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The "Eye of the tiger sign" in Progressive Supranuclear Palsy: Is it a coincidence or not?

Hamit Genç[1*], Nevra Oksuz[2], Okan Doğu[2]

[1]*Gaziantep Dr. Ersin Arslan Training and Research Hospital, Department of Neurology, Gaziantep, Turkey*

[2]*Mersin University Faculty of Medicine, Department of Neurology, Mersin, Turkey*

Abstract

Progressive supranuclear palsy (PSP); is a neurodegenerative disorder involved in atypical parkinsonism syndromes. The classical clinical presentation is postural instability, falls, downward paralysis, frontal dementia, and symmetric akinetic-rigid parkinsonism. The atrophy of the mesencephalon in magnetic resonance imaging (MRI) is an important marker in diagnosing the disease. Recently, a few PSP cases reported the "eye of the tiger" sign on MRI. The "eye of the tiger" sign, in globus pallidus, is a sign that bilaterally symmetrically located low signal intensity and central longitudinal hyperintensity are observed. While previously a specific finding for the pantothenate kinase-associated neurodegeneration (PKAN), it is no longer considered specific because of the reported cases of non-PKAN with the "eye of the tiger" sign such as neuropherritinopathy, multi-system atrophy, corticobasal degeneration. In this report, we aimed to contribute to the literature by presenting two PSP cases in which the "eye of the tiger" sign was observed.

Key words*: Progressive supranuclear palsy; the "eye of the tiger" sign; iron accumulation*

*** Corresponding author:** Hamit Genç, E-mail: hgenc8987@gmail.com, ORCID ID: 0000-0002-6198-2883

Background

Progressive supranuclear palsy (PSP) is a degenerative disorder of the central nervous system and one of the Parkinson-plus syndromes. The classic clinical features of PSP are postural instability, falls, supranuclear palsy with downgaze paralysis, frontal dementia, and symmetric akinetic-rigid parkinsonism (1).

Despite several diagnostic studies, the diagnosis of PSP is made only by history, neurological examination, and magnetic resonance imaging (MRI). In MRI studies, distinctive atrophy of mesencephalon tegmentum is a sign of disease (2). Recent MRI studies have shown the "eye of the tiger" sign in some PSP patients (3). The eye of the tiger sign is typically seen in iron accumulation diseases such as Pantothenate Kinase-Associated Neurodegeneration (PKAN) and neuroferritinopathy (4). In this article, we aimed to present two PSP patients with the "eye of the tiger sign" finding on MRI.

Case 1

An 83-year-old man admitted to the nephrology department with acute renal failure was referred to our clinic because of disorientation, hallucinations, and loss of consciousness. He had been suffering from forgetfulness for the last three years. His daily activities worsened, and he has dysphagia, dysarthria, and behavioral changes. His son had noticed that he had significantly slowed down while walking and sometimes fell. For the last year, complaints of urinary incontinence have appeared. His previous records indicated ongoing problems with myelodysplastic syndrome for the last year. On neurologic examination, he was apathic. Upward gaze paralysis, hypomimia, antecollis, axial rigidity, and bradykinesia were present. No tremor was evident on examination. No pyramidal symptoms were detected. His standardized mini-mental test score was 14/30 (Orientation: 3/10, memory: 3/3, attention and calculation: 0/5, recall: 0/3, language 8/9). On cerebral MRI, a "hummingbird sign "in the sagittal T1 section and a "mickey mouse" appearance in the axial T2 section were seen (Figure 1).

In addition, the eye of the tiger sign on the axial T2 section and iron accumulation in globus pallidus, substantia nigra, and red nucleus on SWI (Susceptibility Weighted Imaging) was seen (Figure 2).

