow). (C) MRS brain showing no abnormal metabolite peaks. (D) DTI showing significantly reduced fractional anisotropy in anterior part of corpus callosum. (E) DTI showing decreased oriental coherence of fiber tracts. (F) MRI dorsal spine axial T2 Weighted image showing spinal cord atrophy and hyperintensity in left posterolateral aspect of the cord (open white arrow)



Figure 2 (A and B): (A) MRI brainaxial T2 FLAIR showing white matter hyperintensities in bilateral centrum semiovale region (white open arrow). (B) MRI cervical spine axial T2-weighted image showing spinal cord atrophy and hyperintensity in the centrolateral aspect of the cord (open white arrow)

0.72, respectively, and MD was 1.01 and  $0.87 \times 10^{-6}$  mm<sup>2</sup>/s in the genu and corpus callosum, respectively). MRS, however, showed normal metabolites. There was evidence of mild atrophy of cord in cervicothoracic region with hyperintensity in the centrolateral aspect which possibly signifies degeneration in the lateral corticospinal tract [Figure 2B].

In both cases, MRI was primarily done to rule out obvious pathology causing similar symptoms. Clinical mimickers include primary or secondary brain and spinal cord neoplasms, spinal arteriovenous malformations, inherited or acquired disorders of metabolism, motor neuron diseasessuch asamyotrophic lateral sclerosis, and infections such asneurosyphilis and HIV. Final diagnosis was made according to the clinical criteria proposed by Harding in 1984.<sup>[1]</sup> Both patients were clinically classified as "complicated" HSP. Genetic analysis for confirmative diagnosis could not be done due to poor socioeconomic status of the patients.

### Discussion

Hereditary spastic paraplegia (HSP) is a heterogeneous group of familial neurodegenerative disorders characterized by progressive lower limb spasticity. Clinically, they are classified as "pure" when spastic paraplegia exists in isolation and as "complicated" when other major clinical features such as mental retardation, optic atrophy, retinopathy, extrapyramidal symptoms, ataxia, deafness, cerebellar signs, muscle wasting, epilepsy, and ichthyosis are present. Both patients in this case report were clinically classified as "complicated" HSP.Genetically autosomal dominant, autosomal recessive, and X-linked recessive forms of inheritance are seen with both pure and complicated forms.<sup>[1,2]</sup> Pedigree analysis of this family revealed that no other first or second degree relative was affected by this disorder. Because the disease appeared in both sexes with equal frequency and the affected offsprings were born to unaffected parents, inheritance pattern was most likely to be autosomal recessive.Genetic locus is commonly linked to chromosome 15q13-15[SPG11gene] which accounts for 41–77% of reported HSP.  $^{\mbox{\tiny [2]}}$ 

MRI of the neuraxis may appear normal. However, there is a spectrum of MR findings seen in patients with HSP.<sup>[3]</sup> These include mild brain and spinal cord atrophy, high T2 signal intensity in the posterior limb of the internal capsule, thinning of the CC, and nonspecific white matter hyperintense lesions in the periventricular white matter and centrum-semiovale region.<sup>[4,5]</sup> Gray matter changes are unlikely in pure HSP. In the complicated form, there is widespread grey matteratrophy, particularly at the basal ganglia, which explains the more heterogeneous phenotype that frequently includes parkinsonism and dystonia.<sup>[6]</sup> These findings in isolation are not useful in diagnosis but when present simultaneously along with spinal cord changes are highly suggestive of HSP. Additional reported findings include bilateral medial frontal atrophy, widening of interhemispheric fissure, and reduced size of thalamus.

Single-voxel proton MRS may reveal reduced concentrations of N-acetylaspartate (NAA), creatine (Cr), and choline (Cho) and elevated levels of myoinositol. However no such finding was noted in the present study. DTI often shows increased mean diffusivity and reduced fractional anisotropy in the CC and periventricular white matter, compatible with damaged myelinated axons.<sup>[7]</sup> Brain MRI and DTI performed on four HSP patients and 15 age-matched healthy subject by Oğuz et al.<sup>[7]</sup> reported that average FA values in genu and splenium were 0.55 and 0.72, respectively. In comparison, the values in healthy controls were 0.81 and 0.87. Average MD values were 1.07 and  $0.89 \times 10^{-6}$  mm<sup>2</sup>/s in the genu and splenium of CC, respectively.<sup>[7]</sup> Reported values were similar to that in the present study, with the genu and anterior part of the body being most severely affected. Aghakhanyanet al.[8] in a case series evaluating 12 patients with HSP and 12 healthy controls showed decreased FA in multiple regions including the bilateral anterior thalamic radiations, corticospinal tracts, CC with forceps major and minor, and parts of the inferior and superior longitudinal fascicule. Whether the thinning of CC represents a congenital hypoplasia or progressive atrophy remains unknown. However, because the severity of atrophy did not correlate with disease duration, it was more probably considered a hypoplasia.<sup>[5]</sup> Bénézit et al.,<sup>[9]</sup> however, reported that congenital hypoplasia of CC appears as a more homogeneous reduction of the callosal size in which homotopic cortical areas of the two hemispheres are connected, implying a preservation of the callosal subdivisions (rostrum, genu, body, and splenium from its anterior to its posterior extremities), but with a restricted number of axons. Asymmetrical changes in HSP can thus probably be attributed to progressive atrophy.

The two can often be differentiated objectively by means of DTI. Diffusion tensor model thatenables the quantification of diffusion parameters (e.g., fractional anisotropy, mean diffusivity), and reflect the tissue microstructure (fibers organization, compactness, density, and maturation) thus shows abnormalities in both congenital hypoplasia and degeneration. However, Bénézit *et al.* reported that the patients with CC hypoplasia showed less severe changes in diffusion parameters (FA  $\simeq 0.67$  and MD  $\simeq 1.05 \times 10^{-6}$ ) as compared to those with dysgenesis or degeneration.<sup>[7,9]</sup>

Krabbe *et al.*<sup>[10]</sup> reported significant atrophy of the upper spinal cord, especially D3 and D9 levels, in patients with HSP compared with the controls, which corresponded neuropathologically to degeneration of the lateral corticospinal tracts, uncrossed pyramidal tracts, and fasciculus gracilis (posterior columns of the spinal cord) from the lumbar level up to the upper cervical level. The neuroradiologic findings are not constant and vary among the different phenotypes and stage of HSP. Furthermore, in the same family, the degree and location of axonal degeneration may differ depending on the gene penetrance. Despite the odds, it is necessary to be aware of this rare condition. Future longitudinal studies with multiple MRI parameters, increased sample size, and a spectrum of phenotypes will be needed to shed further light on the radiological aspects of this morbid disease.

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#### **Conflicts of interest**

There are no conflicts of interest.

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