Late-Developing Cerebral Arteropathy After Pyogenic Meningitis

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Background: Although vasculopathy is a recognized complication during acute meningitis, to our knowledge, no previous reports have been published of this phenomenon developing months after successful treatment.

Objective: To report a unique case of a late-developing vasculopathy after pyogenic meningitis in an adult.

Report of a Case: A 51-year-old woman was seen with severe headache 2 months after treatment of *Haemophilus influenzae* type C meningitis. Initial arteriography showed no abnormality; a second arteriogram showed progressive multifocal intracranial stenosis affecting mainly the internal carotid arteries. Findings from pathologic examination disclosed diffuse collagenosis consistent with chronic vascular injury from meningitis. The arterial lesions stabilized, and the patient remained asymptomatic.

Conclusion: Progressive intracranial arterial stenosis can evolve months after meningitis and should be added to the list of recognized vascular complications.

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**ARTERIAL INVOLVEMENT** during the acute course of pyogenic meningitis is frequent and can lead to stroke. Long-term cerebrovascular complications, especially in adults, are less well characterized, owing in part to the coexistence of other confounders that may predispose to cerebral ischemia. We report a case of progressive cerebral arteropathy that began and evolved during the months after successful treatment of severe *Haemophilus influenzae* type C meningitis in an adult, resulting in a moyo-moya pattern on cerebral arteriography.

**REPORT OF A CASE**

A 51-year-old healthy, left-handed woman with a history of chronic tobacco smoking and asthma developed confusion, fever, nausea, and vomiting that followed an earache that was treated with otic drops. On admission to the hospital a lumbar puncture showed a white blood cell count of 11.4 × 10^3/μL (11.4 × 10^9/L), with 95% neutrophils; a glucose level of 5 mg/dL (2.8 mmol/L); and a protein level of 643 mg/dL (6.43 g/L) all of which is consistent with pyogenic meningitis. *Haemophilus influenzae* type C grew from cultures of cerebrospinal fluid. She was treated with a combination of antibiotics and corticosteroids and required mechanical ventilation for 10 days, followed by gradual neurological improvement of her condition.

No regular medications were taken prior to hospitalization. A history of avascular hip necrosis and exacerbation of asthma by aspirin use was noted.

Six weeks later, the patient reported recurrent headaches and 2 brief episodes of left-sided numbness. An examination of the patient's cerebrospinal fluid showed a total white blood cell count of 0.13 × 10^3/μL (13.5 × 10^9/L), with 90% lymphocytes; a glucose level of 32 mg/dL (17.8 mmol/L); and a protein level of 195 mg/dL (1.95 g/L).

Two months after the initial hospitalization, persistent headache led to cerebral arteriography that showed no abnormality, except for the presence of a 5-mm aneurysm of the left internal carotid artery near the ophthalmic artery origin, suspected to be a congenital “berry” aneurysm (Figure A and E). Cranial magnetic resonance imaging using radiolabeled gadolinium 64 showed meningeal enhancement and pansinusitis. She was treated with a combination of oral antibiotics.

Seven months after onset, although occurring daily, headaches had improved; she had returned to clerical work.
She underwent a second cerebral arteriogram for endo-
vascular treatment of the aneurysm, but the interven-
tion was curtailed when multiple focal, constrictive, in-
tracranial arterial stenoses were present involving the
supraclinoid carotid arteries bilaterally, the proximal
middle cerebral arteries bilaterally, the intracranial left
vertebral artery, and the proximal right posterior cere-
bral artery (Figure B and F). Cranial magnetic reso-
nance imaging showed no meningeal enhancement. A sec-
ond cerebrospinal fluid examination showed normal
opening pressure, a total white blood cell count of 0.02
× 10^3/µL (all lymphocytes), a glucose level of 53 mg/dL
(29.4 mmol/L), and a protein level of 108 mg/dL (1.08
g/L). Results from extensive serologic studies for under-
lying systemic disorders or vasculitis were unrevealing.

Two weeks after the second arteriogram, she experi-
enced the sudden inability to read that lasted about 15
minutes. Combined treatment with clopidogrel, 75 mg/d,
and prednisone, 100 mg/d, was initiated.

