Journal of the Neurological Sciences 399 (2019) 94–96

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

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

Letter to the Editor

Striatal dopamine transporter abnormalities associated with midbrain hemiatrophy

ARTICLE INFO

Keywords:
Midbrain hemiatrophy
Wallerian degeneration
Dying back
[^{123}I]-FP-CIT
SPECT

Dear Editor,

Single photon emission computed tomography (SPECT) with a dopamine transporter-specific radiotracer, [^{123}I]-N-ω-fluoropropyl-2β-carbomethoxy-3β-(4-iodophenyl) nortropane ([^{123}I]-FP-CIT), is widely used to evaluate presynaptic nigrostriatal degeneration. Direct ischemic changes in the striatum and midbrain are known to reduce striatal [^{123}I]-FP-CIT uptake [1,2]. However, it is unclear whether midbrain hemiatrophy with pyramidal tract degeneration also affects striatal [^{123}I]-FP-CIT uptake. Here, we describe abnormal [^{123}I]-FP-CIT uptake in two patients with midbrain hemiatrophy and secondary ischemic pyramidal damage.

1. Case reports

1.1. Case 1

A 77-year-old man complained of progressive gait instability, and presented with left hemiparesis with bradykinesia. Brain infarction in the right posterior limb of the internal capsule and the occipital lobe occurred 7 years prior to presentation at our hospital. Previous brain magnetic resonance imaging (MRI) revealed no abnormalities in the midbrain region (Fig. 1A). Current brain MRI showed no striatal abnormalities, but showed previous infarctions in the right posterior limb of the internal capsule and occipital lobe (Fig. 1B). Additionally, midbrain hemiatrophy was clearly observed (Fig. 1C). The substantia nigra was almost normal status and appeared as a band of signal hypointensity on MRI (Fig. 1D–F). Despite normal [^{131}I]-meta-iodobenzylguanidine (MIBG) myocardial scintigraphy findings, SPECT revealed severely reduced right striatal [^{123}I]-FP-CIT uptake (Fig. 1G). He was diagnosed with vascular parkinsonism.

1.2. Case 2

A 76-year-old man with old paramedian pontine infarction complained of bradykinesia and cognitive decline, and presented with fluctuating attention. He was diagnosed with clinical probable dementia with Lewy bodies. A T2-weighted MRI performed 4 years prior revealed no abnormalities in the midbrain (Fig. 1H). A diffusion-weighted MRI revealed a right-side paramedian pontine infarction (Fig. 1I). A brain MRI in the current presentation revealed a normal right striatum, a previous infarction in the left striatum, and midbrain hemiatrophy (Fig. 1J, K). The substantia nigra was approximately perceived as the hypointense band, while equivocal (Fig. 1L); though it might have been affected secondary by pyramidal tract degeneration and peduncle atrophy (Fig. 1K, L). The right peduncle presented a slightly hyperintense lesion. The presence of a longitudinally continuous hyperintense lesion along the right pyramidal tract, spanning the lower pons to the mesencephalon, is more consistent with degeneration than ischemia (Fig. 1M). This change might have had a significant influence in the vicinity of the substantia nigra.

SPECT revealed remarkably decreased [^{123}I]-FP-CIT uptake, and mildly decreased uptake in the right and left striatum respectively (Fig. 1N). MIBG myocardial scintigraphy revealed a clear decrease in the heart-to-mediastinum ratio. However, in this case, despite a remarkably asymmetric [^{123}I]-FP-CIT uptake, the presence of a laterality of parkinsonism was unclear, even though the patient demonstrated left hemiparesis.

2. Discussion

Asymmetric striatal [^{123}I]-FP-CIT uptake has been reported in direct midbrain infarction [1,2]. Hemiparkinsonism-hemiatrophy syndrome, characterized by unilateral parkinsonism with ipsilateral body atrophy, is reportedly associated with striatal alterations in [^{123}I]-FP-CIT uptake, and midbrain hemiatrophy [3,4]. However, our patients did not demonstrate any overt direct midbrain infarction, remarkable unilateral parkinsonism, or unilateral body atrophy. Ischemia and atrophy in the midbrain have been reported to affect [^{123}I]-FP-CIT uptake [3–6]. Therefore, ipsilateral nigral abnormalities should always be explored when a patient displays striatal dopamine transporter abnormalities, especially when [^{123}I]-FP-CIT SPECT reveals prominent asymmetric presynaptic damage.

