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Case Report

Nine Syndrome in Acute Pontine Ischemic Stroke: A Rare Case Report and Literature Review

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ABSTRACT

Background: Nine syndrome is a rare condition with a manifestation of one and a half syndrome (OAHS) with facial nerve damage and hemiparesis. We aimed to present the first published nine syndrome case from Indonesia with a comprehensive physical examination, radiological diagnosis, and pathological pathway explanation. A case report analysis and literature review were conducted.

Case Presentation: A 71-year-old male patient presented with the sudden onset of blurred vision and diplopia, with 'one' ipsilateral conjugate horizontal gaze palsy and 'half' ipsilateral internuclear ophthalmoplegia; a typical OAHS condition. Nine syndrome was diagnosed as ipsilateral lower motor neuron type facial nerve palsy and contralateral hemiparesis. It was radiologically confirmed by acute right pontine ischemic stroke, where the medial longitudinal fasciculus, abducens nucleus, and paramedian pontine reticular formation anatomically contribute to horizontal gaze. Eye movement and hemiparesis improved significantly after ischemic stroke management.

Conclusion: Nine syndrome is a neuro-ophthalmological manifestation that rarely occurs, and understanding the neuroanatomy and its possible causes may help clinicians in dealing with OAHS and its various disorders.

Keywords: One and a half syndrome, Nine syndrome, Ophthalmoplegia, Pontine stroke, Brainstem stroke, Internuclear ophthalmoplegia

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Highlights

- Nine syndrome is a rare variant of OAHS, presented with additional ipsilateral hemifacial palsy and contralateral hemiparesis.
- Understanding the neuroanatomy of pontine stroke helps prevent misdiagnosis of the nine syndrome.
- The prognosis for nine syndrome is good with isolated, unilateral pontine infarction.
- Early detection of OAHS and nine syndrome enables targeted treatment and better outcomes.

Introduction

Charles Miller Fisher first reported one and a half syndrome (OAHS) in 1967. He described a brainstem lesion patient with clinical manifestations of preserved vertical eye movements but with complete horizontal movement paralysis in one eye that lies centrally abducted and another eye that fails to adduct past the midline of the horizontal axis [1]. Patients with OAHS usually present with visual complaints of diplopia, blurred vision, oscillopsia, one-sided horizontal eye movement difficulty, eye-twitching, and several ocular motility problems, including nystagmus (gaze-evoked upbeat/downbeat nystagmus, horizontal ipsilateral gaze nystagmus, rotary component to ipsilateral gaze nystagmus, or contralateral side spontaneous nystagmus), skew-deviation, convergence insufficiency, saccadic-vertical pursuit, exotropia, esotropia, or orthotropic eye [2]. OAHS might also be associated with other neurologic deficits, including other cranial nerve involvement, muscle incoordination and asymmetric reflexes, muscle weakness, and sensory deficits [2, 3]. We present a comprehensive physical examination, radiological diagnosis, literature review, and pathological pathway explanation of a very rare case of nine syndrome. This syndrome was previously reported only in four cases: Three cases due to pontine infarction reported by Rosini et al. (2013) in Italy and Mahale et al. (2015) in India, and one case due to pontine intracerebral hemorrhage reported by Yadegari et al. (2018) in Iran [4-6]. Therefore, the exact global prevalence of epidemiology reports was still unknown.

Case Presentation

A 71-year-old male patient, Javanese-Indonesian, was admitted with the chief complaint of the sudden onset of blurred vision and diplopia along with sudden left-sided hemiparesis, right-sided upper motorneuron facial palsy, and slurred speech after waking up from a nap 1 hour before the admission. He has difficulty moving his eyes to the right, and the diplopia worsens when looking to the left. Complaints were also accompanied by spinning-sensation dizziness, nausea, and vomiting twice. He had experienced a transient ischemic attack one year before, with resolved similar symptoms of hemiparesis and slurred speech within 24 hours of onset. He had never had a similar complaint in his family history. He has an overweight body mass index (29 kg/m^2), sedentary lifestyle, is a smoker, non-alcoholic, and has a medical history of uncontrolled dyslipidemia, diabetes mellitus type 2, and hypertension with a history of non-routine medication with simvastatin, metformin, insulin injection, amlodipine, and captopril.

