International Journal of Research in Medical Sciences
*Mondal S et al. Int J Res Med Sci. 2014 Feb;2(1):370-372*
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: 10.5455/2320-6012.ijrms20140277

**Case Report**

# Eye of the tiger sign in neurodegeneration with brain iron accumulation: a case report

**Sumantro Mondal[1]*, Debasish Dey[2], Tony Ete[1], Debanjali Sinha[1], Arijit Nag[1], Atanu Chakraborty[1], Amod Prasad[3]**

[1]Department of Medicine, Institute of Post Graduate Medical Education and Research, Kolkata, West Bengal, India
[2]Department of Radiology, Bangur Institute of Neurosciences, Kolkata, West Bengal, India
[3]Department of Medicine, R. G. Kar Medical College and Hospital, Kolkata, West Bengal, India

**Received:** 23 December 2013
**Accepted:** 7 January 2014

***Correspondence:**
Dr. Sumantro Mondal,
E-mail: drmsumantro@gmail.com



## ABSTRACT

Neurodegeneration with brain iron accumulation (NBIA) is a rare autosomal recessive disorder characterized by abnormal accumulation of ferritin in globus pallidus of brain. Magnetic resonance imaging (MRI) of brain demonstrates a characteristic 'eye-of-the-tiger' sign. We describe a case of NBIA in a child with classical clinical and MRI of brain features.

**Keywords:** Neurodegeneration with brain iron accumulation, MRI, Eye of the tiger

## INTRODUCTION

The classic form of NBIA is manifested as extra pyramidal symptoms and retinal degeneration. This condition encompasses a variety of disorders. The clinical phenotype of Wilson disease, neuroacanthocytosis shares some similarity with NBIA and offers diagnostic challenges to the physician. MRI of brain is particularly helpful in this scenario to differentiate NBIA from its mimickers. Our patients presented with early onset progressive extra pyramidal features and final diagnosis of NBIA was secured from characterized MRI findings.

## CASE REPORT

A nine years old boy presented with intermittent abnormal flexor posturing of face, both upper limbs and involuntary jerky movements along with increased stiffness of all four limbs for last eight months. The symptoms hampered his walking and other daily normal activities. The disease course was progressive. He also had mild coarse tremor. Abnormal posturing, movements and tremor were relieved during sleep. There was no history of fever, convulsion, and jaundice preceding or during his current illness. His birth history was uneventful and his elder brother was having normal health. Examination showed normal higher mental functions, increased tone in all four limbs, exaggerated deep tendon reflexes with bilateral extensor planter response. Coarse tremor of limbs was present at rest. Sensory, cerebellar and bladder bowel functions were unremarkable. Examinations of the other systems were normal. Ophthalmoscopic examination was normal. Routine blood investigations, liver and renal function tests were normal. Serum ceruloplasmin and ferritin level were within normal limits with a normal 24 hour urinary copper excretion value (48 microgram/day). Peripheral blood smear did not reveal any acanthocyte. Slit lamp examination of eye was negative for Kayser-Fleischer ring. Magnetic resonance imaging (MRI) of brain revealed marked hypo intensity in bilateral globus pallidus surrounding an area of hyperintensity at its

medial portion producing the classical 'eye-of-the-tiger' sign in axial T2 weighted images (Figure 1). Marked hypo intensity of bilateral globus pallidus region was also evident on gradient echo sequence indicative of accumulation of highly paramagnetic substance (Figure 2). Typical clinical presentation and classical MRI features clinched the final diagnosis of pantothenate kinase associated neurodegeneration with brain iron accumulation, a subset of NBIA.

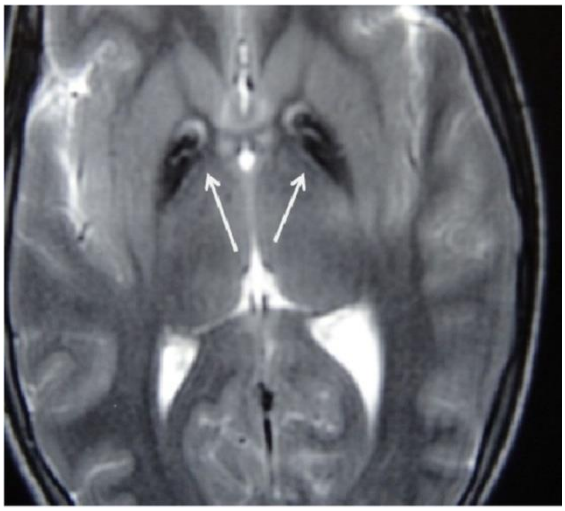

**Figure 1: Axial T2 weighted MRI of brain at the level of basal ganglia showing - hypo intense rim surrounding the antero medial hyper intense signal in bilateral globus pallid (white arrows).**

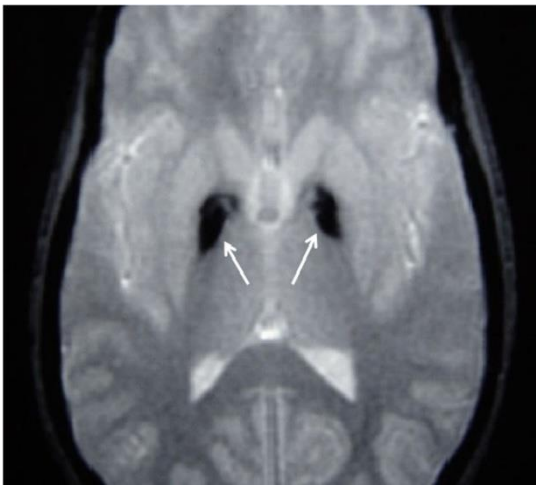

**Figure 2: Axial GRE image of brain showing - hypo intense signals in bilateral globus pallidi sparing the antero medial aspects (white arrows).**

