Paramedian Midbrain Infarction Presenting with Bilateral Ptosis and Unilateral Median Longitudinal Fasciculus Syndrome: A Peculiar Midbrain Syndrome

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Keywords
Blepharoptosis · Median longitudinal fasciculus · Median longitudinal fascicle syndrome · Central caudal nucleus · Oculomotor nucleus

Abstract
We report a case of bilateral ptosis due to paramedian midbrain infarction, which was associated with ipsilateral impaired adduction of the eye and contralateral ataxia. T2-weighted magnetic resonance imaging of the brain revealed a right paramedian midbrain infarction. The ptosis rapidly improved without a difference between the left and right sides, while the other symptoms mostly resolved within a month following treatment with antiplatelet agents and rehabilitation. An infarction of the paramedian dorsocaudal portion of the midbrain can involve both the central caudal nucleus and the median longitudinal fasciculus (MLF), causing a peculiar combination of symptoms, bilateral ptosis, and unilateral MLF syndrome.

Introduction

Pure midbrain infarction can be caused by the occlusion of the branches arising from the posterior cerebral artery, upper basilar artery, and superior cerebellar artery; however, this form of infarction is relatively rare, contributing to only 0.6% of the total patients admitted...
with ischemic stroke in a previous study [1]. The oculomotor nucleus located in the midbrain at the level of the superior colliculus sends efferent fibers to the medial, superior, and inferior rectus and inferior oblique extraocular muscles. The levator palpebrae superioris muscle is also innervated by the oculomotor nerve, and the responsible nerve fibers originate from the central caudal nucleus (CCN) [2]. Midbrain lesions involving the CCN have been reported to cause bilateral ptosis [3]. Additionally, pure midbrain infarction involving the anteromedial areas can cause bilateral ptosis in addition to the median longitudinal fasciculus (MLF) syndrome and contralateral cerebellar ataxia [1]. However, the peculiar combination of bilateral ptosis and unilateral MLF syndrome due to pure midbrain infarction has rarely been addressed. Herein, we report a case of bilateral ptosis due to paramedian midbrain infarction, which was associated with ipsilateral impaired adduction and contralateral ataxia.

Case Report

A 79-year-old man with a history of hypertension, dyslipidemia, and hyperuricemia was brought to the emergency department with a chief complaint of sudden inability to open his eyes. He was regularly taking olmesartan medoxomil, pitavastatin calcium, allopurinol, and potassium citrate with sodium citrate hydrate for the underlying diseases. At around midnight on the day of admission, he suddenly noticed that he could not open his eyes. Furthermore, he developed slurred speech in the morning and was subsequently transported to the hospital by ambulance. No headache or vomiting was reported. On admission, he was alert, with stable vital signs, and was able to walk without any paralysis of the extremities. On ocular examination, there was no anisocoria, and the pupillary light reflex was maintained. However, impaired adduction of the right eye on looking toward the left and severe bilateral ptosis were observed, and he could not open his eyes voluntarily. Convergence was preserved. The patient also had mild dysarthria and ataxia of the left upper extremity. No other neurological abnormalities were observed. Blood tests and electrocardiography did not reveal any abnormal findings. Diffusion-weighted magnetic resonance imaging (MRI) of the brain performed 12 h after symptom onset showed a high-intensity lesion in the right paramedian region of the midbrain (Fig. 1a), and the lesion had a low apparent diffusion coefficient value (Fig. 1b). Fluid-attenuated inversion recovery MRI showed no intensity change.

He was diagnosed with acute midbrain infarction and hospitalized, followed by intravenous administration of a thromboxane synthase inhibitor (ozagrel sodium 160 mg/day). The next day, he could gradually open his eyes, and there was no difference between the left and right-sided ptosis. On the sixth day of hospitalization, the oral antiplatelet agent (aspirin 100 mg/day) was substituted for ozagrel. On day 20 of hospitalization, T2-weighted MRI revealed an infarct of the paramedian midbrain region 13 mm in length in the ventrodorsal direction, from the substantia nigra to the cerebral aqueduct, and 9 mm in length in the rostrocaudal direction, from the superior colliculus level to the caudal border of the midbrain (Fig. 1c–h). Bilateral ptosis was resolved in 3 days, and impaired right eye adduction, dysarthria, and ataxia mostly improved within a month.

