

Locked-in Syndrome: A Rare Manifestation of Pediatric Stroke

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ABSTRACT

Locked-in syndrome is characterized by upper motor neuron quadriplegia, paralysis of lower cranial nerves, bilateral horizontal gaze palsy and anarthria, with preserved consciousness. It is due to a ventral pontine lesion following a basilar artery occlusion. We report the first Indian case report of locked-in syndrome, a 10-year old girl in whom the syndrome was preceded by a 'herald hemiparesis'. Although the exact etiology for the basilar artery occlusion could not be determined, treatment with low molecular weight heparin and warfarin was followed by partial recovery. [Indian J Pediatr 2009; 76 (10): 1053-1055] E-mail: drdm@rediffmail.com

Key words : Basilar artery occlusion; Childhood stroke; Herald-hemiparesis; Hemiplegia; India

Pediatric stroke can have varied presentations and locked-in syndrome is one of the rarer presentations,¹ with no pediatric cases previously reported from India. First reported by Plum and Posner,² the first case of the syndrome in children was reported by Golden *et al.*, in 1976.³ Anatomically the lesion is confined to the ventral pons, and the posterior region, which has the reticular activating system, is uninvolved. As a result, patient maintains sleep-wake cycle and consciousness, but typically has a quadriplegia and expressive aphasia. Patients retain vertical eye movement, facilitating non-verbal communication.⁴ Locked-in syndrome (LIS) is frequently preceded by a hemiparesis ('herald hemiparesis') and convulsions, thereby leading to a misdiagnosis of cortical involvement.^{5,6} A high index of suspicion initial, can predict the onset of a later life threatening illness. If diagnosed at the right stage, the patient can be started on therapy with reasonably good results. We herein present the clinical findings and course of illness of a pediatric patient.

REPORT OF CASE

A 10-year old, developmentally normal female child presented with chief complaints of 5-6 episodes of vomiting followed by unconscious for 30 minutes, three days prior to admission. She continued to be drowsy since then and on the third day, parents noticed that the patient could not turn in bed. She was then brought to the hospital and on examination had stable

vital parameters and a normal fundus picture. Neurological examination revealed a child with normal higher mental functions, no cranial nerve deficits, and a left-sided hemiparesis with hypotonia, normal deep tendon reflexes and left-sided extensor plantar response. There were no sensory deficits but cerebellar signs in the form of hypotonia, nystagmus and truncal ataxia were present. There were no features of raised intracranial pressure. In view of the rapid onset of the neurological deficit, a diagnosis of stroke was made. A computed tomography (CT) scan at admission did not reveal any abnormality. An MRI with an MRA was planned but could not be done immediately in view of logistic problems. Investigations for stroke were planned pending MRI confirmation.

During the hospital stay over the next three days, there was no more vomiting, her ataxia improved and the hemiparesis became more obvious. On day 4 of hospital stay, the patient had an episode of abnormal laughter without provocation and with non-responsiveness, lasting 30-45 seconds, followed by an inability to move all 4 limbs with complete loss of spoken language. Neurological examination revealed motor aphasia with a weak gag reflex and quadriplegia. The child could respond only by blinking or some horizontal movements of her eyes. There was no bladder or bowel involvement. Thus, a clinical diagnosis of a locked-in state was made.

An MRI done on the 5th post-admission day revealed areas of hypointensity involving the ventral pons, middle cerebellar peduncle and cerebellum on T1 images and hyperintensity on T2 images. Diffusion weighted images also revealed hyperintensity in the same areas (Fig.1a). An MRA revealed non-visualization of the left vertebral artery, the

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basilar artery and its various branches suggestive of a complete occlusion by a thrombus; the possibility of an underlying vasculitis could not be excluded (Fig. 1b). A digital subtraction angiography was planned to evaluate for vessel pathology, but could not be done due to lack of parental consent. A complete blood count with a peripheral smear, serum iron studies, lipid profile, Serum C3, ANA, coagulation profile (PT, PTT, Proglobac C), antiphospholipid antibody, RA Factor, echocardiography, chest X-ray, and urinary homocystiene were with in normal limits.

Following the MRI, the Patient was started on low

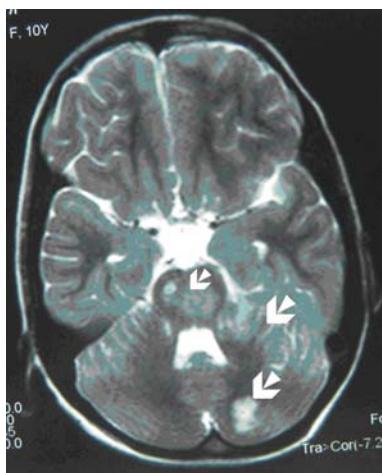


Fig. 1(a). Axial T₂W MR image showing hyperintense areas in the pons, middle cerebellar peduncle and the left cerebellar hemisphere.