In our cases, peduncular hemiatrophy progressed after brain infarction involving the pyramidal tracts. This phenomenon is known as anterograde or orthograde degeneration (i.e., Wallerian degeneration

https://doi.org/10.1016/j.jns.2019.02.026
Received 1 December 2018; Received in revised form 15 February 2019; Accepted 15 February 2019
Available online 16 February 2019
0022-510X/

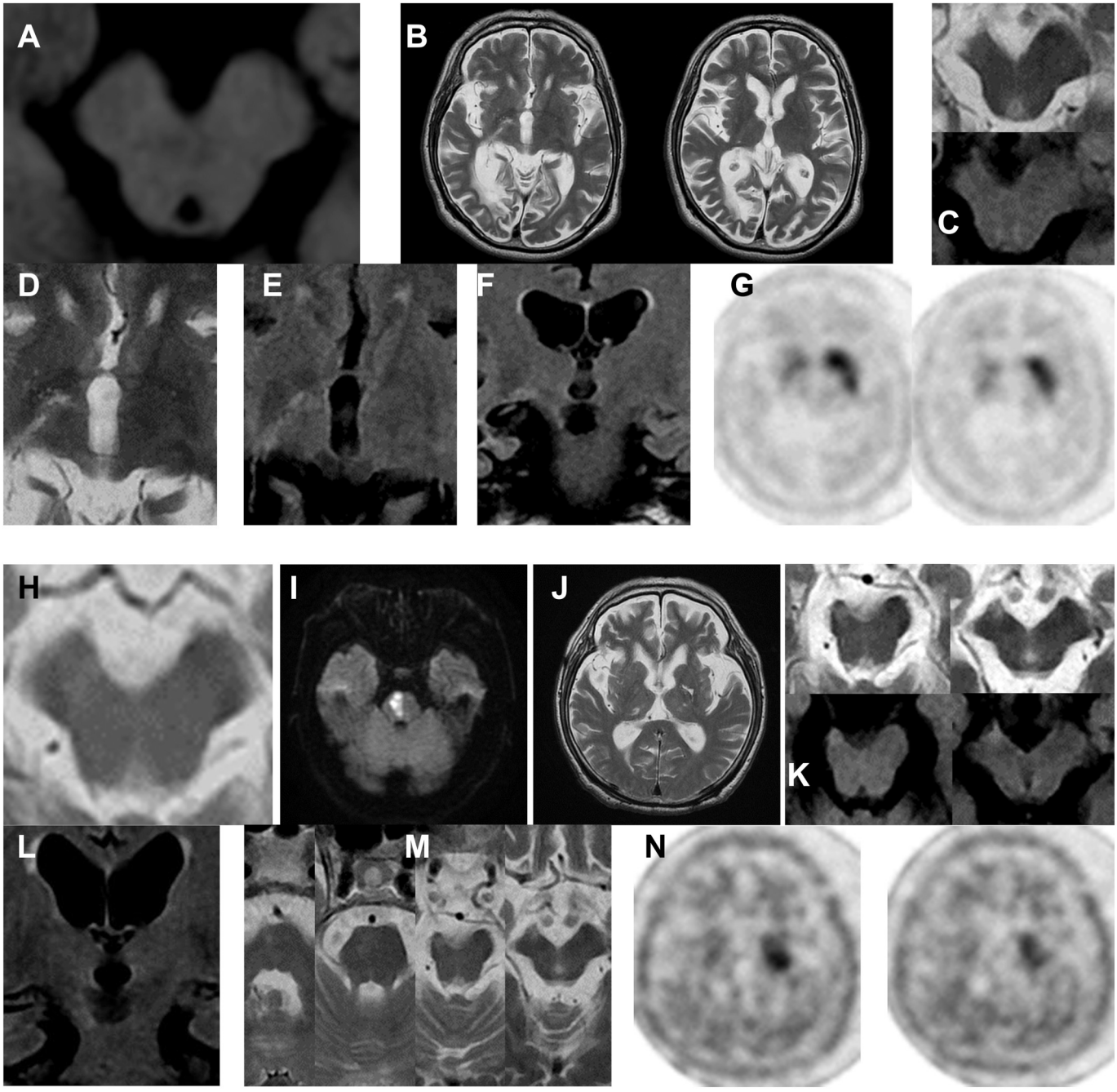

Fig. 1. A–N: Radiological findings in the 2 cases.
A–G depict scans of Case 1, and H–N depict scans of Case 2.
A: A T1-weighted magnetic resonance image obtained 7 years prior to presentation reveals a healthy midbrain.
B: A T2-weighted magnetic resonance images demonstrates a normal striatum, despite the patient exhibiting old infarctions in the right posterior limb of the internal capsule and the occipital lobe.
C: Upper and bottom panels show a T2-weighted magnetic resonance image, and a fluid attenuated inversion recovery image, respectively. Both images reveal right cerebral peduncle atrophy.
D: An axial T2-weighted magnetic resonance image shows that the substantia nigra is almost normal, revealed as a band of signal hypointensity. The right pyramidal tract is hyperintense with old infarction.
E, F: An axial fluid attenuated inversion recovery image (E) reveals equivocal hypointense band of the substantia nigra. The coronal image (F) reveals normally retined hypointense band as well as a right cerebral peduncle atrophy.
G: [^{123}I]-N-ω-fluoropropyl-2β-carbomethoxy-3β-(4-iodophenyl) nortropane single photon emission computed tomography ([^{123}I]-FP-CIT SPECT) shows severely reduced uptake in the right striatum.
H: A T2-weighted magnetic resonance image obtained 4 years prior to presentation reveals a normal midbrain.
I: A diffusion-weighted magnetic resonance image shows a 4-year-old right-sided paramedian pontine infarction.
J: A T2-weighted magnetic resonance image shows a normal right striatum and ischemic lesions in the left putamen.
K: Upper and bottom panels show a T2-weighted magnetic resonance image and a fluid attenuated inversion recovery image, respectively. Both images reveal right cerebral peduncle atrophy.
L: Coronal fluid attenuated inversion recovery image shows the substantia nigra is approximately perceived as the hypointense band, while equivocal. The substantia nigra may be affected secondarily by pyramidal tract degeneration and peduncle atrophy.

M: T2-weighted magnetic resonance images from the lower pons to the mesencephalon show a continuous hyperintense band along the right pyramidal tract. The longitudinal lesion is more likely to be degenerative than ischemic.