Discussion

Our patient displayed complete but transient bilateral ptosis associated with partial MLF syndrome, mild dysarthria, and ataxia. The ptosis quickly improved without a difference between the left and right eyes, while the other symptoms mostly resolved within a month. Bilateral ptosis is a rare manifestation and has been reported in 5% of patients with pure
Fig. 1. a–b MRI performed 12 h after symptom onset. a Diffusion-weighted MRI with a 128 × 128 matrix, a 5-mm thickness, and a 1.5-mm gap showing hyperintensity in the right paramedian area of the midbrain (white arrows). b The lesion had a low ADC value. c–h MRI performed 20 days after onset. T2-MRI axial sections (c–f) and frontal sections (g–h) with a 384 × 384 matrix, a 3-mm section thickness, and a 0.9-mm gap revealed an infarct of the paramedian midbrain region located rostrocaudally from the superior colliculus level to the caudal border of the midbrain (white arrows). ADC, apparent diffusion coefficient.
midbrain infarction in a previous case series [1]. Isolated bilateral ptosis has also been reported in a few cases [3–6], and the majority of these patients had small lesions in the paramedian or central regions of the midbrain. The CCN, which is a single structure and located in the midline dorsomedial to the caudal pole of the oculomotor nucleus in the midbrain, emits crossed and uncrossed fibers that innervate the bilateral levator palpebrae muscles [2]. Accordingly, as observed in our patient, bilateral ptosis can occur with paramedian lesions, if the lesion involves the CCN. Importantly, bilateral ptosis due to bilateral paramedian midbrain infarction did not improve after conservative care in a previously reported case [7]. Therefore, the recovery of our patient’s ptosis might be explained by the partial involvement of the CCN. Similar symptoms have been reported previously in the literature [1]. In 1 case report, transient nuclear midbrain blepharoptosis associated with mildly restricted adduction of the left eye was described [3]. Notably, MRI demonstrated an infarction which was located predominantly on the left side of the dorsal caudal midbrain and was 10 × 10 mm in diameter [3]. This case also appeared to have a CCN and MLF infarction, as in our case.

Our patient presented with ipsilateral impaired adduction with preserved convergence due to the right paramedian midbrain infarction. This phenomenon was compatible with internuclear ophthalmoplegia due to the lesion in the right MLF (MLF syndrome). The MLF is a paired, highly specialized, and heavily myelinated nerve bundle traveling in a craniocaudal direction near the midline within the tegmentum of the midbrain and dorsal pons [8]. In the midbrain, the MLF is located in the paramedian and lower portion [1], which is anatomically close to the CCN. Thus, the paramedian dorsocaudal portion of a midbrain infarction can involve both the MLF and CCN. Furthermore, the other symptoms of dysarthria and left upper limb ataxia in our patient could be explained by the partial involvement of the superior cerebellar peduncles, which is also located in the paramedian region of the midbrain [2, 9]. The majority of midbrain infarctions have been attributed to atherothrombotic diseases of the large or small vessels [1]. The MLF in the dorsal tegmentum of the midbrain is supplied by small perforating branches of the P2 segment of the posterior cerebral artery [8]. In our patient, since no atrial fibrillation was observed, cardiogenic embolism did not seem to be involved in the pathogenesis. Accordingly, small vessel disease, presumably involving the branches of the posterior cerebral artery, was thought to be the etiology. We have described a case of a peculiar combination of symptoms, bilateral ptosis, and unilateral MLF syndrome, caused by a unilateral paramedian midbrain lesion involving the MLF and CCN.

**Statement of Ethics**

This research was conducted ethically in accordance with the Declaration of Helsinki. Ethics approval was not required by the Aizawa Hospital Research Ethics Committee because this is a case report. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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Author Contributions

Yoshihiro Aoki: conceptualization, methodology, and writing – original draft preparation. Takao Hashimoto: conceptualization, supervision, and writing – reviewing and editing. All authors have read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1. Kim JS, Kim J. Pure midbrain infarction: clinical, radiologic, and pathophysiologic findings. Neurology. 2005 Apr;64(7):1227–32.
2. Porter JD, Burns LA, May PJ. Morphological substrate for eyelid movements: innervation and structure of primate levator palpebrae superioris and orbicularis oculi muscles. J Comp Neurol. 1989 Sep;287(1):64–81.
3. Yazici B, Ucan Gunduz G, Yargic N. Isolated and transient nuclear midbrain blepharoptosis in a young and healthy adult. Neuroophthalmology. 2019 Mar;44(2):111–3.
4. Liu GT, Carrazana EJ, Charness ME. Unilateral oculomotor palsy and bilateral ptosis from paramedian midbrain infarction. Arch Neurol. 1991 Sep;48(9):983–6.
5. Saito T, Asanome A, Sawada J, Katayama T, Hasebe N. A case of midbrain infarction causing ipsilateral mydriasis, contralateral superior rectus palsy, and bilateral ptosis. Neurol Sci. 2013 Sep;34(9):1683–4.
6. James S, Thozhuthumparambil KP. Brainstem stroke presenting as isolated bilateral ptosis. BMJ Case Rep. 2021 Jul;14(7):e243220.
7. Kim SY, Park HK, Song DH, Chung ME, Kim YM, Woo JH. Management of severe bilateral ptosis in a patient with midbrain infarction: a case report. Ann Rehabil Med. 2013 Dec;37(6):891–5.
8. Fiester P, Baig SA, Patel J, Rao D. An anatomic, imaging, and clinical review of the medial longitudinal fasciculus. J Clin Imaging Sci. 2020 Dec;10:83.
9. Mossuto-Agatiello L. Caudal paramedian midbrain syndrome. Neurology. 2006 Jun;66(11):1668–71.