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Locked-in syndrome as an unusual complication of acute otitis media

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Abstract. *Locked-in syndrome as an unusual complication of acute otitis media. Background*: A 32-year-old woman developed altered consciousness two days after initial symptoms of acute otitis media, with purulent discharge from the right ear. She was quadriplegic, with spontaneous eye opening, mild neck stiffness, and lacking vestibular-ocular reflexes. *Methodology*: Upon admission, the patient was subjected to brain computed tomography (CT), magnetic resonance imaging (MRI), and lumbar puncture.
Results: CT was consistent with pansinusitis, right middle ear otitis, mastoiditis, and sphenoiditis. No brainstem lesion was evident; brain MRI demonstrated ischemic and secondary hemorrhagic lesions in the pons and cerebral peduncles. The dura mater in the petroclival space was intensely inflamed, and likely responsible for reduced basilar arterial blood flow. Lumbar puncture yielded clear cerebrospinal fluid; gram stain examination was negative and culture remained sterile. *Streptococcus pneumoniae* and *Haemophilus influenzae* were cultured from the purulent ear discharge.
Conclusion: The final diagnosis was locked-in syndrome consecutive to inflammatory changes compressing the basilar artery.

Introduction

Intracranial arterial complications following acute otitis media (AOM) appear to be rare in adults. Focal or diffuse brain infarctions are usually of venous origin and mainly occur as complications of bacterial meningitis. We present a case of AOM complicated by acute brainstem ischemia resulting in locked-in syndrome (LIS). The paucity of meningeal signs and clear, sterile cerebrospinal fluid made this case particularly interesting.

Case report

A 32-year-old woman without significant past medical history was referred to the Emergency Department for altered consciousness. Two days before hospital admission, she had developed fever, earache, and right ear discharge; she did not consult her general practitioner and took paracetamol for pain relief. The patient's vital signs at admission were: temperature 38°C, heart rate 89 beats/min, arterial blood pressure 115/90 mmHg, and oxygen saturation 99%. Physical examination revealed spontaneous eye opening and lack of any verbal response or motor response in the four limbs; the Glasgow Coma Score was calculated at 6/15 (E4,V1,M1). Pupils were equal in size and reacted to light stimulation; however, the left corneal reflex was absent. Vertical and horizontal vestibular-ocular reflexes were abolished. Tonus was spastic with hyperreflexia, ankle clonus, and Babinski sign. Mild neck stiffness was observed. Purulent discharge was observed at the right ear. Because the patient's respiratory rate was decreasing and peripheral oxygen saturation was low, orotracheal intubation was required for mechanical ventilation.

Routine laboratory investigations were not relevant, with the exception of C-reactive protein at 7.95 mg/dl. A non-contrast computed tomography (CT) scan of the head revealed pansinusitis, lack of aeration of the right mastoid cavity, and soft tissue swelling of the mastoid and middle ear.

A lumbar puncture yielded clear cerebrospinal fluid (CSF); the opening pressure was normal. Examination of the CSF revealed the presence of 72 white blood cells (81% neutrophils), with glucose level 59 mg/dl and protein level 33 mg/dl. CSF gram stain showed no bacteria and culture remained sterile. The gram stain examination of the pus discharged from the right ear showed gram-positive cocci. The culture was ultimately positive for *Streptococcus pneumoniae* and *Haemophilus influenzae*. Antimicrobial therapy was initiated from hospital admission with ceftriaxone and ampi-

cillin, together with dexamethasone 40 mg/day. General anesthesia was performed to obtain secretions from the maxillary sinuses, which the CT scan revealed were inflamed. Swab samples were taken from both maxillary sinuses, as well as from the right middle ear via paracentesis, and ruled out any mycotic infection.

Brain magnetic resonance imaging (MRI) was performed on the second hospital day (Figure 1A-C). The main findings (aside from the confirmation of right-side mastoiditis) were ischemic and hemorrhagic changes visible in the pons and cerebral peduncles. The basilar artery was surrounded by an intense inflammatory reaction of the dura mater in the petroclival area, and there was no flow in the left vertebral artery. Brain CT had also revealed some focal bone discontinuity of the clivus (Figure 1D). There was no evidence of epidural abscess or lateral sinus thrombosis.

