Journal of the Neurological Sciences 399 (2019) 1–2

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Letter to the Editor

The “eye of the tiger” in a patient with multiple sclerosis

ARTICLE INFO

Keywords:
Eye of the tiger sign
Multiple sclerosis

Dear Editor,

The eye-of-the-tiger sign has been classically associated with pantothenate kinase-associated neurodegeneration (PKAN), also called neurodegeneration with brain iron accumulation (NBIA) type 1, and formerly known as Hallervorden-Spatz syndrome [1]. Two clinical forms of PKAN exist: the classic phenotype presents within the first decade of life and rapidly progresses, while the atypical phenotype manifests in the second to third decade of life and slowly deteriorates. Clinical features of PKAN include chorea, dystonia, bradykinesia, tremor, gait dysfunction, ataxia, rigidity, and dementia [1,2].

I am writing to describe a 45-year-old relapsing-remitting multiple sclerosis (RRMS) patient with the “eye-of-the-tiger” sign on MRI, who has been under my care for the past four years. He first experienced difficulty walking when he was 19, and although it improved, he had residual right leg weakness. When he was 21-years-old, he suffered an episode of bilateral lower extremity paresthesiae and numbness that lasted for several weeks before resolving. At age 28, he was diagnosed right optic neuritis. His neurologist diagnosed him with RRMS, and started on interferon beta-1a but due to severe flu-like reactions, he was switched to glatiramer acetate, and remained stable on this.

At age 41, he consulted with me for a second opinion regarding treatment. The neurologic deficits he described were neurogenic bladder (necessitating intermittent self-catheterization), erectile dysfunction, right leg weakness (resulting in gait dysfunction), and heat-induced fatigue. His examination revealed right leg weakness and impaired vibration sense in both lower extremities. No other findings, including Parkinsonism, dystonia, tremor, rigidity, or ophthalmoparesis were present. He had no family history of neurologic or autoimmune diseases.

I reviewed available brain MRIs. The most recent MRI available at my initial visit was a 3-Tesla brain MRI preformed when he was 37, which revealed ovoid lesions perpendicularly aligned to the lateral ventricles, typical of MS plaques. The T2-weighted images also showed bilateral symmetrical areas of high signal intensity in the anteromedial globus pallidi, surrounded by regions of low signal intensity, producing the eye-of-the-tiger sign (Fig. 1). Laboratory investigations including complete blood count, comprehensive metabolic panel, B12, ceruloplasmin, copper, and iron levels were unremarkable.

He decided to transition to oral dimethyl fumarate due to injection fatigue. Over the ensuing four years under my care, his MS-related symptoms and two follow-up 3-Tesla brain MRIs have remained unchanged. He has not developed parkinsonism, dystonia, tremor, seizures, or cognitive impairment.

While the eye-of-the-tiger sign has been classically associated with PKAN, it is by no means pathognomonic for this disorder. It has been described in other NBIA subtypes (including mitochondrial membrane protein associated neurodegeneration, and neuroferritinopathy), Wilson's disease, progressive supranuclear palsy, multiple system atrophy, corticobasal degeneration, pure akinesia with gait freezing, mutation of the manganese transporter gene SLC39A14, cervical dystonia, and organophosphate poisoning (please refer to the e-component for a complete list of references). Although these disorders do not directly affect iron metabolism, their etiopathogenetic processes can be localized to the basal ganglia, and as such, the eye-of-the-tiger could possibly be attributed to basal ganglial changes.

The eye-of-the-tiger sign has also been observed in the 3-Tesla brain MRI of a healthy adult [3], which remained stable over a two-year period, similar to how my patient's brain MRI has remained stable for four years. It is unclear why the eye-of-the-tiger sign may appear on MRIs of patients without an apparent basal ganglial disorder. It is plausible that a preclinical neurodegenerative disorder was incidentally detected by MRI; however, the eye-of-the-tiger sign is usually absent in early PKAN and can even be absent in some cases of PKAN [4,5]. Alternately, and most likely, it may represent a normal anatomical variant that is more easily detected by the higher image quality and spatial resolution of the 3-Tesla MRI.

