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A case report of fifteen-and-a-half syndrome

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Abstract

Background Fifteen-and-a-Half Syndrome is an uncommon clinical presentation characterized by the coexistence of one-and-a-half syndrome and bilateral facial palsy. In this study, we provide a comprehensive description of symptom evolution and imaging changes in a patient with Fifteen-and-a-Half Syndrome.

Case presentation A 54-year-old male presented with sudden onset of one-and-a-half syndrome, which gradually progressed to fifteen-and-a-half syndrome. The final diagnosis was confirmed to be pontine infarction which occurred at the midline of the pontine tegmentum.

Conclusion This case highlights the diverse and progressive early clinical manifestations associated with Fifteen-and-a-half Syndrome. Currently, all reported cases of this syndrome are linked to brainstem infarction; however, early differential diagnosis is crucial to ensure prompt initiation of appropriate treatment for affected patients.

Keywords Fifteen-and-a-half syndrome, Pontine infarction, Bilateral facial nerve palsy

Background

Fifteen-and-a-half syndrome is a rare brainstem syndrome first proposed by Bae in 2005 [1]. Clinically, it manifests as one-and-a-half syndrome (restricted adduction and abduction in the ipsilateral eye, restricted adduction in the contralateral eye, accompanied by nystagmus during abduction) combined with bilateral facial nerve palsy. To date, only a limited number of cases of Fifteen-and-a-Half syndrome have been reported, all of which are attributed to pontine infarction. Theoretically, any lesion involving the pons tegmentum can potentially cause this syndrome, not solely brainstem infarction. Due to its clinical rarity, previous reports lack comprehensive understanding and differential diagnostic evidence. Herein, we present a case of progressive stroke in which a patient initially presented with one-and-a-half syndrome that evolved into eight-and-a-half syndrome before ultimately developing into fifteen-and-a-half syndrome. The patient underwent cranial MR imaging, facial electromyography, and additional tests for demyelinating antibodies and cerebrospinal fluid analysis to exclude other diseases, eventually leading to the diagnosis of pontine infarction. To date, four cases of fifteen-and-a-half syndrome have been reported, all occurring in Asian populations. This case is the only one solely associated with hypertension and demonstrates a progressive nature in its disease course.

Clinical report

A 54-year-old male patient was admitted to the hospital due to a one-day history of dizziness and diplopia. The patient presented with sudden onset vertigo accompanied by horizontal diplopia, nausea, and vomiting for the past day. He had well-controlled blood pressure despite

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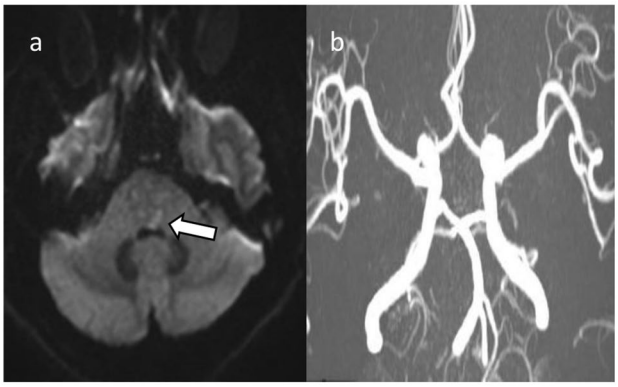

Fig. 1 Cranial magnetic resonance image 2 day after disease onset revealed restricted diffusion (arrow) in the pons on the DWI sequence (**a**) without significant arterial stenosis on cranial MRA (**b**)

his 10-year history of hypertension treated with nifedipine. Physical examination revealed restricted abduction and adduction in the left eye, restricted adduction in the right eye, and horizontal nystagmus during right eye abduction. Cranial CT revealed no significant abnormalities, while neck artery ultrasound indicated plaque formation in the right common carotid artery. Cardiac ultrasound and electrocardiogram results were normal. Blood tests, including routine blood workup, coagulation profile, urine analysis, thyroid function test, liver function test, kidney function test, lipid panel screening for blood lipid level assessment along with glucose level measurement for diabetes evaluation, hepatitis B virus infection screening, syphilis testing, and HIV antibody detection, all yielded normal results. The patient was diagnosed with "One-and-a-Half Syndrome", which is highly suggestive of pontine infarction based on clinical presentation and findings from diagnostic imaging studies. Treatment included aspirin administration alongside clopidogrel sulfate and atorvastatin.

On the 2nd day after symptom onset, the patient developed shallow left frontal striae, a shallow left nasolabial groove, and left oral angle skew. Physical examination revealed peripheral facial palsy on the left side in addition to manifestations of one-and-a-half syndrome. Further cranial MR imaging revealed restricted diffusion in the pons on the DWI sequence without significant arterial stenosis on cranial MRA (Fig. 1), and no significant pontine lesions were observed on the T2 and T2-FLAIR sequences. Considering the high possibility of infarction in the pontine region resulting in eight-and-a-half syndrome, we continued administering antiplatelet aggregation therapy.