On examination, he was compos mentis and had high blood pressure of 160/90 mm Hg. Neurological examinations (Figure 1) on primary position revealed fixation of his right eye parallel to the sagittal plane of the head, and abduction of his left eye slightly to the left. Horizontal right-gaze showed both eyes unable to move past the midline of the primary position axis. In contrast, left-gaze showed a still fixated right eye on the primary position, and the left eye abducting to the left with horizontal nystagmus. These conditions are hallmarks of OAHS, which showed complete horizontal gaze palsy for the voluntary and tracking movement or vestibular-ocular reflex to the right direction. Both eyes have a normal accommodation, 20/20 visual acuity score, and a normal direct and indirect pupillary light reflex. He also had a lower motor neuron type of right facial nerve palsy. Other cranial nerve examinations were normal. In the motor examinations, left-sided hemiparesis with the Medical Research Council (MRC) scale for the left-upper extremity muscle strength scored 2/5 and the left-lower extremity scored 3/5. On sensory examination and physiologic reflexes, no abnormalities were found.

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Laboratory testing showed hyperglycemia and hypercholesterolemia. Brain magnetic-resonance imaging (MRI) without contrast in the diffusion-weighted imaging (DWI) sequences showed a hyperintense lesion in the right pontine, which indicated hyperacute ischemia in the right pontine (Figure 2). Furthermore, there was an old right corona radiata infarction.

The final diagnosis was nine syndrome due to pontine ischemic stroke, with risk factors being uncontrolled hypertension, diabetes, and dyslipidemia. In the emergency room, he was given a loading dose of dual-antiplatelet therapy (DAPT) using aspirin and clopidogrel. He was then admitted to the neurology ward and was given a treatment of maintenance DAPT, flunarizine, captopril, amlodipine, simvastatin, metformin, and insulin injection. In addition to physical rehabilitation, an eye patch has also been used to close his eyes alternately every day to reduce complaints of diplopia.

After six days, he was recovered well, and his right gaze began to be carried out, even though it was minimal. Also, the patient started to raise his hands and walk using assistive devices with an MRC scale of 3/5 for the left upper extremity and 4 /5 for the left lower extremity. His initial NIHSS (National Institutes of Health Stroke-scale) score before admission was 12 (moderate stroke), and follow-up post-hospitalization showed a recovery with only a slight disability, MRS (modified Rankin-scale) scored 2. He had no worsening symptoms during admission and proceeded with outpatient care within 7 days after admission by continuing therapy with a scheduled follow-up and physical rehabilitation program.

Discussion

OAHS that is concurrent with other neurologic deficits form a new spectrum disorder: The eight and a half syndrome (EHS), nine syndrome, thirteen and a half syndrome, fifteen and a half syndrome, and sixteen and a half syndrome. EHS is OAHS with a lesion in the ipsilateral paramedian pontine tegmentum, presenting with additional ipsilateral hemifacial paralysis due to facial nerve damage. At the same time, nine syndrome is EHS with an additional lesion in the ventromedial pons or ventrolateral medipeduncle, presenting with additional hemiparesis, hemihypesthesia, or ataxia [3, 4, 7]. Sudden onset of nine syndrome and neurological deficit in our patient was due to acute ischemic stroke in the right pontine extending from the pontine tegmentum to the base. OAHS happened due to a brainstem lesion, particularly near or in the pontine region, related to vascular pathology (mostly brainstem infarction and a few due to arteriovenous-malformation, pontine-hemorrhage, and basilar-artery aneurysm) than neoplasm or demyelination (multiple-sclerosis), and in a few rare cases due to infection (neurocysticercosis, brainstem encephalitis, and tuberculomas) [1-3, 8, 9]. Pontine infarction is one of the most common subtype of posterior circulation strokes [10]. Pontine infarction is reported to be related to both branch atheromatous disease and small vessel disease, with hypertension and diabetes as an independent risk factors being significantly related to its recurrency [11, 12]. These symptoms were in accordance with our patient, with aging, diabetes, hypertension, and dyslipidemia being the risk factors leading to pontine ischemic stroke as the cause of the nine syndrome.