It has been proposed that the eye-of-the-tiger sign be limited to MRIs that show (1) bilateral low signal in the pallidi completely surrounding an area of high signal on T2-weighted images, and (2) no other MRI abnormalities aside from generalized atrophy [6]. My patient met the first but not the second criteria (due to the presence of MS plaques), which is why he has the “eye-of-the-tiger” sign (with inverted commas), or a pseudo-eye-of-the-tiger sign.

In conclusion, it is likely that the “eye-of-the-tiger” sign on my patient's MRI is an incidental finding, similar to that reported in a healthy adult male [3], and is not related to RRMS. More studies are needed to elucidate the anatomical reasons why this striking and memorable neuro-radiologic sign may be incidentally detected by 3-Tesla MRIs in patients without basal ganglial disorders.

Funding

None.

https://doi.org/10.1016/j.jns.2019.02.003
Received 7 November 2018; Received in revised form 3 January 2019; Accepted 1 February 2019
Available online 05 February 2019
0022-510X/

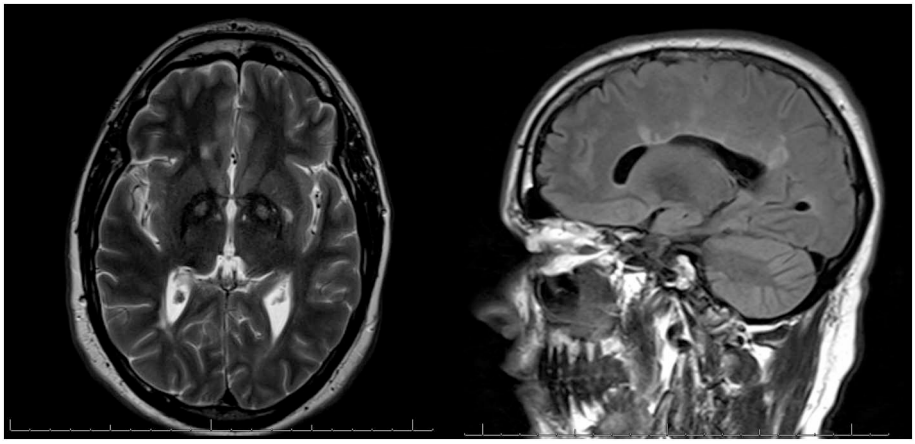

Fig. 1. The axial view T2-weighted MR image on the left panel reveals bilateral symmetrical areas of high signal intensity in the anteromedial globus pallidi, surrounded by regions of low signal intensity, producing the eye-of-the-tiger sign. The sagittal view fluid attenuated inversion recovery (FLAIR) sequence in the right panel demonstrates the ovoid lesions oriented perpendicularly to the surface of the lateral ventricles, which are typical of multiple sclerosis plaques.

Financial disclosures and conflicts of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2019.02.003.

References

[1] K.D. Sethi, R.J. Adams, D.W. Loring, et al., Hallervorden-Spatz syndrome: clinical and magnetic resonance imaging correlations, Ann. Neurol. 24 (1988) 692–694.
[2] S.J. Hayflick, M.A. Kurian, P. Hogarth, Neurodegeneration with brain iron accumulation, Handb. Clin. Neurol. 147 (2018) 293–305.
[3] S.J.A. Van den Bogaard, M.C. Kruit, E.M. Dumas, R.A.C. Roos, Eye-of-the-tiger-sign in a 48 year healthy adult, J. Neurol. Sci. 336 (2014) 254–256.
[4] R.F. Delgado, P.R. Sanchez, H. Speckter, et al., Missense PANK2 mutation without "eye of the tiger" sign: MR findings in a large group of patients with pantothenate kinase-associated neurodegeneration (PKAN), J. Magn. Reson. Imaging 35 (2012) 788–794.
[5] L. Chiapparini, M. Savoiardo, S. D'Arrigo, et al., The "eye-of-the-tiger" sign may be absent in the early stages of classic pantothenate kinase associated neurodegeneration, Neuropediatrics 42 (2011) 159–162.
[6] K.D. Sethi, S.H. Mehta, J.C. Morgan, Defining the eye-of-the-tiger sign, JAMA Neurol 72 (2015) 606.

Shin C. Beh*
Department of Neurology, University of Texas Southwestern Medical Center, United States
E-mail address: scjbeh@gmail.com.

* Corresponding author at: Department of Neurology, 5323 Harry Hines Blvd, Dallas, TX 75390, United States.