On the 9th day after onset, in addition to presenting with one-and-a-half syndrome and left facial nerve palsy, the patient exhibited clinical signs of right facial nerve palsy. The patient experienced weakness in eyelid closure without any impairment in speech, swallowing, limb movement, or coordination. Subsequent cranial MR re-examination revealed a slightly enlarged area of restricted diffusion extending ventrally along the midline in the pons, with high signal intensity observed on T2 and T2-FLAIR sequences (Fig. 2). On the 10th day, bilateral peripheral facial nerve damage was confirmed through facial electromyography testing, which assessed facial nerve conduction and blink reflexes. On the 11th day, tumor marker levels, serum M protein levels, ANCA antibodies, antinuclear antibodies, and Bence-Jones protein levels in the urine were all negative. Cerebrospinal fluid routine examination revealed no abnormalities or protein-cell separation. Furthermore, no oligoclonal bands were detected in either the serum or cerebrospinal fluid samples. The final diagnosis was a pontine infarction. On the 13th day after symptom onset, the dizziness and diplopia resolved, and subsequently, the patient was discharged.

After a three-month interval, the patient returned for a follow-up examination, which demonstrated complete resolution of dizziness and diplopia. Moreover, there was notable improvement in facial palsy symptoms.

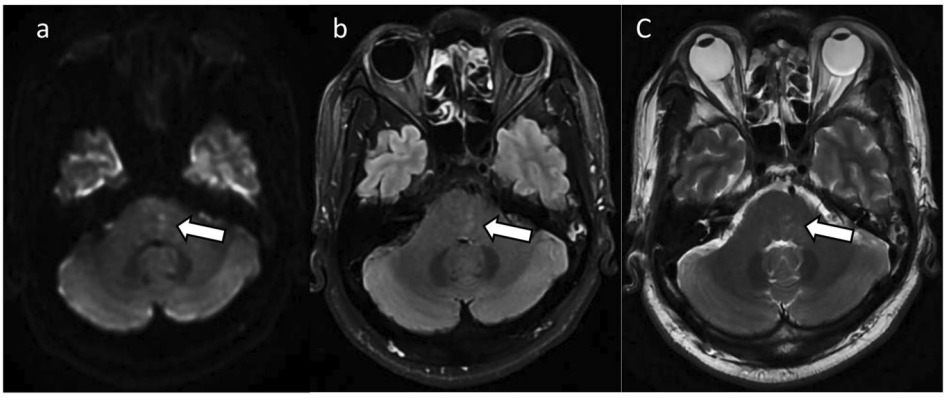

Fig. 2 On the 9th day after onset MR re-examination revealed a slightly enlarged area of restricted diffusion (arrow) extending ventrally along the midline in the pons (**a**), with high signal intensity observed on T2 (**b**) and T2-FLAIR sequences (**c**)

Discussion

One-and-a-half syndrome, first described by Fisher [2], arises from lesions affecting either the paramedian pontine reticular formation (PPRF) or the abducens nucleus, and is typically accompanied by involvement of the medial longitudinal fasciculus. Clinically, it is characterized by a horizontal gaze palsy on the side of the lesion and an internuclear ophthalmoplegia on the opposite side, resulting in an inability to move the eye horizontally toward the side of the lesion. Vertical eye movements and convergence are typically preserved. It is most commonly observed in patients with stroke and multiple sclerosis. The addition of ipsilateral facial nerve palsy to this syndrome results in eight-and-a-half syndrome (1½+7), which was first reported by Eggenberger in 1998 [3] and has been observed in conditions such as pontine infarction [4], pontine hemorrhage [5], and multiple sclerosis [6]. In 2005, Bae reported a case of one-and-a-half syndrome combined with bilateral facial nerve palsy and introduced the concept of Fifteen-and-a-half syndrome (1½+7+7) [1]. This syndrome is based on anatomical proximity between the paramedian pontine reticular formation, abducens nucleus, medial longitudinal fasciculus, and bilateral facial nerves. In our reported case, the patient presented with left horizontal gaze palsy, restricted adduction of the left eye during right gaze, and bilateral peripheral facial palsy consistent with clinical manifestations of fifteen-and-a-half syndrome.

Fifteen-and-a-half syndrome is an extremely rare condition, with only a few documented cases. Reported patients have shown variations in the onset time of facial palsy along with accompanying symptoms and the extent of cranial MR lesions. In Bae's report [1], bilateral peripheral facial palsy occurred on day two after one-and-a-half syndrome onset, while cranial MR revealed bilateral tegmental pontine infarction. Feiyan Zhu reported a patient who presented with one-and-a-half syndrome along with left-sided facial nerve palsy on day one accompanied by dysarthria; right peripheral facial palsy appeared on day fifteen alongside cranial MR, indicating left-sided tegmental pontine infarction [7].

