

Pearls & Oy-sters: Upbeat Nystagmus and Quadriplegia in a Young Girl with Bilateral Medial Medullary Syndrome

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Pearls

- The presence of nystagmus differentiates a high cervical cord and a brainstem lesion in a quadriplegic patient.
- Upbeat nystagmus commonly occurs due to a lesion involving bilateral anteromedial medulla.
- In medial medullary syndrome (MMS), brain MRI with diffusion-weighted imaging (DWI) is crucial to visualize the hyperacute changes of ischemia.

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Oy-sters

- Bilateral MMS due to vascular occlusion can rarely occur in very young patients without atherosclerosis risk factors, and the diagnosis should not be missed.
- Early ischemic changes at the paramedian region of the bilateral medulla in brain imaging might incorrectly be interpreted as a midline artifact by untrained eyes.
- Neurologists and radiologists should be alert for the characteristic MRI features of heart appearance in patients presenting with bilateral medial medullary infarction and neuroimaging should be repeated in highly suspicious cases.

A 13-year old girl, without prior illness, presented with an abrupt onset of severe neck pain and occipital headache while resting, followed by bilateral upper extremity numbness, which progressed to bilateral lower extremity numbness within a few minutes. Half an hour afterward, she rapidly developed quadriplegia and breathlessness. She was immediately brought to the hospital.

The patient did not complain of spinning sensation, vomiting, dysphagia, or double vision during the event. There was no history of fever, trauma, or cardiac symptoms. She had no history of antecedent infection, vaccination, or drug abuse, or any family history of young stroke.

On examination, the patient was drowsy, with normal blood pressure and pulse rate. She had weak neck movements and was quadriplegic, with muscle strength of MRC grade 0/5, hypotonia, and areflexia in all her extremities. Plantar reflexes were absent bilaterally. Sensory level was not able to be determined as the patient was unable to cooperate during the examination. Extraocular muscle movements were intact in all directions, but upbeat nystagmus, which was aggravated upon upward gaze, was noted (video). No bruit was heard over the neck vessels. Cardiovascular and other system examinations were unremarkable.

The patient was immediately intubated due to respiratory failure and right lung collapse. The right lung collapse occurred as a result of respiratory muscle weakness in quadriplegia, in combination with hypoxia and drowsiness, which further led to aspiration pneumonia and accumulation of mucous plug within the airway.

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Emergent brain CT scan was unremarkable. The results of the brain and cervical spine MRI, which was performed within 4.5 to 6 hours of onset, but without a DWI sequence, were also reported as normal. No contrast enhancement was seen after gadolinium. Magnetic resonance angiography (MRA) of bilateral carotid, vertebro-basilar arteries, and its branches showed normal vasculature.

A nerve conduction study, performed to rule out Guillain-Barré syndrome, was also normal. CSF was acellular, with normal protein and glucose content. CSF screening for infections was negative. The patient was treated with IV methylprednisolone (1 g) daily for 5 days, in view of the differential diagnoses of immune-mediated brainstem encephalitis with acute transverse myelitis. No clinical improvement was noted.

As the diagnosis was not well-established, brain and cervical MRI was repeated on day 5 of the illness, in view of the possibility of vascular occlusion evidenced by a very sudden and abrupt onset of clinical presentation. The MRI showed features of bilateral medial medullary infarction that extended down to the C5 cervical cord (figure, A). DWI sequence showed hyperintense lesion (figure, B) with hypointensity on apparent diffusion coefficient, consistent with restricted diffusion within the medulla with the characteristic heart appearance sign. It was also hypointense on T1-weighted and hyperintense on T2-weighted and fluid-attenuated inversion recovery (figure, C) images. Axial T2-weighted MRI of the cervical cord showed that the abnormalities were confined to the anterior part of the cord, which is compatible with anterior spinal artery infarction (figure, D). Both MRA and CT angiography were repeated and showed a normal intracranial and extracranial vascular system. The cervical spine and intervertebral discs appeared normal.

