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Case Report

Radiology Section

Hallervorden-Spatz Syndrome: A Case Report

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ABSTRACT

Hallervorden-Spatz syndrome is a rare disease entity with only a few cases reports available in radiological literature. Though, the definitive diagnosis of the disease is by histopathological examination, radiological investigations by detecting certain near pathognomonic features play an important role in narrowing down to the diagnosis in patients who present with vague symptoms, signs and thus vast clinical differential diagnoses.

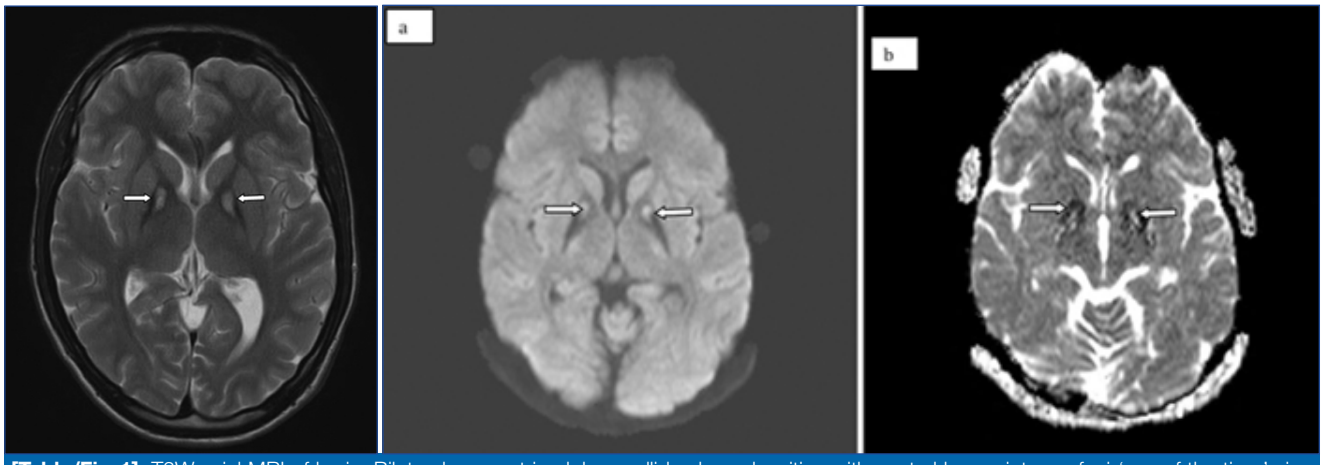
Keywords: Bilateral globus pallidi, Dystonia, Eye of the tiger sign

CASE REPORT

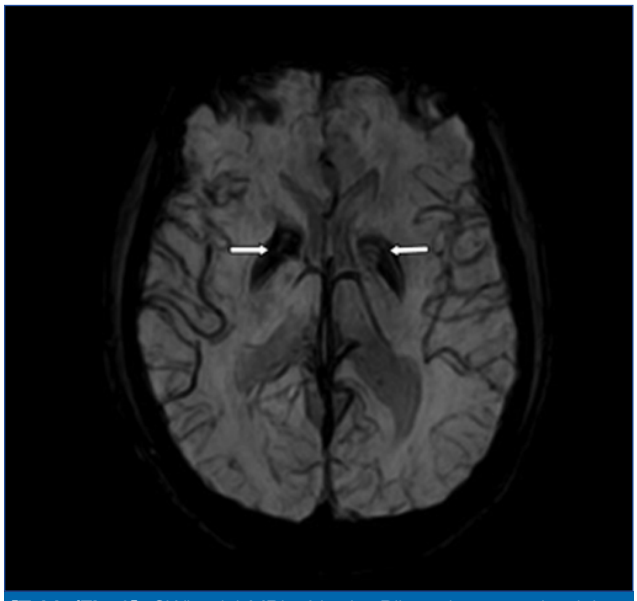
A 17-year-old male presented to the Paediatric Department of our hospital with complaints of slurred speech, involuntary movements of his neck, left upper limb, decrease in intelligence and social interaction for the past 12 years. The boy was born from a non consangineous marriage, youngest among the three children in the family with no similar history in his siblings. The birth of the boy was a full term institutional normal vaginal delivery and the perinatal period was uneventful. There was no history of hospitalisation during his childhood or any recent change in vision. The boy has not received any treatment for similar complaints in the past.

On examination, the boy was found to have cervical and left upper limb dystonia with increased tone of the neck, left upper limb muscles. Laboratory investigations showed mildly increased serum iron values of 186 µg/dL and total iron binding capacity was found to be normal. Ophthalmological investigations were found to be normal.