Electrophysiological investigations were performed on hospital day 4. The electroencephalogram (EEG) showed diffuse slowing (8 Hz) with beta waves predominating, although theta and delta waves were also observed; alpha waves were also obtained after stimulation. Multimodality (visual, auditory, somatosensory) evoked potentials were also investigated on hospital day 4. The visual evoked potentials were normal. When brainstem auditory evoked potentials were examined, peak V could not be identified after stimulation of the left ear. When somatosensory evoked potentials were examined, medullar cervical and lemniscal activities (P14 wave) were normal after median nerve bilateral stimulation. However, no cortical parietal activities (N20 wave) could be recorded from the left hemisphere. At follow-up (hospital day 26), no lemniscal (P14) or parietal (N20) activities could be recorded on the left side. No peripheral activities were obtained following transcranial stimulation of the motor cortex (motor evoked potentials).

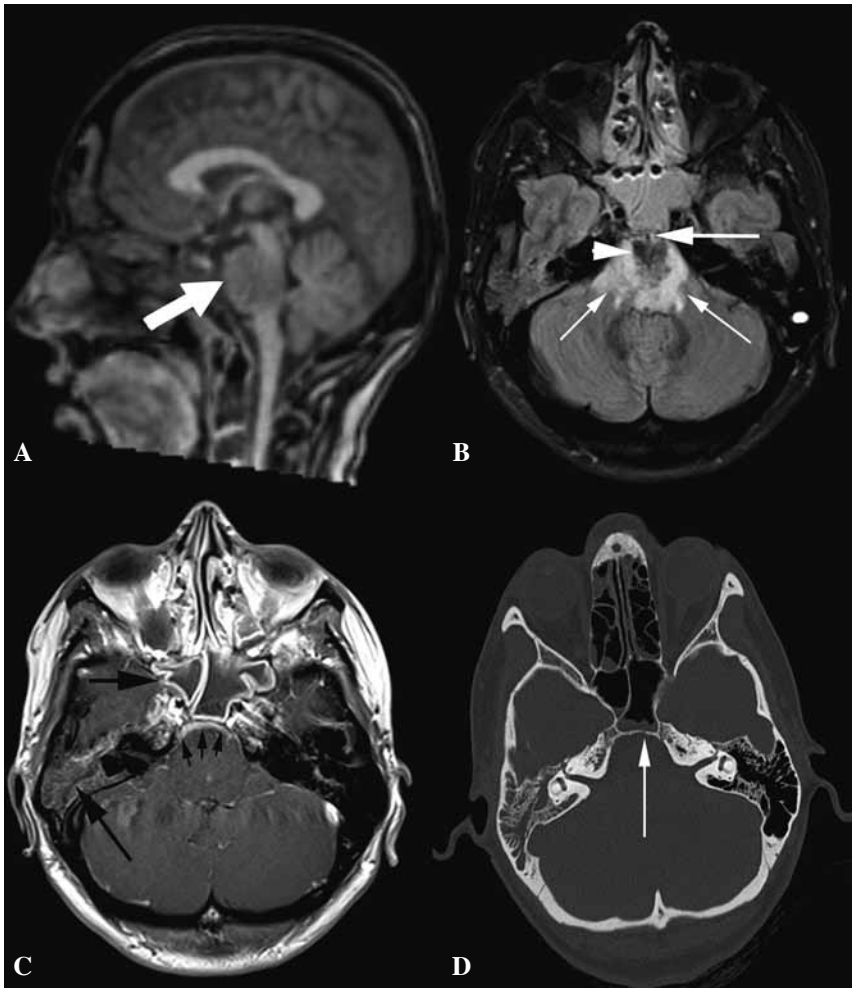

Figure 1A-D

MRI of the head (hospital day 2). A: Sagittal T1-weighted image showing diffuse hypointensity of the pons (arrow). B: Axial FLAIR MRI. Ischemic and hemorrhagic lesions of the pons and middle part of cerebral peduncles. The edematous changes appear hyperintense (thin arrows), while hypointense signal changes are consistent with hemorrhagic lesions (arrow head) and occlusion of the basilar artery (thick arrow). C: Axial T1 post-gadolinium, showing localized enlargement and hyperhemia of the dura mater in the petroclival space (small arrows). Abnormal soft-tissue attenuation of the right mastoid air cells, petrous apex, and sphenoidal sinus (large arrow). D: High resolution CT (axial image) demonstrating a focal bone discontinuity of the clivus (arrow).