Screening tests for underlying thrombophilia, vasculitis, autoimmune diseases, and antiphospholipid syndrome were negative. Aquaporin-4 antibody was not tested due to the normal CSF results, as well as the MRI findings of ischemic areas following the vascular distribution of the anterior spinal artery, rather than acute transverse myelitis. Urine toxicology was not performed as there was no history of drug abuse. No abnormalities were seen on the ECG, 24-hour cardiac rhythm monitoring, or echocardiogram. Dabigatran was started because the full cardiac workup was not yet completed. After 3 months of rehabilitation, the muscle power improved to Medical Research Council grade 2/5, but with a modified Rankin Scale score of 5. The patient was discharged with continued rehabilitation in an outpatient unit.

Discussion

Our patient presented with abrupt onset of neck pain, quadriplegia, sensory loss, and respiratory failure, which usually indicates a complete high cervical cord transection or vascular pathology involving the brainstem, such as in acute vascular dissection. Brain and cervical spine MRI were performed immediately, but DWI, which could show early changes of an

infarct, was missed in the imaging sequence. Spontaneous vessel occlusion leading to ischemia or infarction was not emphasized early, because of the patient's very young age at onset with the absence of common risk factors for stroke.

In this case, the finding of nystagmus in a quadriplegic patient helped to localize the lesion to the brainstem instead of being a purely cervical cord disease. In a medulla oblongata lesion, horizontal gaze-evoked nystagmus is commonly reported in lateral medullary syndrome due to the involvement of the vestibular nuclei and its projection.¹ The neural integrators responsible for horizontal gaze are the medial vestibular nuclei and the nucleus prepositus hypoglossi.² Medullary lesions located in the paramedian region usually manifest as an up-beat nystagmus (UBN).^{3,4} UBN beats upward in the primary position and can be aggravated by looking in an upward direction of gaze. Its common etiologies include tumor, stroke, multiple sclerosis, and Wernicke encephalopathy.³

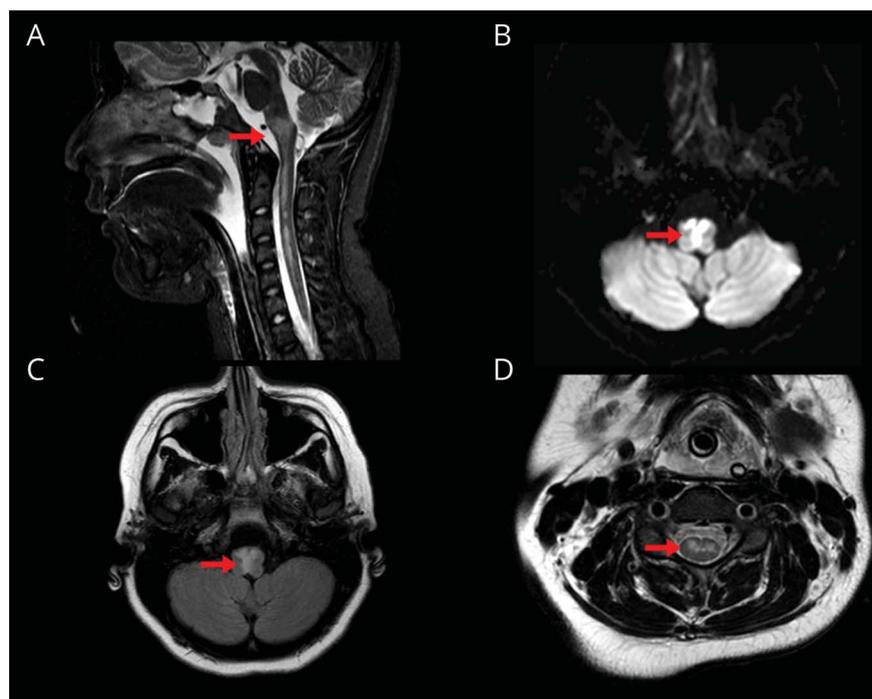
On the other hand, vertical gaze-evoked nystagmus (GEN) can also be prominent in upward or downward direction of gaze, but it disappears in the primary eye position. Vertical GEN occurs primarily in midbrain lesions, where the interstitial nucleus of Cajal serves as the primary neural integrator.² The flocculus and nodulus of the cerebellum also play a role in maintaining an eccentric position of gaze.²

