Extensive Brainstem Ischemia on Neuroimaging Does Not Preclude Meaningful Recovery from Locked-In Syndrome: Two Cases of Endovascularly Managed Basilar Thrombosis

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ABSTRACT

We report 2 patients with angiographically demonstrated basilar artery thrombosis who received emergent intra-arterial thrombolysis with successful recanalization of the basilar artery. In the ensuing weeks after the procedure, both patients were in a locked-in state and had sustained large bilateral regions of pontine ischemia on brain imaging. Following aggressive supportive care and rehabilitation, outcomes obtained prospectively revealed that both patients made a remarkable recovery, becoming fully independent with Barthel scores of 20 and modified Rankin scores of 2.

Background and Significance

Locked-in syndrome is the neurologic constellation of anarthria, quadriplegia, horizontal gaze paresis, and preserved consciousness usually engendered by a ventral pontine lesion. The most common cause of locked-in syndrome is pontine infarction secondary to basilar artery thrombosis.[1] Patients with the classic form of locked-in syndrome can communicate solely through vertical eye movements and blinking. Mortality reported from one of the largest series of locked-in patients was 60%,[2] but more recently, 10-year survival rates of 80% have been achieved with early, intensive rehabilitation.[1] It therefore behooves physicians to make this diagnosis and therefore to distinguish the patient's condition from other prognostically distinct states of diminished responsiveness.

Case series of patients with locked-in syndrome have reported motor recovery rates ranging from 55% to 91% in addition to less frequent improvements in respiration, bladder/bowel continence, swallowing, and verbal communication.[3] Moreover, although the mortality of patients with locked-in syndrome has proved highest when the etiology is vascular, ie, secondary to basilar artery thrombosis, complete or near-complete recovery has been reported in patients locked-in following several hours of basilar artery thrombosis.[4-7] However, in these few published reports of vascular locked-in syndrome reversibility, the extent of brain ischemia is poorly documented and it is unclear if recovery was associated with rapid (spontaneous or therapeutic) basilar artery recanalization that preserved large brainstem regions or occurred despite severe brainstem ischemia. We present 2 cases of meaningful neurological recovery in patients who had evidence of extensive bilateral ischemic insult to the brainstem and an initial locked-in syndrome examination after endovascular basilar artery thrombolysis.

Methods

This case series was performed with Institutional Review Board approval. Patients with locked-in syndrome were retrospectively identified from a prospectively acquired database composed of patients with acute ischemic stroke admitted to the University of Pittsburgh Medical Center Presbyterian Hospital stroke service between 2000 and 2003 who were enrolled in the prospective "stroke outcome study" ongoing at our institution during that period. Outcomes at 3, 6, 9, and 12 months were obtained independently from caretakers by a group of nurses and occupational therapists trained in performing neurological outcome scales. Clinical and radiological data were obtained retrospectively through chart review.

Case Report 1

A 46-year-old man with no significant past medical history developed severe headache and slurred speech. He became unresponsive and was taken to a local hospital where his neurological exam showed extensor posturing and an absent left corneal reflex. The patient was transferred to our facility where he exhibited unresposiveness, abnormal eye movements, and quadriparesis. Noncontrast head computed tomography (CT) demonstrated a hyperdense basilar artery. Emergent cerebral angiography revealed thrombus in the distal two-thirds of the basilar artery just above the AICA origin (Fig 1), high-grade stenosis of the right vertebral artery (VA) origin with an occlusive thrombus from approximately the C2-C5 vertebral levels,
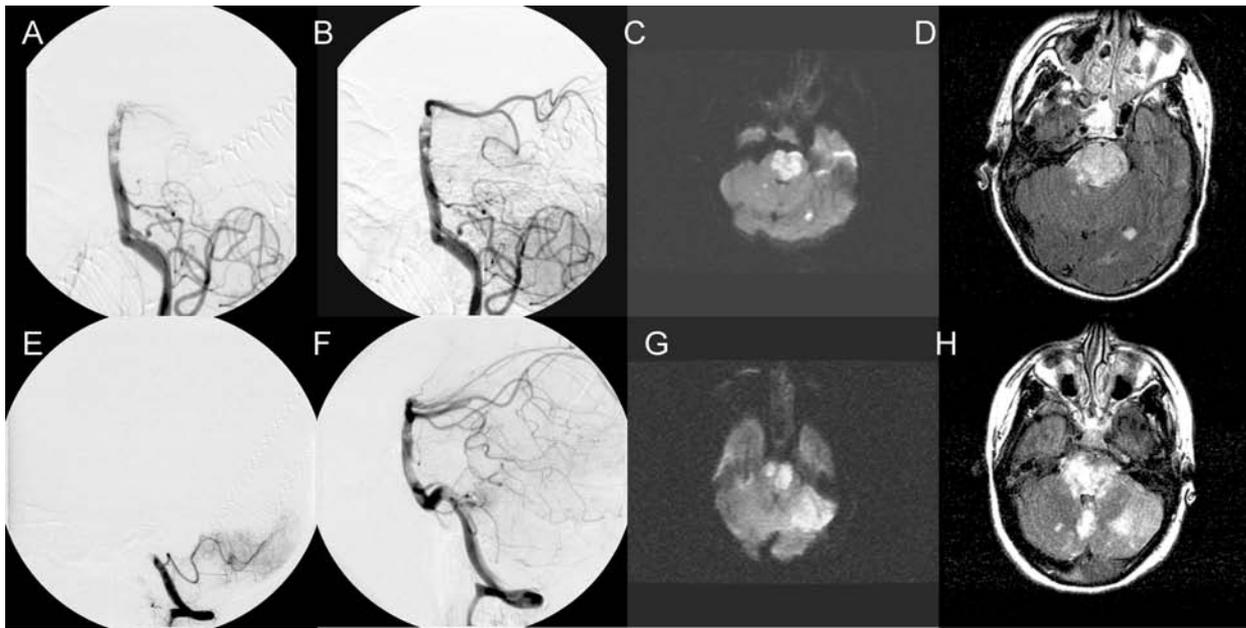
Fig 1. Cerebral angiography (A, B, E, F) diffusion weighted MRI (C, G), and axial FLAIR sequence MRI images (D, H) of patient 1 (A, B, C, D) and patient 2 (E, F, G, H) showing basilar artery thrombosis, recanalization, and extensive pontine infarctions.