OAHS is just as literal and clear, a self-explanatory term. It refers to ‘one’ ipsilateral conjugate horizontal-gaze palsy because of pontine lesion combined with another ‘half’ ipsilateral internuclear-ophthalmoplegia with its typical characteristic of adduction deficit and abducting nystagmus because of lesion on the medial-longitudinal fasciculus (MLF) where pontine lesion crosses the midline to the vestibular nucleus contralaterally [1, 3]. MLF is a highly specialized fiber tract in the brainstem that serves as the main central connection for cranial nerves (CN) III (oculomotor), IV (trochlear), and VI (abducens), which primarily coordinate the eyes’ movement. Horizontal gaze was controlled in the pontine of the central subcortical level, while vertical gaze was controlled in the rostral of the midbrain level. The final pathway of horizontal gaze is in the CN-VI nucleus, which has two groups of cells: Motor neurons that innervate the ipsilateral lateral rectus muscle and internuclear neurons that innervate the contralateral medial rectus muscle via MLF [3, 7]. Movements resulting from this system are abduction of the ipsilateral eyeball and adduction of the contralateral eyeball. The horizontal-gaze command was processed in the paramedian pontine reticular formation, which serves as a supranuclear center that receives impulses from the visual areas of the frontal and parietal lobes and regulates horizontal conjugate movements [3]. To perform a conjugate lateral horizontal gaze, the CN-VI nucleus transmits the signal to the contralateral CN-VI nucleus through the connecting fibers in the contralateral MLF. Our patient showed right (ipsilateral) horizontal gaze paralysis, right-eye internuclear-ophthalmoplegia, exotropia of the left (contralateral) eyeball (Figure 1), a typical condition of OAHS with supported findings of acute right pontine ischemic stroke during brain MRI-DWI diagnosis (Figure 2) that was consistent with the clinical manifestation with area of lesion in the right pontine tegmentum, including the damaged structure of right MLF, right CN-VI nucleus, and right paramedian pontine reticular formation (Figure 3).