The patient remained quadriplegic with progressive spasticity of the lower limbs. She was able to communicate using vertical eye movements. The patient was diagnosed with LIS with preserved cognitive functions. Because of swallowing disorders and the absence of upper airway protection, a tracheostomy and gastrostomy were performed and the patient was discharged from the intensive care unit on hospital day

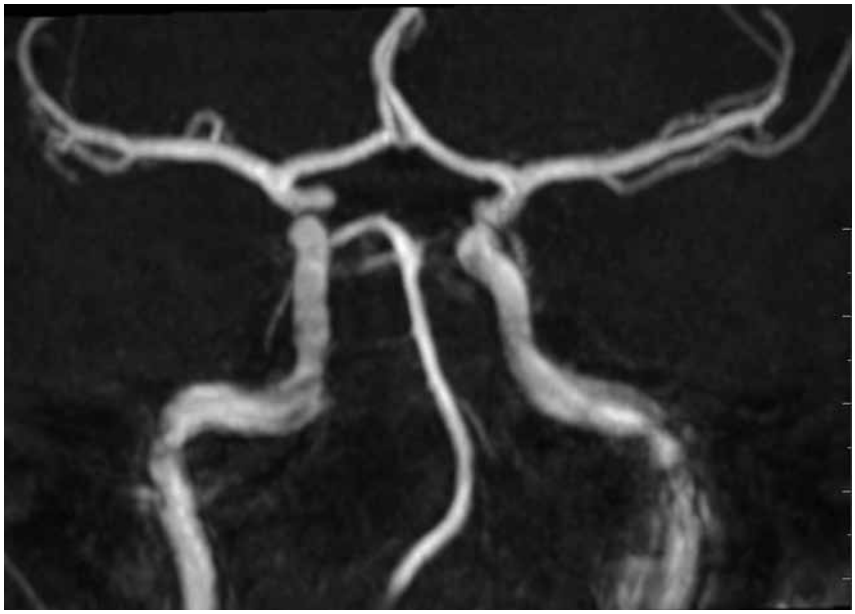

Figure 2
MR angiography performed on hospital day 39. Note that the basilar artery has recovered a normal diameter. The left vertebral artery appears narrowed, particularly in the V4 segment.

10. Further investigation did not reveal any prothrombotic tendency.

A control MR angiography was performed on hospital day 39 (Figure 2). This investigation demonstrated that the basilar artery had recovered a normal diameter. The right vertebral artery appears large (which may simply be an anatomic variant), while the distal part of the left vertebral artery remains narrowed, but is not occluded.

When followed up after 3 months in a neurological rehabilitation unit, the patient still presented spastic quadriparesis. She was able to move the fingers of her left hand slightly, and to communicate via an electronic tablet. Some improvement was noted in head rotation and flexion. The tracheostomy tube was removed and oral feeding was reintroduced.

Discussion

LIS was first defined in 1966 as quadriplegia, lower cranial nerve paralysis, and mutism with preservation of consciousness, vertical gaze, and upper eyelid movement. Typically, LIS is caused by an insult to the ventral pons of vascular origin (basilar artery occlusion or hemorrhage within the pons). Occasionally, other etiologies may be observed, including: trauma, tumor, metabolism, or infection.[1] Sometimes, LIS may be incomplete, with remnants of voluntary movement other than vertical eye movement. LIS-associated mortality and morbidity can be reduced with the aggressive treatment of complications. Ten-year survival rates as high as 80% have been reported, and quality of life can be improved with an early rehabilitation program. MRI is the most helpful technique to confirm diagnosis of LIS. Preserved EEG reactivity of a posterior alpha rhythm is a cardinal feature of LIS, while somatosensory evoked potentials have limited diagnostic value, ranging from fully normal to unilateral or bilateral abnormalities.[2] Although lemniscal activities (P14 wave) are typically preserved, cortical activities (N20 wave) are usually abolished. This pattern is highly suggestive of a pontine lesion, particularly when brainstem auditory evoked potentials appear pathological.

The association between AOM and acute brainstem stroke appears exceptional, and the possible mechanisms will be briefly presented.

The first hypothesis is that acute brainstem ischemia was not related to AOM. Our patient had no significant risk factor for cerebrovascular diseases (no smoking, drug use, etc.). A hypercoagulable state due to an inherited prothrombotic tendency (protein S deficiency, mutation of factor II or V, etc.) was also ruled out. The patient also never presented significant arterial hypotension during her stay in the intensive care unit.