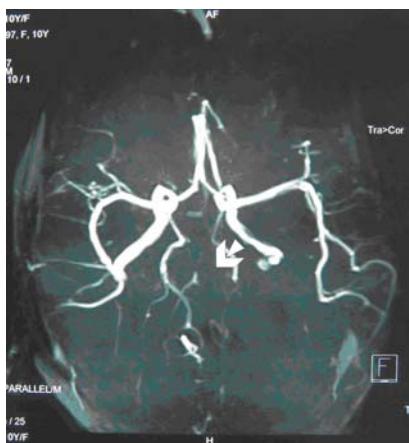


Fig. 1(b). MR angiogram showing non-visualization of the left vertebral artery, basilar artery and its branches, suggestive of vascular occlusion.

molecular weight heparin and warfarin. She has been followed up for three months and has shown considerable improvement in her aphasia and quadriplegia (Category 3, Patterson and Grabs classification⁷).

DISCUSSION

The annual incidence of pediatric stroke is estimated to be around 10.7 cases per 100,000 children per year.⁸ Among the causes of pediatric stroke, occlusion of the basilar artery is rare, and the locked-in presentation still rarer.¹ Two recent reviews of literature have yielded less than 15 cases of locked-in syndrome (LIS) in children.^{1,9} No previous Indian report of locked-in syndrome (LIS) exists in the literature, although basilar artery occlusion has previously been reported in a 16-year old girl.¹⁰

LIS refers to the condition in which patient retains consciousness and cognition but is unable to move or communicate because of severe paralysis. It results from bilateral destruction involving rostral and middle pontine segment, interrupting the descending corticospinal and corticobulbar pathways. Lack of involvement of the mesencephalon permits preservation of convergence and eye movements in the vertical plane. Bauer, et al.¹¹ in 1979, classified LIS into three categories: the '*classical*' variety, which includes patients with all characteristics of LIS as described before, the '*incomplete*' category, which resembles the classical variety, except that patients have other voluntary movements besides upper eyelid and vertical eye movement; and the '*total*' variety, which includes patients who are completely motionless and unable to communicate. According to this classification, our patient had incomplete locked-in syndrome, as she had partial horizontal eye movements in addition to upper eyelid and vertical eye movements. To maintain consciousness, the bulk of the rostral pontine tegmentum must be spared. Severe peripheral nervous system involvement as in Gullain Barre syndrome and myasthenia gravis can occasionally lead to a locked-in state. This condition needs to be differentiated with conditions like vegetative state, akinetic-mutism, and minimally conscious state. The most common cause of LIS is ventral pontine infarction due to basilar artery obstruction. Other causes include pontine hemorrhage, brain stem trauma, pontine tumor, central pontine myelinosis, pontine abscess and multiple sclerosis. The leading cause of basilar artery occlusion in children is vertebral artery dissection,¹² with a history of trivial neck/head trauma being elicited in quite a few patients. Such a history was not available in this child. The site of basilar artery occlusion in majority of the children presenting with a LIS is the mid-third of the artery.¹ The site of BA occlusion is important as it has been correlated with the outcome in adults; more distal the occlusion, less favorable is the outcome.¹³ When the occlusion is located at the proximal part of basilar artery, there is a better chance for good outcome mainly due to the preservation of the blood flow into the brainstem.¹³ Motor recovery in LIS is assessed by Patterson and Grabs classification⁷ and was assessed to be grade 3 (Moderate recovery: moderate motor return, independence in some but not all ADLs) in this patient, 12 weeks after onset. The involvement at the proximal part possibly explains the good outcome in this child.

Two 'classic' pitfalls have been reported to be responsible for delayed diagnosis of LIS patients *viz.*, hemiparesis and convulsions. The hemiparesis was mistakenly interpreted as cortical in origin by us, as has been commonly reported both in children and adults with acute basilar artery occlusion.^{1,5,6} The hemiparesis associated with basilar artery occlusion has been referred to as '*herald hemiparesis*' and is presumably because the growing thrombus blocks the orifices of the paramedian basilar branches first on one side of pons (and several hours later on the other side).⁵ There are many minor accompanying brainstem signs, the recognition of which will arouse the suspicion leading to a correct interpretation. Some of these are: unduly severe dysarthria, transient diplopia, bilateral extensor plantar responses, slight cerebellar dysmetria in the contralateral arm and leg, *etc.*⁵ Convulsive movements at the onset can be either unilateral or bilateral.⁶ Pathological laughter (*fou rire prodromique*) has also been reported previously to herald the development of a brainstem stroke as a result of basilar artery occlusion.¹⁴

Management of acute basilar artery occlusion (BAO) is by recanalisation using intraarterial fibrinolysis.⁹ Only 5 of the previously reported 10 pediatric patients had received primary endovascular treatment. The same was not an option for us due to delayed diagnosis and the parental refusal for continuing management. The outcome of locked-in syndrome with basilar artery occlusion for patients who receive conservative treatment is grim, with most remaining locked-in or with severe neurological impairment.¹ In early literature, mortality was estimated at 60%, being greatest in the first four months and higher in patients with vascular insult than non-vascular causes.⁷ Survivors tended to be younger at age of onset. Earlier rehabilitation and more effective nursing care have been reported to reduce mortality from acute locked-in syndrome.¹⁵