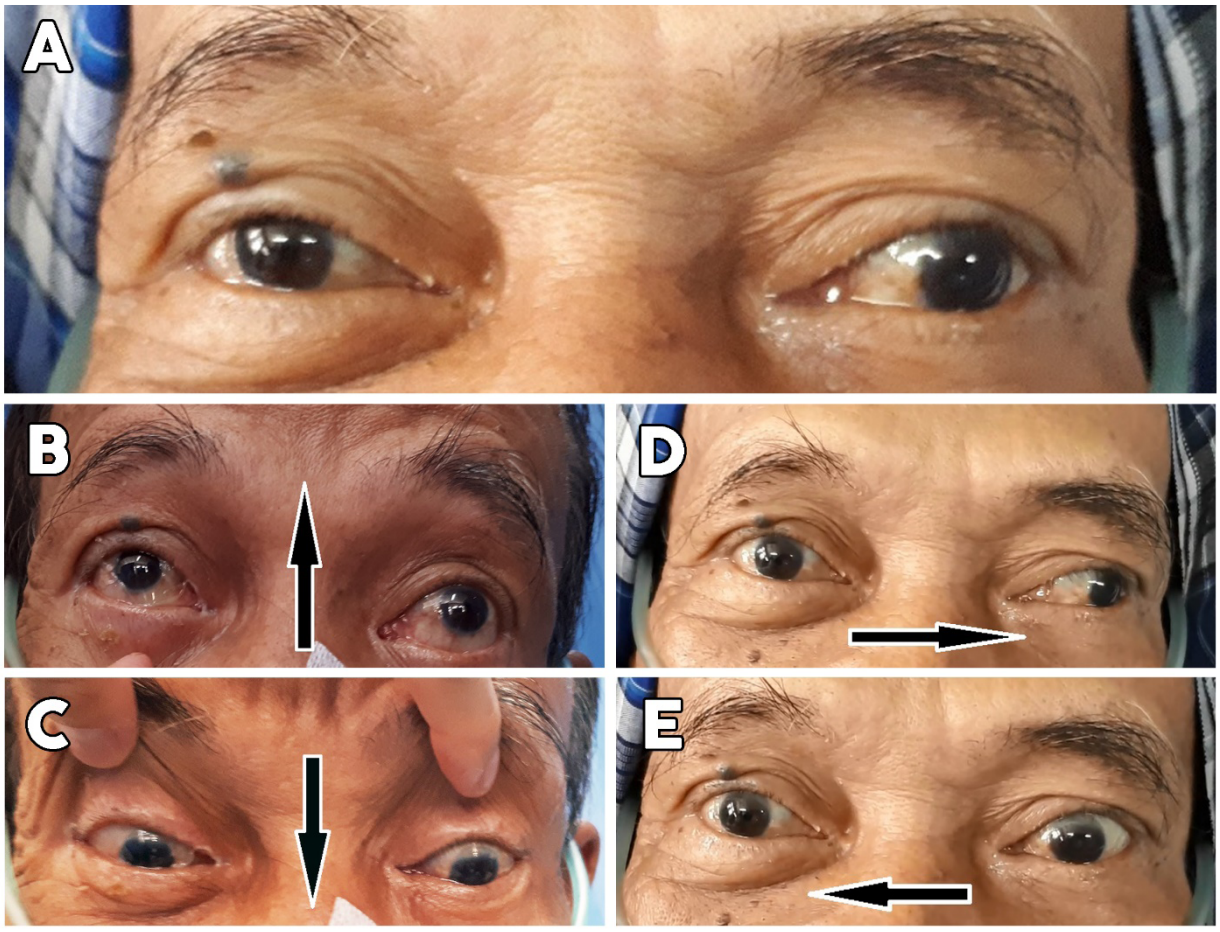

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Figure 1. Eye examination of (A) primary position, vertical movement of (B) upgaze and (C) downgaze, and horizontal movement to the (D) left and (E) right

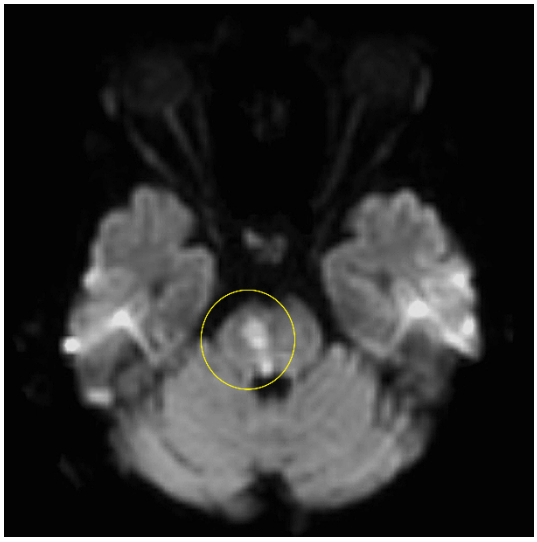

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Figure 2. Brain MRI diffusion weighted imaging sequence showing a hyperintense lesion in the right pontine (yellow circle)