N: [^{123}I]-N-ω-fluoropropyl-2β-carbomethoxy-3β-(4-iodophenyl) nortropane single photon emission computed tomography ([^{123}I]-FP-CIT SPECT) shows a remarkably decreased striatal uptake, particularly in the right hemisphere.

and "dying-back" degeneration). In our cases, midbrain hemiatrophy was not confined to the pyramidal tracts but extended across the entire cerebral peduncle, possibly included the substantia nigra. Moreover, the damaged peduncle may have induced functional and structural abnormalities in the substantia nigra, altering the availability of the nigrostriatal system. Consequently, SPECT showed reduced striatal [^{123}I]-FP-CIT uptake ipsilateral to the midbrain hemiatrophy.

We cannot exclude an alternative explanation for MRI and [^{123}I]-FP-CIT SPECT abnormalities in our cases. Axial T2-weighted MRI revealed a lesion localized to the anterolateral portion of the right cerebral peduncle (Fig. 1D, M), corresponding to the ipsilateral nigrostriatal tract. Previous cerebral infarctions in both patients occurred in the posterior circulation. It is possible these ischemic infarcts affected the cerebral peduncle region. In addition, the ischemic damage in nigrostriatal tract might result from dopaminergic neuron degeneration, with a consequent equivocal hypointense band of the substantia nigra. Consequently, SPECT revealed reduced ipsilateral striatal [^{123}I]-FP-CIT uptake.

It is not possible to accurately determine whether degeneration and/or ischemia affected the nigrostriatal tract, as we have not examined the detailed radiological study, owing to ordinary clinical setting circumstances. Nevertheless, the longitudinal continuous hyperintense lesion along the right pyramidal tract and frontopontine fibers is more consistent with degeneration than ischemia. Therefore, we believe that nigral abnormalities represent secondary effects of pyramidal tract degeneration and peduncle atrophy.

Previous literature reports that sudden-onset hemiparkinsonism is characteristic of parkinsonism resulting from a direct midbrain infarction [1,2,7]. Patient responses to levodopa treatment vary as per the reports; however, its efficacy was unclear in our cases. Slow disease progression, observed in our cases, is also rare. To date, there is no report of dementia with Lewy bodies, with midbrain hemiatrophy demonstrating asymmetric [^{123}I]-FP-CIT uptake. Peduncle lesions sometimes elicit "peduncular hallucinations" [8]; however, there were no overt hallucinations in our cases.