Another type of vertical nystagmus is spontaneous downbeat nystagmus, in which the fast phase beats in a downward direction in the primary eye position.³ It can be aggravated by looking down and to the side while in a prone position. It is mainly due to bilateral disease of the cerebellar flocculus, but has rarely been reported in paramedian medullary lesions.³

MMS is a rare form of posterior circulation stroke that occurs in fewer than 1% of cases.⁵ It occurs even more rarely bilaterally in a young patient without underlying diseases. MMS is more commonly seen in elderly men, and the main mechanism of stroke is atherosclerosis involving the vertebral artery.⁵⁻⁷ Large artery disease is more common than small penetrating arteries occlusion.^{6,7} Occlusion of the anterior or posterior spinal arteries can be associated with cervical cord ischemia or infarction, as demonstrated in our case.¹ Clinical presentations of MMS include motor weakness, dysarthria, and hypoglossal nerve palsy.^{4,5} Other reported symptoms of bilateral MMS are rapidly progressive quadriplegia, generalized numbness, nystagmus, giddiness or vertigo, and mild impairment of consciousness.^{1,4,7,8}

The medulla oblongata has a unique arterial supply from the branches of the vertebral artery, namely from the anterior and posterior spinal arteries, in addition to the perforating arteries and the long circumferential artery.⁶ The medulla oblongata is divided into few vascular territories: the anteromedial, anterolateral, lateral, and posterior territories.⁶

The characteristic brain MRI finding of heart appearance in bilateral MMS has been described in multiple case reports.^{1,4,8}



(A) MRI shows features of bilateral medial medullary infarction that extend down to C5 cervical cord. (B) Diffusion-weighted imaging sequence shows hyperintense lesion with hypointensity on apparent diffusion coefficient, consistent with restricted diffusion within the medulla with the characteristic heart appearance sign, also hypointense on T1-weighted and hyperintense on T2-weighted and fluid-attenuated inversion recovery images (C). (D) Axial T2-weighted MRI of the cervical cord shows that the abnormalities were confined to the anterior part of the cord, which is compatible with anterior spinal artery infarction.

The heart appearance sign is considered to appear when the infarct occurs in the bilateral anteromedial medulla, which is supplied by branches of vertebral artery and anterior spinal artery and may extend to the anterolateral territory, which is fed by short and long transverse branches of the vertebral artery.¹ Lesions involving the anteromedial vascular territory are common in the rostral part of the medulla oblongata.^{1,6,7} Unilateral vertebral artery occlusion may also cause a bilateral infarction, because the rostral median branches of the vertebral artery penetrate the midline to supply the contralateral anteromedial arterial territory.^{1,6}

We postulated that our patient had MMS with anterior spinal artery (ASA) infarction due to emboli of an unrecognized source, which possibly dislodged to multiple distal branches rather than causing blockage of the main vessels, as evidenced by a normal MRA of the main cerebral vessels. A rare cause of ASA infarction in a young patient is fibrocartilaginous emboli (FCE), due to the migration of the nucleus pulposus material from the intervertebral disc to the nearby vessels and subsequent embolization to the spinal arteries.⁹ In one review of histopathology-confirmed FCE, 6 out of 41 cases presented with an abrupt onset of neck pain and quadriplegia due to ASA infarction involving the medulla oblongata and cervical cord. A total of 40% of deaths in these cases were attributable to respiratory complications.⁹ FCE can occur even with a very minimal or unnoticed injury to the neck and without degenerative spine changes seen on MRI. FCE can only be confirmed by biopsy of the occluded vessels, mostly taken during the autopsy, and no specific treatment was available.⁹