and moderate stenosis of the left VA origin. Approximately 11 hours after ictus, defined as the sudden onset of unresponsiveness, his basilar artery was recanalized to thrombolysis in myocardial ischemia (TIMI) grade 2 flow (minimal residual thrombus with brisk antegrade flow) via the administration of 32 mg tissue plasminogen activator (t-PA) into the occlusive thrombus. Brain magnetic resonance imaging (MRI) obtained 2 days after ictus demonstrated ischemia within large areas of the pons and extending into the cerebral peduncles (Fig 1). Magnetic resonance angiogram showed a patent basilar artery. The patient's neurological examination confirmed by several neurologists revealed a locked-in state with preserved blinking and vertical eye movement superimposed on a background of quadriplegia, anarthria, and horizontal gaze paresis. The patient was discharged to a standard rehabilitation program after a 3-week hospitalization during which his condition had not changed significantly. Following discharge he started to steadily improve and at 6 months after hospitalization, his Barthel score and modified Rankin scores obtained independently from physician caretakers were 20 and 2, respectively. Today the patient is fully independent, walks with a cane, and continues to enjoy activities including hunting, lake fishing, and woodwork.

Case Report 2

A 27-year-old woman presented to her local hospital with a 2-day history of intermittent vertigo, neck pain, nausea, and vomiting. Her only medication was an oral contraceptive and she had no significant past medical history. While being evaluated at the hospital, the patient developed sudden anarthria, urinary incontinence, and left hemiparesis followed rapidly by unresponsiveness and decerebrate posturing. Noncontrast head

CT showed hyperdensity in the lower basilar artery and distal right vertebral artery. Cerebral angiography showed dissection of the right VA at the C1-C2 level, a patent left VA, and complete occlusion of the proximal basilar artery (Fig 1). Approximately 7 hours after ictus, the basilar artery was recanalized to a TIMI grade 2 flow with 22 mg intra-arterial t-PA. Brain MRI obtained 4 days after ictus showed substantial bilateral pontine as well as cerebellar ischemic lesions (Fig 1). On examination performed by several neurologists, she was locked-in with preserved vertical eye movements and appropriate blinking to different commands. Eight days after admission the patient regained some lateral gaze capability but remained otherwise unchanged. The patient was discharged to a standard rehabilitation program and eventually became fully independent. Her recovery was quantified independently of physician caretakers at 6 months as a Barthel score of 20 and modified Rankin score of 2. The patient became fully independent and returned to work as a software instructor. She currently drives a car, walks with a cane, and is able to engage in about 50% of previous leisure activities.

Discussion

Although the reversibility of locked-in syndrome has been described, this is the first report of patients achieving functional recovery from vascular locked-in syndrome in the context of near-complete pontine ischemic insult on neuroimaging. Understanding that diffusion weighted imaging hyperintensity in the setting of acute ischemic stroke may be a reversible imaging finding, which overestimates final histological infarct volume, we confirm the impressive magnitude of irreversible brainstem ischemic damage in these 2 patients by displaying corresponding regions of hyperintensity on brain MRI FLAIR

(Fluid-attenuated inversion recovery) sequences.[8-11] Diffusion-perfusion MRI of patients with acute basilar artery occlusion has revealed that intra-arterial thrombolytic recanalization of the basilar artery can salvage substantial volumes of hypoperfused brain tissue, preventing the lethality of total basilar artery territory infarction.[12] Our report suggests that early revascularization of basilar artery thrombosis may not spare patients the morbidity of locked-in state, which may be only temporary, but may permit them to sustain a recoverable type of basilar artery stroke limited primarily to paramedian ventral pontine perforator territory.[13]

Given the known poor natural history of basilar thrombosis, the outcomes observed in these 2 cases lends credence to the expectation that the mortality and morbidity of vascular locked-in syndrome may decline in parallel with technological advances that enable rapid revascularization of the posterior circulation. The time window during which recanalization of the basilar artery remains beneficial is poorly defined. Yet, it is likely that the time windows for thrombolytic therapy in the basilar circulation are significantly longer than most anterior circulation occlusions. While recent studies have suggested beneficial effects of recanalization even after 79 hours of basilar thrombosis, our patients were revascularized relatively early.[14] Our study adds meaningful prospective outcomes to a list of vascular locked-in patients that have been aggressively revascularized. Similar to patients with intracerebral hemorrhage in whom withdrawal of care ensures dismal self-fulfilling prophecies,[15] it is possible that the poor outcomes in locked-in patients may in part derive from a reluctance to provide aggressive care.