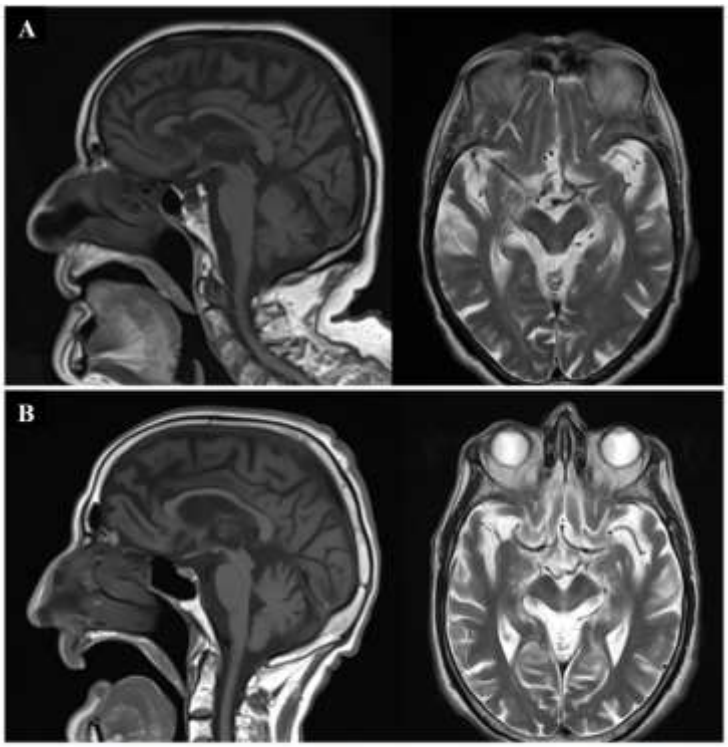

Figure 1: A; Case 1, **B;** Case 2, In cerebral MRI, it has shown" hummingbird sign" at mesencephalon in T1 midsagittal section examination, and "mickey mouse sign" in axial T2 section.

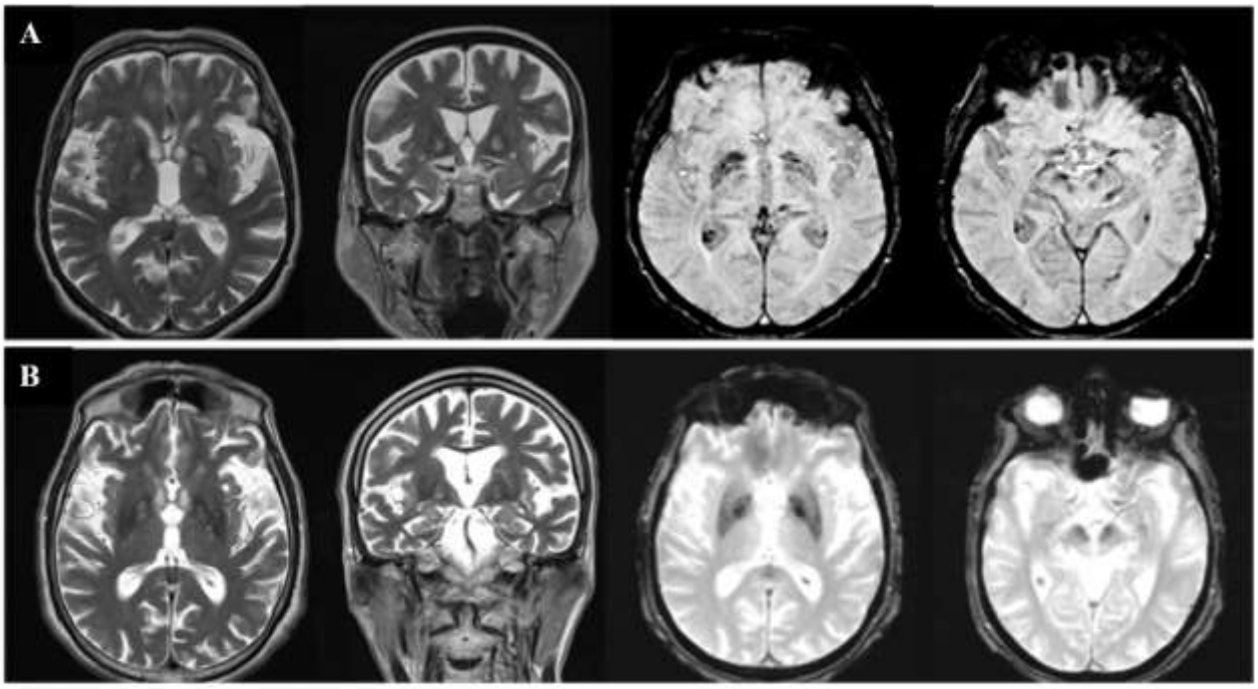

Figure 2: A; Case 1, **B;** Case 2, Cerebral MRI examination shows a view consistent with the eye of the tiger sign in the left-sided axial T2 section and next to the coronal section of the same area. In the two sections on the right, observed view consistent iron accumulation in axial examinations of case 1 with SWI and case 2 with gradient echo in bilateral globus pallidus, substantia nigra, and red nucleus.