The patient reported in our study presented with one-and-a-half syndrome on the first day of onset. Ipsilateral peripheral facial palsy manifested on the second day, suggesting either an expansion of the lesion affecting the facial nerve or compression of the facial nerve due to brainstem edema. On the ninth day after onset, contralateral peripheral facial palsy emerged. Subsequent re-examination via cranial MR revealed ventral extension of the pontine infarction without abnormal signals in the right pontine region. We speculate that this might be due to ischemia or edema affecting the right facial nerve adjacent to the median structures following pontine infarction, leading to secondary demyelination or axonal degeneration of the right facial nerve (Fig. 3).

Demyelinating patients can present with one-and-a-half syndrome, eight-and-a-half syndrome, or sixteen syndrome [8, 9]. However, to date, all fifteen-and-a-half patients were caused by brainstem infarction [1, 7, 10]. We reviewed three reported cases and found that all fifteen-and-a-half cases were reported in Asian regions (Table 1). The patients all had hypertension, and most had diabetes. The initial clinical manifestations were mostly dizziness and diplopia. Except for the case reported by Li [10], the progression of the other fifteen-and-a-half cases was relatively slow. Based on the progressive nature of posterior circulation stroke, it is evident that initial symptoms can rapidly worsen, as observed in cases where early interventions did not prevent further neurological deterioration [1, 7]. This highlights the importance of continuous monitoring and adaptive treatment strategies to manage posterior circulation strokes effectively [11].

Although patients with fifteen-and-a-half syndrome are exceedingly rare, with limited reported cases, fortunately, this patient received an accurate diagnosis and exhibited

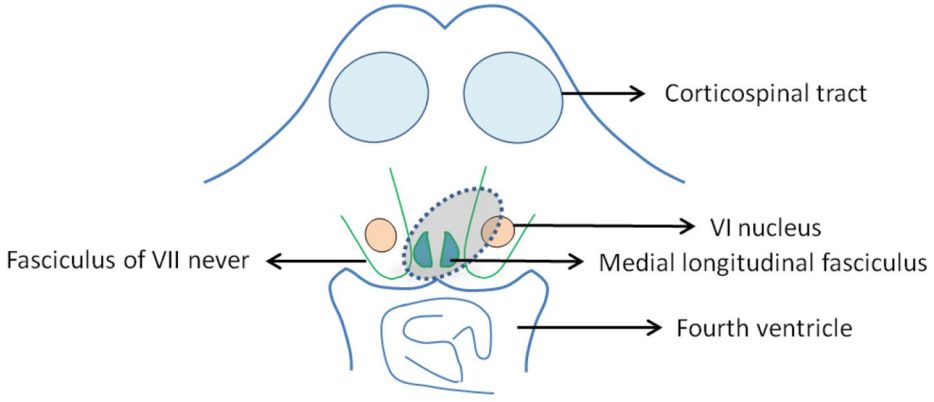

Fig. 3 Schematic diagram of fifteen-and-a-half syndrome. The shadow area revealed the responsible lesion that involves the left abducens nucleus, bilateral medial longitudinal fasciculus, and bilateral fasciculus of VII never

Table 1 Clinical characteristics in cases of fifteen-and-a-Half syndrome

Characteristics / Case	Case 1 [10]	Case 2 [7]	Case 3 [1]
Patient Information	54-year-old female	55-year-old male	67-year-old male
Medical History	Hypertension, type 2 diabetes, ischemic stroke	Hypertension, type 2 diabetes	Type 2 diabetes, heavy smoking
Admission Symptoms	Diplopia, slurred speech, and slightly distal numbness of the left upper limb for four days	Sudden onset of dizziness, double vision, and slurred speech	Sudden onset of dizziness, nausea, and blurring of vision
Disease Progression	No disease progression	Bilateral peripheral facial paralysis on day 15	Bilateral peripheral facial palsy developed on day 2
Follow-Up Results	Significant improvement in speech and ocular movement, bilateral facial paresis improved after 2 months	Slurred speech and dizziness disappeared, diplopia gradually improved after 4 months	Minimal deficit in right horizontal gaze after 2 months

favorable recovery following treatments such as antiplatelet aggregation therapy.

Abbreviations

MR Magnetic resonance imaging
CT Computed tomography
DWI Diffusion-weighted image

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Author contributions

YZ designed the study. HZ and XY drafted the manuscript. CL collected the data. XH revised the manuscript. The authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The Ethics Committee of Weifang People's Hospital stated that ethics approval was not necessary for case report.

Consent for publication

Written consent to publish the information was obtained from the patient. The participant has consented to the submission of the case report to the journal.

Competing interests

The authors declare no competing interests.

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