Wallerian degeneration after cerebral infarction is generally observed on MRI after two weeks. A delay of 4–7 years between ischemic lesions and the manifestation of parkinsonism in our cases can be explained by the parkinsonism prodromal period. Symptoms typically do not develop until 40–60% of substantia nigra neurons are lost [9]. Furthermore, a decrease in the number of dopamine transporters and midbrain atrophy are known to advance with aging [10,11]. With time, parkinsonism symptoms in our cases may have reached the threshold of progressive presynaptic dopaminergic impairment. Moreover, the extrapyramidal symptoms may have been masked by the hemiparesis caused by the cerebral infarctions.

In conclusion, midbrain abnormalities should always be examined when prominent asymmetric presynaptic damage is revealed on [^{123}I]-FP-CIT SPECT. Our observations suggest that midbrain hemiatrophy, secondary to pyramidal degeneration, may influence presynaptic dopaminergic function. Neurologists should consider the association of midbrain hemiatrophy with secondary pyramidal degeneration when asymmetric striatal [^{123}I]-FP-CIT uptake is observed.

Relevant conflicts of interest/financial disclosures

None.

Funding sources for study

None.

Conflict of interest

None to declare.

Contributions

Drs. Nakajima and Ueda contributed equally to the case report.

References

[1] E. Peña, C. Fernandez, Abnormal DAT SCAN in a patient with parkinsonism after a midbrain ischemic lesion, Mov. Disord. 27 (2012) 205, https://doi.org/10.1002/mds.24890.
[2] P. Solla, A. Cannas, R. Arca, D. Fonti, G. Orofino, F. Marrosu, Focal (123) I-FP-CIT SPECT abnormality in midbrain vascular parkinsonism, Case Rep. Neurol. Med. (2015) (2015) 642764, , https://doi.org/10.1155/2015/642764.
[3] V. Pisani, A. Nicoletti, A. Meschini, et al., Putaminal, but not nigral alterations, characterize hemiparkinsonism-hemiatrophy syndrome: a case report, Mov. Disord. 26 (2011) 352–354, https://doi.org/10.1002/mds.23357.
[4] G. Barbagallo, G. Arabia, A. Lupo, U. Sabatini, A. Quattrone, Midbrain hemiatrophy and nigral rarefaction in a patient with hemiparkinsonism-hemiatrophy syndrome, Mov. Disord. 31 (2016) 1756–1757, https://doi.org/10.1002/mds.26811.
[5] B. Costa, G. Zanette, L. Bertolasi, A. Fiaschi, Hemiparkinsonism-hemiatrophy syndrome: neuroradiological and neurophysiological findings, Eur. Neurol. 34 (1994) 107–109, https://doi.org/10.1159/000117019.
[6] K. Ohta, K. Obara, Hemiparkinsonism with a discrete lacunar infarction in the contralateral substantia nigra, Mov. Disord. 21 (2006) 124–125, https://doi.org/10.1002/mds.20747.
[7] S. Peters, E.G. Eising, H. Przuntek, T. Müller, Vascular Parkinsonism: a case report and review of the literature, J. Clin. Neurosci. 8 (2001) 268–271, https://doi.org/10.1054/jocn.2000.0807.
[8] R. De la Fuente Fernandez, J. López, P. Rey del Corral, F. De la Iglesia Martinez, Peduncular hallucinosis and right hemiparkinsonism caused by left mesencephalic infarction, J. Neurol. Neurosurg. Psychiatry 57 (1994) 870, , https://doi.org/10.1136/jnnp.57.7.870.
[9] J.M. Fearnley, A.J. Lees, Ageing and Parkinson's disease: substantia nigra regional selectivity, Brain 114 (1991) 2283–2301, https://doi.org/10.1007/s00415-009-5226-z.
[10] J. Lavalaye, J. Booij, L. Reneman, J.B. Habraken, E.A. van Royen, Effect of age and gender on dopamine transporter imaging with [123I]FP-CIT SPET in healthy volunteers, Eur. J. Nucl. Med. 27 (2000) 867–869.
[11] Y.H. Sung, K.H. Park, Y.B. Lee, et al., Midbrain atrophy in subcortical ischemic vascular dementia, J. Neurol. 256 (2009) 1997–2002.

Nobuhito Nakajima[a,*], Masayuki Ueda[b]
[a] Department of Neurology, Kitamurayama Hospital, Japan
[b] Department of Neurology and Stroke Medicine, Tokyo Metropolitan Tama Medical Center, Tokyo, Japan
E-mail address: s7066@nms.ac.jp (N. Nakajima).

* Corresponding author at: Department of Neurology, Kitamurayama Hospital, 2-15-1 Onsen-machi, Higashine-shi, Yamagata 999-3792, Japan.