The patient was diagnosed with PSP-Richardson syndrome (RS) according to the 2017 MDS (The Movement Disorder Society) criteria, and his UPDRS (Unified Parkinson's Disease Rating Scale) score was 71 points. 62.5 mg madopar (combination of levodopa and benserazide hydrochloride) three times per day was given to the patient, and after one week, his UPDRS score decreased to 50 points.

Case 2

A 77-year-old man presented to our clinic with a 5-month history of dizziness, complaining of walking difficulties, dysarthria, and dysphagia. He reported that he would suddenly fall without a trigger. He did not have any disease in his history. On examination, he had dysarthria, hypophonia, palilalia, and dysphagia. There was moderate bilateral rigidity, bradykinesia, and reduced blinking frequency and facial expression. He had impaired vertical gaze, predominantly on upward gaze. He had a stooped posture and reduced arm swing without a tremor on gait examination. On the pull test, he had significant retropulsion and would have fallen if not caught by the examiner. His blood tests, including ferritin and ceruloplasmin, were within normal limits. On cerebral MRI, a "hummingbird sign "in the sagittal T1 section and a "mickey mouse" appearance in the axial T2 section were seen (Figure 1). The eye of the tiger sign on axial T2 and iron accumulation in globus pallidus, substantia nigra, and red nucleus were also seen on gradient echo (Figure 2). According to the 2017 MDS criteria, the patient was diagnosed with PSP-RS, and his UPDRS score was 54. After a mild response to the levodopa test, a combination of levodopa and carbidopa 125/12,5 mg three times per day and rasagiline 1 mg per day was begun.

Discussion

The "eye of the tiger sign" is a radiological sign. This sign indicates abnormally low signal intensity and central longitudinal hyperintensities symmetrically located in the globus pallidus in T2-weighted MR images. This sign is the most prominent radiological feature of iron accumulation in the brain, formerly called Hallervorden-Spatz disease. Iron is not present in the central nervous system at birth; however, it occurs throughout life in healthy adults. The highest concentration is reached in the globus pallidus, primarily in the form of the metalloprotein ferritin (5).

Differential diagnosis of symmetrical basal ganglion involvement, except PKAN, includes mitochondrial diseases (Leigh disease), methylmalonic acidemia, Wilson's disease, toxin exposure (CO, Methanol, Cyanide), and hypoxic damage. The

exciting part of our cases was MRI findings, including the "eye of the tiger sign" and iron deposition in the bilateral basal ganglia and the substantia nigra (Figure 2) (6). Nevertheless, our patients' history, age, and other clinical findings were inconsistent with these situations.

The eye of the tiger sign was observed in almost all patients with PKAN. This sign was also observed in some patients with a multi-system atrophy-parkinsonian type (MSA-P) (7), corticobasal degeneration (CBD) (8), and pure akinesis (9). Davie CA et al. also reported the "eye of the tiger sign" in a few PSP patients, as in our cases. Iron accumulation was not evaluated in MSA, pure akinesia, and CBD patients in these cases (7-9). Tokunori ve Ikeda has reported a case of atypical parkinsonism in which iron accumulation was evaluated and seemed to be the "eye of the tiger sign"; there was no evidence of iron deposition. For this reason, they called this sign the "pseudo eye of the tiger sign" and emphasized the need for research on iron accumulation in these cases (10).

Besides, Akashi et al. described a 60-year-old male patient who was clinically diagnosed with PSP and detected changes of spesific to the PKAN and changes in the typical PSP in the postmortem examinations (11). Then, Yamamoto et al. conducted a case of a patient with the characteristics of both pathologies has been reported (12).

