Fatal Basilar Vasculopathy Complicating Bacterial Meningitis

James R. Perry, MD; Juan M. Bilbao, MD; and Trevor Gray, MD

Background: Bacterial meningitis complicated by thrombosis, vasculitis, and aneurysm formation affecting both small and distal branches of cerebral vessels has been well described. Involvement of major cerebral vessels is rare and has only been documented late in the course of disease.

Case Description: We describe the clinical and pathological findings in a young man who presented with pontine infarction as an early manifestation of bacterial meningitis. Streptococcus milleri, an unusual organism in this setting, was cultured. Despite improvement with antibiotic therapy, the patient experienced fatal subarachnoid hemorrhage. A ruptured inflammatory aneurysm of the basilar artery, evidence of residual meningitis and vasculitis, and basilar thrombosis associated with pontine infarction were found.

Conclusions: Bacterial meningitis, which may be associated with severe vasculopathy of the basilar artery and lead to cerebral infarction, aneurysm formation, and subarachnoid hemorrhage, should be considered in the differential diagnosis of these conditions. The role of S. milleri in meningitis and its vascular complications merits further study. (Stroke 1992;23:1175-1178)

Key Words • cerebral infarction • meningitis • thrombosis

Cerebrovascular complications of meningitis, including stroke, are usually manifested during the course of well-established illnesses. Stroke as an early manifestation of meningitis, particularly that due to bacterial organisms, has rarely been reported. We document the clinical findings and pathological examination of a young man who developed pontine infarction as an early manifestation of bacterial meningitis. Despite treatment, his course was also complicated by subarachnoid hemorrhage from a ruptured inflammatory aneurysm of the basilar artery. The mechanism of the severe vasculopathy in this case included vasculitis, venous and arterial thrombosis, and destruction of the basilar artery by inflammation leading to aneurysm formation. These pathological processes, although known to affect small vessels and distal branches of cerebral arteries, rarely involve the major vessels at the base of the brain. These findings may be related to properties of an unusual and controversial Streptococcus species (S. milleri) recovered from the cerebrospinal fluid in this case.

Case Report

A 34-year-old man from Northern Ontario was admitted to our hospital following sudden collapse with right hemiparesis. He had been unwell the previous 10 days with fever, nonproductive cough, and mild headache. A physician prescribed oral penicillin, which had been taken for 8 days without improvement. The patient experienced no further symptoms until he collapsed on the day of admission. His medical history was significant only for depression treated 5 years previously. There was no history of neurological disease, head trauma, travel, infectious contacts, dental work, or surgical procedures. He denied drug use and risk factors for human immunodeficiency virus infection.

Upon transfer to our institution, he appeared toxic and had an oral temperature of 39.4°C. Marked meningismus was present. General physical examination was normal. He was drowsy but able to give a coherent history. Extraocular movements were abnormal, with a gaze palsy sparing only abduction of the right eye. An upper motor neuron-type facial palsy, hemiplegia, and extensor plantar response were present on the right side.

Peripheral blood revealed a white blood cell count of $20.8 \times 10^9/l$ with 87% neutrophils, 125 mmol/l sodium, and 6.3 mmol/l glucose. Plain and contrast-enhanced computed tomographic (CT) scan of the brain was normal. Lumbar puncture yielded turbid cerebrospinal fluid (CSF) under an elevated opening pressure of 31 cm water. Results of CSF analysis were white blood cell count of 1,189/mm$^3$ (all neutrophils), 1.35 g/l protein, and 0.4 mmol/l glucose. A gram stain documented numerous neutrophils but no organisms. Latex agglutination for cryptococcal antigen, smear for mycobacteria, and assays for syphilis were negative. Blood cultures for bacteria, fungi, and viral studies were negative. The CSF grew a pure culture of S. milleri sensitive to penicillin.

The patient was treated with $2.4 \times 10^7$ IU i.v. penicillin and 16 mg dexamethasone daily. Twenty-four hours after admission, he had improved markedly, with reso-
lution of fever and drowsiness and normalization of the gaze palsy; however, the hemiparesis persisted. Magnetic resonance imaging of the brain on day 2 revealed an abnormal signal in the region of the left ventral pons consistent on all sequences with recent ischemic infarction (Figure 1). Continued improvement occurred over the following days. Chest and sinus x-ray films and dental examination were unremarkable.

On day 8 he complained of severe headache and abruptly deteriorated. He required intubation and ventilation and developed fixed midposition pupils. A CT scan revealed fresh subarachnoid hemorrhage in the basal cisterns of the brain. Clinical signs of brain death were normal. The temporal bones and mastoids, after grossly and histologically normal. The paranasal sinuses were normal at this level.