MRI brain was performed on a 1.5T scanner. The study showed symmetric hypointensity in bilateral globus pallidi, with a central hyperintensity on T2W images which has been described as 'eye of the tiger sign' in literature [Table/Fig-1]. Similar hypointensities were also seen on the FLAIR and diffusion weighted imaging [Table/Fig-2a,b]. Susceptibility effect seen as marked hypointensity in bilateral globus pallidi on Susceptibility Weighted Imaging (SWI) images suggest deposition of iron [Table/Fig-3]. Based on the clinical assessment and the typical MRI findings, was considered as



[Table/Fig-1]: T2W axial MRI of brain: Bilateral symmetric globus pallidus hypodensities with central hypereintense foci-'eye of the tiger' sign (white arrows); **[Table/Fig-2a,b]:** DWI and ADC axial MRI of brain also show 'Eye of the tiger' sign (white arrows) with no evidence of diffusion restriction.



[Table/Fig-3]: SWI axial MRI of brain: Bilateral symmetric globus pallidus susceptibility artefacts (white arrows) suggesting deposition of iron which is a paramagnetic substance.

provisional diagnosis of Hallervorden- Spatz syndrome.

Consent: This case report has been produced with consent from the parents.

DISCUSSION

Hallervorden-Spatz disease also known as Pantothenate Kinase-Associated Neurodegeneration (PKAN) is caused by mutations in the gene which encodes Pantothenate Kinase 2 *(PANK 2)*. *PANK 2* is responsible for the production of coenzyme A in mtiochondria.

The diagnosis of Hallervorden-Spatz syndrome is done based on clinical features, imaging findings, laboratory parameters while the definitive diagnosis of a Hallervorden-Spatz disease is established with the help of histopathological examination. Genetic testing could not be performed in this patient due to unavailability of such tests in our institution and hence differentiation from other types of Neurodegeneration associated with Brain Iron Accumulation (NBIA) could not be made.

The findings in our case were similar to radiological findings of PKAN described by Kruger MC et al., [1]. The clinical features and radiological findings in our case were also found to be similar to that of the case reported by Asumal KB et al., [2].

The syndrome is categorised under NBIA-Classic NBIA' has an early onset in infancy and manifests as dystonia, rapidly progressive gait impairment, choreoathetoid movements, dysarthria, and decline in cognition. 'Atypical NBIA' has a late onset in adolescence or adulthood with slower progression and was found to occur due to similar genetic mutations. The clinical manifestations of the disease reflect the involvement of basal ganglia and striatum [3-5]. Approximately, one fifth of the cases have retinitis pigmentosa. Blephrospasm, ballism, and ptosis of eyelid are rare presentations. The closest differential diagnosis on the basis of clinical presentation is Wilson's disease [2,6].

The histopathological basis of the disease is explained by the deficiency of coenzyme A which results in the accumulation of cysteine containing enzyme substrates, these in turn result in chelation of iron. Vacuolisation, regions of neuronal loss, gliosis, and axonal swelling are present in the central nervous system and peripheral nerves. These pathologic changes combine to form signal abnormality in the globus pallidus [3,4].

The radiological findings in the disease can be explained by accumulation of iron in the globus pallidus which causes dramatic T2 shortening (hypointense signal). Within these hypointense areas, regions of vacuolisation and gliosis occur centrally causing T2 prolongation (hyperintense signal). These changes produce an "eye of the tiger" appearance on MRI brain sequences [3]. Recent studies suggest that "eye of the tiger" is not pathognomonic for PKAN [7].

Neuroaxonal degeneration can be assessed by proton MR Spectroscopy focussing on N-Acetyl-Aspartate (NAA) and myoinositol. Generally, NAA reflects presence of neuronal tissue and in PKAN, NAA/Cr ratio is increased in the affected regions. Myoinositol is considered a marker of glial proliferation and myoinositol/Cr ratio is reduced in the affected regions.

The differential diagnoses for the "eye of the tiger" appearance on MRI are corticobasal ganglionic degeneration, early onset levodopa-responsive Parkinsonism, aceruloplasminaemia and neuroferritinopathy. Mitochondrial encephalopathies, Leigh disease and Wilson's disease also show lentiform nucleus involvement in which predominant putamen involvement is seen rather than the globus pallidus [8,9].

The diagnosis of Hallervorden-Spatz syndrome is done based on clinical features, imaging findings, laboratory parameters while the definitive diagnosis of a Hallervorden-Spatz disease is established with the help of histopathological examination.

There is no specific treatment for Hallervorden-Spatz disease and the management is mostly symptomatic. Recent studies show that marked improvements in quality of life, dystonia have been achieved with drugs like intrathecal Baclofen and oral deferiprone [9]. Surgical procedures like stereo pallidotomy and thalamotomy have also been used for reduction of dystonia [10].

CONCLUSION

Hallervorden-Spatz syndrome, a rare disease is caused by genetic mutations in gene encoding for *PANK 2*. The disease

causes neurodegeneration which is associated with brain iron accumulation commonly involving the basal ganglia and striatum. In this case, "eye of the tiger" sign which is near pathognomonic sign for the disease in radiology is well demonstrated. This case report emphasises the importance of radiological investigations in being an important aid in prompt diagnosis of the disease. Deferring radiological investigations in such patients can cause misdiagnosis of the disease and deterioration of quality of life.

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