Iron accumulation secondary to myelodysplastic syndrome accompanied by PSP disease as coincidence may be developed in the first case. Iron accumulation occurs due to excessive iron absorption from the intestinal tract caused by chronic anemia and recurrent blood transfusions. Therefore, iron accumulation exists in both parenchymal tissues and reticuloendothelial system. Even if there is no transfusion in these patients, iron accumulation occurs (13). Both cases had no transfusion history, and the ferritin level was within the normal range. In the second case, there was no history of disease-causing iron accumulation. It was demonstrated iron deposition with MRI in both patients indirectly.

Conclusion

These cases bring to mind a question "Are the patients with PSP with the "eye of tiger sign" another part of a spectrum of iron accumulation diseases." Another question is, "Does iron accumulation originate secondary to the accompanying diseases or increased iron accumulation due to advanced age?". If iron accumulation is due to advanced age in case, why do we not see the same sign in all patients with PSP? We

only think more case reports and studies can resolve this uncertainty.

References

1. Morris, H. R., N. W. Wood, and A. J. Lees, 2016, "Progressive supranuclear palsy (Steele-Richardson-Olszewski disease)." *Neurology Update: Reviews for Continuing Professional Development*: 185.

2. Righini, A., Antonini, A., De Notaris, R., et al., (2004). MR imaging of the superior profile of the midbrain: differential diagnosis between progressive supranuclear palsy and Parkinson disease. *American J of neuroradiol*, *25*(6), 927-932.

3. Davie, C. A., Barker, G. J., Machado, C., Miller, D. H., & Lees, A. J. (1997). Proton magnetic resonance spectroscopy in Steele-Richardson-Olszewski syndrome. *Mov Dis: Official Journal of the Movement Disorder Society*, *12*(5), 767-771. https://doi.org/10.1002/mds.870120525

4. McNeill, A., Birchall, D., Hayflick, S. J., et al., 2008, T2* and FSE MRI distinguishes four subtypes of neurodegeneration with brain iron accumulation. *Neurol*, *70*(18), 1614-1619. https://doi.org/10.1212/01.wnl.0000310985.40011.d6

5. Guillerman, R. Paul, 2000, "The eye-of-the-tiger sign." *Radiol* 217.3: 895-896. https://doi.org/10.1148/radiology.217.3.r00dc31895

6. Osborn, A. G., 1994, "Acquired metabolic, white matter, and degenerative diseases of the brain." *Diagn neuroradiol. St. Louis, Mosby*: 748-784.

7. Strecker, K., Hesse, S., Wegner, F., Sabri, O., Schwarz, J., & Schneider, J. P. (2007). Eye of the tiger sign in multiple system atrophy. *European J of Neurol*, *14*(11), e1-e2. https://doi.org/10.1111/j.1468-1331.2007.01925.x

8. Molinuevo, J. L., Muñoz, E., Valldeoriola, F., & Tolosa, E. (1999). The eye of the tiger sign in cortical-basal ganglionic degeneration. *Mov dis: official journal of the Movement Disorder Society*, *14*(1), 169-171. https://doi.org/10.1002/1531 8257(199901)14:1%3C169::AID MDS1033%3E3.0.CO;2-%23

9. Erro, R., Amboni, M., Vitale, C., et al., 2011, The “eye of the tiger” sign in pure akinesia with gait freezing. *Neurol Sci 32*, 703-705. https://doi.org/10.1007/s10072-011-0589-1

10. Ikeda, T., Matsuo, Y., Ueda, A., & Hirano, T. (2013). Pseudo eye of the tiger sign in atypical Parkinsonism. *Neurol Sci*, *34*, 777-778. https://doi.org/10.1007/s10072-012-1113-y

11. Akashi, T., Arima, K., Maruyama, N., Ando, S., & Inose, T. (1989). Severe cerebral atrophy in progressive supranuclear palsy: a case report. *Clin neuropath*, *8*(4), 195-199.

12. Yamamoto, T., Kawamura, J., Hashimoto, S., et al., 1991, Pallido-nigro-luysian atrophy, progressive supranuclear palsy and adult onset Hallervorden-Spatz disease: a case of akinesia as a predominant feature of parkinsonism. *J Neurol Sci*, *101*(1), 98-106. https://doi.org/10.1016/0022-510X(91)90023-Z

13. Yurci, A., & All, A., 2002, MİYELODİSPLASTİK SENDROMDA DEMİR BİRİKİMİ VE TEDAVİSİ: OLGU SUNUMU. *J of Istanbul Faculty of Med*, *65*(4).