At autopsy, significant findings were limited to the brain. A focal acute bronchopneumonia was present in the lungs, but they were otherwise normal. Examination of the heart showed no evidence of endocarditis, thrombus, or structural abnormality. The major organs were grossly and histologically normal. The paranasal sinuses were normal. The temporal bones and mastoids, after removal en bloc, revealed no abnormality. A large clot was present in the basal cisterns and extended to the third and fourth ventricles. A 10-mm fusiform aneurysm was found arising from the midportion of the basilar artery, projecting ventrally. It had ruptured, with a clot forming one third of the outer wall (Figure 2A). No other aneurysms were present. The pons was softened, and histological examination revealed a large infarction 10–14 days of age mainly confined to the left ventral region (Figure 2A). The basilar artery was involved by an angiodestructive inflammatory process in all wall layers (Figure 2B). An organizing thrombus had occluded ad-

Discussion

Cerebrovascular complications of meningitis include vasculitis, vasospasm, venous and arterial thrombosis, intracranial aneurysm formation, and rarely, subarachnoid hemorrhage. Stroke may be the result of any one or combinations of these processes. In a large, community-based review of over 1,300 patients with meningitis, Geiseler et al found focal neurological deficits in 6.6% of cases across the course of disease. Rarely, as documented in this report, stroke may be an early manifestation of meningitis. Saul et al described sudden hemiparesis as the presenting sign in a case of cryptococcal meningitis; however, imaging studies were normal and the mechanism speculative. Vasculitis associated with cryptococcal infection, variella-zoster virus, and possibly human immunodeficiency virus may play a role in producing transient ischemic neurological deficits and stroke at the onset of infection. The mechanism of stroke in this case includes thrombosis in the setting of a severe, widespread vasculopathy with prominent basilar artery involvement.

Despite improvement with therapy, our patient abruptly worsened owing to rupture of an infected basilar aneurysm. Karsner grouped bacterial aneurysms into embolic, extravascular, and cryptogenic subtypes. Embolic aneurysms, typical of infective endocarditis, form from within the artery as septic material lodges at branch points. Extravascular aneurysms form “from without” because of extension of infection through the adventitia toward the lumen. This mechanism has been seen in cavernous sinus infection causing carotid artery aneurysm formation, and adjacent to foci of osteomyelitis and otitis. Meningitis due to Mycobacterium and Aspergillus infection occasionally forms aneurysms in this fashion; however, bacterial causes remain less well described. In 1966 Ojemann et al first reported angiographic evidence of aneurysm formation in distal branches of major cerebral vessels in a case of bacterial meningitis. Such lesions have since become well known but notably involve distant vessels rather than the circle of Willis. Watson et al reported a case somewhat similar to ours in which thrombosis occurred in the basilar artery secondary to Pseudomonas infection. In that case, the mechanism of thrombosis involved local extension of infection from external otitis rather than meningitis and was a late manifestation of the patient’s illness. Although a preexisting vessel wall defect cannot be ruled out in our case, the angiodestructive process secondary to meningitis was overwhelming and led to aneurysm formation “from without,” with fatal rupture.

Another unique aspect of this case is the isolation of S. milleri from the CSF despite “partial” treatment with oral penicillin, a drug to which this organism is usually sensitive. The taxonomy and pathogenicity of S. milleri (now recognized as S. anginosus) is controversial. Similar to S. viridans, it is an oral commensal and pathogen in infective endocarditis. In the central ner-
Figure 2. Panel A: Axial section through midpons at level of basilar aneurysm. Large area of pallor is present in left ventral pons associated with focal hemorrhage. Organizing thrombus occupies the basilar artery, and aneurysm wall is formed by clot and destroyed by inflammation at the point of rupture (arrow). Hematoxylin, orcein, phloxin, and saffron (HOPS) stain. Original magnification, ×5. Panel B: Higher magnification of basilar wall from area marked in panel A. Chronic, mainly lymphocytic, infiltrate is present in adventitia. Internal elastic lamina (darkly stained) and intima are disrupted by inflammatory process. HOPS stain. Original magnification, ×80.

Veous system, it is the most common isolate from brain abscesses. Several previous cases of *S. milleri* meningitis have been reported. All cases with pathological confirmation have been associated with a parameningeal focus of infection or dental manipulation. Presence of this organism in CSF should prompt a search for such a process. Clinical and subsequent autopsy search for associated infection was negative in this case. *S. milleri* is rarely found as a contaminant in CSF or in cultures from lumbar puncture sites. These facts, along with the CSF findings and evidence of residual meningitis with gram-positive cocci, argue a pathogenic role for *S. milleri* in this case.

Treatment of serious *S. milleri* infection has not been standardized; however, most authors recommend high-dose penicillin (2.4×10⁷ IU/day) or intravenous ampicillin as used in this patient during his hospitalization. Oral penicillin, used in our patient before presentation with stroke, may have contributed to the progression of the vasculopathy. Although the patient was relatively asymptomatic, a smoldering meningitis with vasculitis may have continued because of inadequate treatment. Clinically, he responded well to intravenous penicillin but died abruptly because of aneurysmal rupture, a complication of the inflammatory angiodestructive process. No primary source of infection was noted; however, a subclinical bacteremia or small abscess, although unlikely, may have been missed. These facts do not alter the overall implication of *S. milleri* infection in the causation of the unusually severe vasculopathy and neurological sequelae in this case.

In summary, we document a case of bacterial meningitis complicated by pontine infarction resulting from thrombosis within the basilar artery. Despite therapy, an inflammatory process continued and led to aneurysm formation and rupture. Bacterial meningitis should be considered in the differential diagnosis of both ischemic stroke and subarachnoid hemorrhage. The role of *S. milleri* as a pathogen in purulent meningitis and its cerebrovascular complications merits further study.

Acknowledgments
The authors wish to thank Sandra Cohen and Wayne Ozanne for expert technical assistance.
References

Fatal basilar vasculopathy complicating bacterial meningitis.

J R Perry, J M Bilbao and T Gray

*Stroke.* 1992;23:1175-1178
doi: 10.1161/01.STR.23.8.1175

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1992 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/23/8/1175