Spinal cord infarction is often mistaken for and treated as acute transverse myelitis. In this case, the clues to support infarction rather than myelitis include very abrupt onset, with maximal neurologic deficit within the first hour, normal CSF examination, distribution of lesion area following vascular territory of ASA (anterior 2/3 of the cord), no contrast enhancement on MRI with relatively normal initial scan, and absence of clinical response to early administration of high-dose methylprednisolone.⁹ In neuromyelitis optica, the long segment lesion is usually located centrally in the gray matter. It enhances with contrast and might also show restricted diffusion on DWI.¹⁰ Other causes of restricted diffusion on brain MRI include immune encephalitis, multiple sclerosis, venous infarction, and brain abscess.¹⁰

Few case reports highlight that early MRI features of MMS might be missed if the MRI is not thoroughly interpreted.^{4,8} Similar to our case, a retrospective review of the first MRI, which was initially read as normal, actually showed early changes of infarct in the paramedian region of the medulla, which sometimes can be misinterpreted as midline artifacts. As the prognosis of bilateral MMS is guarded, it is crucial to recognize the early imaging features of MMS, because urgent reperfusion therapy might help to salvage the ischemic area in selected cases.^{5,7} In our case, further investigations with conventional cerebral angiography, extended duration of cardiac Holter monitoring, and transesophageal echocardiogram would be helpful to look for the source of emboli in a young patient.

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Disclosure

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Appendix Authors

Name	Location	Contribution
Intan Aaroni Md Isa, MBBS	Universiti Sains Malaysia, Kelantan	Major role in acquisition of data, interpreted the data, drafted the manuscript
Sanihah Abdul Halim, MD, MMed	Universiti Sains Malaysia, Kelantan	Design and conceptualization, analyzed and interpreted the data, drafted and revised the manuscript

References

1. Gupta A, Goyal MJ, Vishnu VY, Ahuja CK, Khurana D, Lal V. Bilateral medial medullary infarction: the 'heart' reveals the diagnosis. *Int J Stroke* 2014;9:e18.

Appendix (continued)

Name	Location	Contribution
Chee Yong Chuan, MBBS, MRCP	Universiti Sains Malaysia, Kelantan	Design, acquisition, and interpretation of data

2. Sanchez K, Rowe FJ. Role of neural integrators in oculomotor systems: a systematic narrative literature review. *Acta Ophthalmol* 2018;96:e111–e118.
3. Strupp M, Hufner K, Sandmann R, et al. Central oculomotor disturbances and nystagmus: a window into the brainstem and cerebellum. *Dtsch Arztebl Int* 2011;108:197–204.
4. Lee ES, Sung KB, Lee TK. Teaching Video NeuroImages: upbeat and horizontal gaze-evoked nystagmus in bilateral medial medullary infarction. *Neurology* 2017;89:e238.
5. Pongmoragot J, Parthasarathy S, Selchen D, Saposnik G. Bilateral medial medullary infarction: a systematic review. *J Stroke Cerebrovasc Dis* 2013;22:775–780.
6. Kim K, Lee HS, Jung YH, et al. Mechanism of medullary infarction based on arterial territory involvement. *Clin Neurol* 2012;8:116–122.
7. Kim JS, Han YS. Medial medullary infarction: clinical, imaging, and outcome study in 86 consecutive patients. *Stroke* 2009;40:3221–3225.
8. Torabi AM. Bilateral medial medullary stroke: a challenge in early diagnosis. *Case Rep Neurol Med* 2013;2013:1–3.
9. AbdelRazek MA, Mowla A, Farooq S, Silvestri N, Sawyer R, Wolfe G. Fibrocartilaginous embolism: a comprehensive review of an under-studied cause of spinal cord infarction and proposed diagnostic criteria. *J Spinal Cord Med* 2016;39:146–154.
10. Finelli PF. Diagnostic approach to restricted-diffusion patterns on MR imaging. *Neurol Clin Pract* 2012;2:287–293.

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