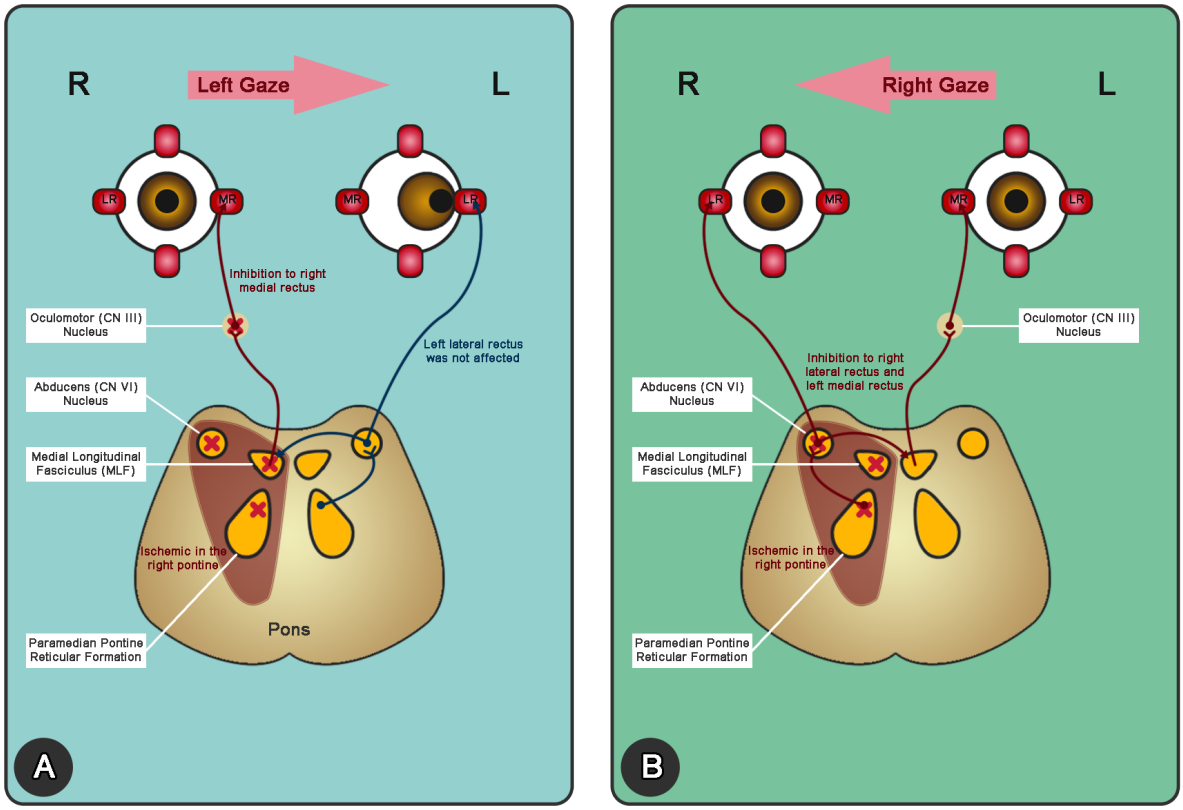

Figure 3. OAHS simplified pathway in our patient with right pontine ischemic stroke

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Note: The stroke affected the right medial longitudinal fasciculus, which blocked the connection pathway from the contralateral (left) abducens nucleus interneurons, resulting in the signal inhibition toward the right oculomotor nucleus, and right medial rectus muscle movement was restricted, leading to right eye left gaze palsy. The signal from the left paramedian pontine reticular formation to the left abducens nucleus was not affected, providing the ipsilateral motor neuron signal toward the left lateral rectus muscle, and left eye left gaze palsy was normal. Right paramedian pontine reticular formation lesion leads to signal inhibition toward right abducens nucleus, leading to signal inhibition toward right lateral rectus muscle and contralateral (left) medial longitudinal fasciculus (which inhibits the motor neuron signal to left oculomotor nucleus to left medial rectus muscle), leading to bilateral right gaze palsy.

The pons generally receives its blood supply from the basilar artery and its branches. Based on region, pontine infarctions are divided into bilateral, unilateral paramedian, tegmental, lateral, combined unilateral, lateral paramedian, and patchy pontine syndrome [7]. In this case, an infarction occurred in the anterior region (anteromedial and anterolateral), which was suspected to be due to atherothrombosis, where this area was supplied by a penetrating artery that emerged from the dorsal surface of the basilar artery. This territory includes most of the pontine base (corticospinal tract) and the ventral tegmentum (part of the medial lemniscus). Paramedian branch occlusion will cause damage to the corticospinal, cortico-ponto-cerebellar, and cortico-bulbar tracts. It can even extend to the medial tegmentum area, including the CN nucleus, fasciculus, and MLF [7]. In our patient, disturbances occurred in the corticospinal tract and corticobulbar tract at the pontine base, which manifested as left-sided (contralateral) hemiparesis, lower motor neuron lesion-type right-sided (ipsilateral) CN-VII palsy, and CN-XII nerve palsy, together with OAHS forming the nine syndrome [4].

The management of nine syndrome was focused on its underlying cause, with an additional symptomatic treatment that might be needed depending on the clinical findings. Generally, the short-term functional prognosis of patients with unilateral small vessel infarction of the pons is good. Factors contributing to a better prognosis are isolated lateral or tegmental location, lacunar morphology, and upper to midpontine lesions. Bilateral infarctions, multiple unilateral infarctions, and lesions in the lower part of the pons contribute to a worse prognosis. In this case, the patient's prognosis can be considered

good, as his infarct was unilateral and isolated in the tegmental and lateral parts.

Conclusion

OAHS is a neuro-ophthalmological manifestation that rarely occurs, with the nine syndrome even rarer. Understanding the neuroanatomy contributing to ocular movements is an essential basis for understanding the pathophysiology and possible causes. Therefore, in dealing with OAHS and its various disorders, including EHS and nine syndrome, the clinician must suspect a process along the neuraxis and look for the underlying etiology so that appropriate treatment can occur.

Ethical Considerations

Compliance with ethical guidelines

All study procedures were in compliance with the ethical guidelines of the 2013 Declaration of Helsinki.

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Authors contributions

Writing the original draft: Robert Shen; Patient management, data collection, interpretation, and final approval: All authors.

Conflict of interest

The authors declared no conflict of interest.

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