A second hypothesis is that this brainstem injury was a consequence of intracranial hypertension. This hypothesis is not supported by the MRI findings. Only one measurement of opening pressure was obtained at the time of the first lumbar puncture. However, the patient did not present purulent meningitis as a potential trigger of high intracranial pressure. Pneumococcal meningitis has rarely been associated with brainstem ischemia in the absence of increased intracranial pressure.[3]

Pontine and spinal cord infarcts have been reported.[4-6] Several factors may be involved, such as systemic hypotension; loss of autoregulation of cerebral blood flow; or the occlusion of small blood vessels because of septic embolism, or because of vasculitis after direct invasion by microorganisms.[7,8]

A third possible mechanism is an injury to the brainstem from a local (infectious or vascular) cause.

While approximately 2% of cases of AOM will develop intracranial complications (mostly meningitis), arterial brain infarctions appear exceptional.[9] In 2007, Oestreicher-Kedem *et al*.[10] reported the case of a 30-month-old girl who developed meningitis, brain abscess, orbital cellulitis, and (most notably) arterial brain infarction, all after an AOM due to *Diphteroids*. The brain infarct was located in the territory of the right posterior cerebral artery (RPCA), with subdural abscesses along the cisterns of the right cerebropontine angle, quadrigemina, and ambiens, compressing and obliterating the RPCA. In the present case, there was no evidence of abscess surrounding or infiltrating the ventral pons. We strongly suspect that the spread of the meningeal inflammation to the wall of the intracranial vessels may have resulted in arterial thrombosis with ischemia. Indeed, the brain MRI revealed signs of pachymeningitis in the petroclival area. There was also a focal bone discontinuity in the clivus. The CSF culture remained sterile. Therefore, the intensity of the local inflammatory reaction appears to be responsible for disrupting blood flow in the basilar and left vertebral arteries. This hypothesis is also supported by the follow-up MR angiography findings.

Conclusions

This patient presented with LIS as a rare complication of AOM due to *Streptococcus pneumoniae* and *Haemophilus influenzae*. The functional outcome appears poor. The most likely hypothesis, in the absence of increased intracranial pressure or purulent meningitis, is reduced basilar arterial flow because of petroclival meningeal inflammation.

References

1. Smith E, Delargy M. Locked-in syndrome. *BMJ*. 2005;330(7488);406-409.
2. Gütling E, Isenmann S, Wichmann W. Electrophysiology in locked-in syndrome. *Neurology*. 1996;46(4):1092-1101.
3. Haarman EG, Vermeulen RJ, van Furth AM, Verbeke JI, Plötz FB. Cushing's triad in pneumococcal meningitis due to brainstem ischemia: early detection by diffusion-weighted MRI. *Pediatr Neurol*. 2008;38(4): 276-278.
4. Perry JR, Bilbao JM, Gray T. Fatal basilar vasculopathy complicating bacterial meningitis. *Stroke*. 1992; 23(8):1175-1178.
5. Haupt HM, Kurlinski JP, Barnett NK, Epstein M. Infarction of the spinal cord as a complication of pneumococcal meningitis. Case report. *J Neurosurg*. 1981;55(1):121-123.
6. van Egeraat SC, van Munster ET, Bodewes HW, van der Hoeven JG. Spinal cord infarction as a severe complication of meningococcal meningitis. *Eur J Intern Med*. 2003;14(6): 383-385.
7. Tureen JH, Dworkin RJ, Kennedy SL, Sachdeva M, Sande MA. Loss of cerebrovascular autoregulation in experimental meningitis in rabbits. *J Clin Invest*. 1990;85(2):577-581.
8. Ashwal S, Tomasi L, Schneider S, Perkin R, Thompson J. Bacterial meningitis in children: Pathophysiology and treatment. *Neurology*. 1992; 42(4):739-748.
9. Friedman EM, McGill TJ, Healy GB. Central nervous system complications associated with acute otitis media in children. *Laryngoscope*. 1990;100(2 Pt 1):149-151.
10. Oestreicher-Kedem Y, Ben-Sira L, Grissaru G, DeRowe A. Arterial brain infarction in complicated acute otitis media. *Int J Pediatr Otorhinolaryngol*. 2007;71(4):659-663.

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