## DISCUSSION

NBIA, formerly known as Hallervorden-Spatz syndrome consists of a group of neurodegenerative diseases with autosomal recessive inheritance. It is a very rare disease with an estimated prevalence of 1-3/1,000,000 population.[1] The disease usually affects the children and younger age population, but may also be seen in adults.[2] NBIA encompasses a group of disorders where progressive extra pyramidal features and dementia constitute the clinical phenotype.[3] The subgroups of NBIA consists of PKAN (Pantothenate kinase associated neurodegeneration), HARP syndrome, aceruloplasminemia and neuroferritinipathy. PKAN usually manifests in two forms, the childhood onset classic form with features of dystonia involving face, tongue and limbs, spasticity and abnormal movements with early loss of ambulation. Retinitis pigmentosa and acanthocytosis are other reported associations. The late onset atypical form has a slowly progressive course with features of speech abnormality and dysarthria.[4] Psychiatric problems are also present. The genetic abnormality in PKAN is deficiency or absence of pantothenate kinase 2 which is encoded by chromosome 20p13-p12.3. This enzyme is essential for CoA biosynthesis and deficiency leads to accumulation of N-pantothenoylcystien and pantethene. This may cause cellular toxicity either directly or by free radical mediated damage as an iron chelator.[5] Iron deposition, axonal spheroids, and gliosis in the globus pallidus constitutes the pathologic triad of PKAN.[6] In our patient most of the features were consistent with the classic PKAN although a number of other conditions had to be excluded before making a confident diagnosis of PKAN. Wilson disease (WD) can present with early onset dystonia, choreoathetosis and is an important differential of PKAN and must to be excluded as the treatment protocol and prognosis are distinctly different. Absence of corneal KF ring and a normal serum ceruloplasmin with normal urinary copper excretion virtually excluded the diagnosis of WD in our patient. Aceruloplasminemia, neuroferritinopathy and non PKAN NBIA were the other important diagnostic consideration in our patient. However a normal serum ceruloplasmin level ruled out the possibility of aceruloplasminemia and there was no evidence of visceral iron accumulation which is commonly seen in this condition. Unlike PKAN neuroferritinopathy usually affects elderly population in their fourth to fifth decade.

MRI of brain is the diagnostic modality for NBIA.[7] It can also distinguish PKAN from non PKAN NBIA. The 'eye of the tiger' sign seen in axial and coronal T2 weighted MRI is very characteristic of PKAN, both classical and atypical forms. This sign is produced due to diffuse low signal intensity surrounding an anteromedial area of high signal intensity in T2-weighted images and can also be demonstrated in gradient echo sequence.[8] MRI of the brain revealed the classical 'eye of the tiger' sign in our patient. The T2 hypo intensity is due to the accumulation of iron whereas the antero medial hyper intensity is the result of gliosis and spongiosis. This sign is considered highly sensitive and specific for PKAN and it can be seen in presymptomatic affected individuals.[9] Though this sign can also be found in some other conditions like multiple system atrophy, neuroferritinopathy but the contour is

irregular and the hyper intensity is laterally displaced. In this case the clinical features and the typical MRI 'eye of the tiger' sign led us to the final diagnosis of a rare neurodegenerative disorder.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: Not required*

## REFERENCES

1. Allison M. Georgy, Susan J. Hayflick. Neurodegeneration with brain iron accumulation. Orphanate encyclopedia, 2004. Available at: https://www.orpha.net/data/patho/GB/uk-NBIA.pdf.
2. Wolfang HO, Molter JC. Other degenerative syndromes that cause parkinsonism. In: Watts RL and Koller WC, eds. Movement disorders: neurologic principle sand practice. 2nd ed. New York: McGraw Hill Publishers; 1997:331-344.
3. Guillerman RP. The eye-of-the-tiger sign. Radiology 2000 Dec;217(3):895-6.
4. Benke. T, B. Butterworth. Palilalia and repetitive speech: two case studies. Brain Lang 2001;78(1):62-81.
5. Yang. E.Y, A. Campbell. Configuration of thiols dictates their ability to promote iron-induced reactive oxygen species generation. Redox Rep. 2000;5(6):371-5.
6. Halliday W. The nosology of Hallervorden-Spatz disease. J Neurol Sci. 1995;134(suppl):84-91.
7. Sethi KD, Adams RJ, et al. Hallervorden-spatz syndrome: clinical and magnetic resonance imaging correlations. Ann Neurol 1988;24(5):692-4.
8. Savoiardo M, Halliday WC, Nardocci N, et al. Hallervorden-Spatz disease: MR and pathologic findings. AJNR Am J Neuroradiol 1993 Jan-Feb;14(1):155-62.
9. Hayflick SJ, Penzien JM, Michl W, Sharif UM, Rosman NP, Wheeler PG. Cranial MRI changes may precede symptoms in Hallervorden-Spatz syndrome. Pediatr Neurol. 2001;25:166-9.

DOI: 10.5455/2320-6012.ijrms20140277
**Cite this article as:** Mondal S, Dey D, Ete T, Sinha D, Nag A, Chakraborty A, Prasad A. Eye of the tiger sign in neurodegeneration with brain iron accumulation: a case report. Int J Res Med Sci 2014;2:370-2.