Locked-in syndrome is a devastating condition in which consciousness is preserved despite complete deprivation of voluntary activity. This report establishes the counterintuitive potential for good recovery in locked-in patients with early-revascularized basilar thrombosis even when MRI shows large brainstem strokes. Physicians treating this heterogeneous patient population must remain wary of allowing the magnitude of brainstem ischemia on modern neuroimaging to influence estimates of prognosis and the supportive effort. Identifying those patients who are most likely to recover and in whom aggressive and sustained rehabilitative efforts are justified remains a great challenge.

References

1. Casanova E, Lazzari RE, Lotta S, Mazzucchi A. Locked-in syndrome: improvement in the prognosis after an early intensive multidisciplinary rehabilitation. *Arch Phys Med Rehabil* 2003;84:862-867.
2. Patterson JR, Grabois M. Locked-in syndrome: a review of 139 cases. *Stroke* 1986;17(4):758-764.
3. Smith E, Delargy M. Locked-in syndrome. *BMJ* 2005;330:406-409.
4. Mellado P, Sandoval P, Tevah J, Huete I, Castillo L. Intra-arterial thrombolysis in basilar artery thrombosis. Recovery of two patients with locked-in syndrome. *Rev Med Chil* 2004;132(3):357-360.
5. McCusker EA, Rudick RA, Honch GW, Griggs RC. Recovery from 'locked-in' syndrome. *Arch Neurol* 1982;39(3):145-147.
6. Cabezudo JM, Olabe J, Lopez-Anguera A, Bacci F. Recovery from locked-in syndrome after posttraumatic bilateral distal vertebral artery occlusion. *Surg Neurol* 1986;25(2):185-190.
7. Wijdicks EFM, Nichols DA, Thielen K, Fulgham JR, Brown RD Jr, Meissner I, Meyer FB, Piepgras DG. Intra-arterial thrombolysis in acute basilar artery thromboembolism: the initial Mayo experience. *Mayo Clinic Proceedings* 1997;72:1005-1013.
8. Guadagno JV, Warburton EA, Aigbirhio FI, Smielewski P, Fryer TD, Harding S, Price CJ, Gillard JH, Carpenter TA, Baron JC. Does the acute diffusion-weighted imaging lesion represent penumbra as well as core? A combined quantitative PET/MRI voxel-based study. *J Cereb Blood Flow Metab* 2004;24(11):1249-1254.
9. Noguchi K, Ogawa T, Inugami A, Fugita H, Hatazawa J, Shimosegawa E, Okudera T, Uemura K, Seto H. MRI of acute cerebral infarction: a comparison of FLAIR and T2-weighted fast spin-echo imaging. *Neuroradiol* 1997;39:406-410.
10. Ritzl A, Meisel S, Wittsack H, Fink GR, Siebler M, Modder U, Seitz R. Development of brain infarct volume as assessed by magnetic resonance imaging (MRI): follow-up of diffusion-weighted MRI lesions. *J Magn Reson Imaging* 2004:20:201-207.
11. Kidwell CS, Saver JL, Starkman S, Duckwiler G, Jahan R, Vespa P, Villablanca JP, Liebeskind DS, Gobin YP, Vinuela F, Alger JR. Late secondary ischemic injury in patients receiving intra-arterial thrombolysis. *Ann Neurol* 2002;52:698-703.
12. Thajeb P, Lie LK, Chang TR. Types of basilar artery syndrome: clinicoradiologic correlation. *Angiology* 1993;44:368-375.
13. Cross DT, Moran CJ, Akins PT, Angtuaco EE, Diringer MN. Relationship between clot location and outcome after basilar artery thrombolysis. *Am J Neuroradiol* 1997;18:1221-1228.
14. Ostrem JL, Saver JL, Alger JR, Starkman S, Leary MC, Duckwiler G, Jahan R, Vespa P, Villablanca JP, Gobin YP, Vinuela F, Kidwell CS. Acute basilar artery occlusion: diffusion-perfusion MRI characterization of tissue salvage in patients receiving intra-arterial stroke therapies. *Stroke* 2004;35:e30-e34.
15. Becker KJ, Baxter AB, Cohen WA, Bybee HM, Tirschwell DL, Newell DW, Winn HR, Longstreth WT Jr. Withdrawal of support in intracerebral hemorrhage may lead to self-fulfilling prophecies. *Neurology* 2001;56(6):766-772.