Rosman *et al.*¹ recently presented three cases and reviewed 37 previous cases of basilar artery occlusion in children <18 year (31 males and 9 females), with locked-in presentation in 10 (8 males, 4-13 yr age; 2 females, both 18 yr old). The BAO was associated in these 10 LIS cases with cyanotic CHD in 2, trauma in 1, factor V leiden heterozygosity in 1, and unknown causes in 5. Our patient was much younger than the reported female patients and did not have any evidence of these etiologies. The mode of onset of neurological symptoms in BAO is acute with neurological symptoms without precedent in 60%, and the rest having a history of transient premonitory phenomenon for less than 1 month.¹ The most common presentation of BAO was hemiparesis and abnormal movements (misinterpreted as seizures in 36%). CT scans in 23% (5 of 22, in whom it was done) were normal in the initial phase, and MRI was abnormal in 100% of the cases (done in only 11 patients), as was the case in our patient. Most patients with LIS had some useful recovery, though the outcome ranged from mild quadriplegia (1 case), to persistent LIS 4 years later (1 case), to death from a secondary cause after a prolonged locked-in state (1 case).¹

Locked-in syndrome has been infrequently reported from pediatric patients because of the rarity of the condition itself, the vague and non-specific symptomatology, and the difficulty in separating it from other conditions associated with altered sensorium. Although rare in its occurrence, it is important that this condition not be overlooked. This case-report serves to emphasize the clinical features and also underscores the clinical pitfalls in making an early diagnosis. The prognosis is poor but early intra-arterial fibrinolysis and early intensive multi-disciplinary rehabilitation may aid recovery to a large extent.

Contributions: RJ and SS were involved in patient management, literature search and manuscript preparation. MJ made the initial diagnosis and alongwith DM supervised the patient management and manuscript preparation. SS provided expert opinion on radiological investigations.

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REFERENCES

1. Rosman NP, Adhami S, Mannheim GB, Katz NP, Klucznik RP, Muriello MA. Basilar artery occlusion in children: Misleading presentations, "locked-in" state, and diagnostic importance of accompanying vertebral artery occlusion. *J Child Neurol* 2003; 18: 450-462.
2. Plum F, Posner JB. *The diagnosis of stupor and coma*. Philadelphia, 1966, FA Davis Company, pp. 92-93.
3. Golden GS, Leeds N, Kremenitzer MW, Russman BS. The "locked-in" syndrome in children. *J Pediatr* 1976; 89: 596-598.
4. Smith E, Delargy M. Locked-in syndrome *BMJ* 2005; 330: 406-409.
5. Fischer CM. The 'herald hemiparesis' of basilar artery occlusion. *Arch Neurol* 1988; 45: 1301-1303.
6. Ropper AH. 'Convulsions' in basilar artery occlusion. *Neurology* 1988; 38: 1500-1501.
7. Patterson JR, Grabsos M. Locked-in syndrome: a review of 139 cases. *Stroke* 1986; 17: 758-764.
8. de Veber GA. Cerebrovascular Disease in Children. In Swaiman KF, Ashwal S, Ferriero DM eds. *Paediatric Neurology-Principles & Practice*, 4th ed. St Louis Philadelphia; Mosby Publishers, 2006: 1759-1801.
9. Grigoriadis S, Gomori JM, Grigoriadis N, Cohen JE. Clinically successful late recanalization of basilar artery occlusion in childhood: What are the odds? Case report and review of the literature. *J Neurol Sci* 2007; 260: 256-260.
10. Jain S, Maheshwari MC, Tandon PN, Goulatia RK. Idiopathic basilar artery occlusion in childhood. *Stroke* 1984; 15: 563-565.
11. Baeur G, Gerstenbrand F, Rumpl E. Varieties of locked-in syndrome. *J Neurol* 1979; 221: 77-91.
12. Hasan I, Wapnick S, Tenner MS, Couldwell WT. Vertebral artery dissection in children: a comprehensive review. *Pediatr Neurosurg* 2002; 37: 168-77.
13. De Bray JM, Penisson-Besnier I, Dubas F, Emile J. Extracranial and intracranial vertebralbasilar dissections: diagnosis and prognosis. *J Neurosurg Psychiatry* 1997; 63: 46-51.
14. Gondim FA, Parks BJ, Cruz-Flores S. "Fou rire prodromique" as the presentation of pontine ischaemia secondary to vertebrobasilar stenosis. *J Neurol Neurosurg Psychiatry* 2001; 71: 802-804.
15. Casanova E, Lazzari RE, Latta S, Mazzucchi A. Locked-in syndrome: improvement in the prognosis after an early intensive multi-disciplinary rehabilitation. *Arch Phys Med Rehabil* 2003; 84: 862-867.