Nine months after onset and after 6 weeks of oral
corticosteroids were received, a third cerebral arterio-
gram showed progression of focal areas of intracranial
stenosis to 90% diameter stenosis with new develop-
ment of abundant lenticulostriate collateral vessels and
extracranial collaterals (Figure C and G). The cerebral
aneurysm was unchanged. Subsequently, results from the
evaluation of cerebral blood flow by acetazolamide-
enhanced, single-positron emission computed tomo-
graphic imaging were normal. A cerebral biopsy speci-
men showed marked leptomeningeal collagenosis with

Consecutive (serial) cerebral angiograms showing the progression of left (LICA) and right intracranial carotid artery (RICA) stenosis. A, Three months after meningitis, there was a 4-mm saccular aneurysm on the LICA at the level of the origin of the ophthalmic artery, with no intracranial stenosis. B, Seven months after meningitis, 50% carotid siphon stenosis is noted to have been developing since the initial angiogram. C, Nine months after meningitis, the progression of siphon stenosis to 90% can be seen. D, Twenty-two months after meningitis, 90% of the siphon stenosis is unchanged from the prior angiogram performed 13 months earlier. In A through D, wide arrows indicate involvement of the supraclinoid segment of the LICA; thin arrows, the presence of incidental LICA congenital aneurysm; white arrows, the progressive development of collateral circulation of the lenticulostriate arteries in a moyamoya pattern. Serial angiograms showing the same process seen in A through D, involving the RICA. E, Three months after meningitis, the RICA is normal. F, Seven months after meningitis, moderate stenosis on the RICA involving the siphon can be seen with significant degree of reflux into the external carotid branches. G. Nine months after meningitis, there is 90% stenosis of the RICA siphon. H, Twenty-two months after meningitis, there is 90% stenosis, unchanged from the previous angiogram. In E through H, black arrows indicate progression of RICA stenosis; white arrows, the progressive development of collateral circulation of lenticulostriate arteries.
periadventitial fibrosis of the small arteries, without inflammatory or atherosclerotic changes. Corticosteroid treatment was tapered; however, treatment with clopidogrel was continued.

Twenty-two months later, the patient was generally doing well, with infrequent headaches and no abnormal findings on neurological examination. Arteriography was undertaken to assess the cerebral aneurysm and showed subtle improvement in the degree of intracranial stenoses, persistence of extensive collateral vessels, and no change in the cerebral aneurysm (Figure D and H). The patient remains neurologically asymptomatic 36 months after having acute meningitis. To our knowledge, no information about the natural history of this vasculopathy is available. This process would probably not have been identified in this patient because of its surprisingly benign clinical course, except for the incidental aneurysm that led to repeated arteriograms. Whether late-developing cerebrovascular complications are more related to H influenzae than to other organisms is uncertain. It is likely that late-developing intracranial arterial stenosis may be more frequent than appreciated following severe pyogenic meningitis and should be recognized as a potential vascular complication.

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COMMENT

This case represents a delayed manifestation of postmeningitis vasculopathy. Early vascular involvement, affecting both arterial and venous vasculatures, is a well-known result of acute meningitis. No reliable estimates are available of the incidence of vascular complications in adults with meningitis. A prospective case series reported a 37% prevalence of angiographically documented cerebrovascular complications in patients with meningitis who have either focal neurological signs or persistent coma. The most common organisms involved are Streptococcus pneumoniae, Neisseria meningitidis, and Mycobacterium tuberculosis.

Most evidence of vascular complications associated with H influenzae meningitis comes from reports involving children. Arteriographic involvement includes multiple stenoses of the arterial trunks at the base of the brain and predominantly the supraclinoid segment of the internal carotid artery. Interestingly, the posterior circulation seems to be less affected both clinically or angiographically and is consistent with the findings in our case. Other signs of vascular involvement include the development of collateral circulation (sometimes in a moyamoya pattern) and slowing and retrograde circulation. The severity of stenosis seems to improve in follow-up angiograms after the acute stage.

Regarding the late-developing vascular complications, we identified a published report of delayed cerebral infarction in a child 6 years after H influenzae meningitis. Arteriography showed moderate stenoses of the proximal middle cerebral and anterior cerebral arteries, but the time course of evolution of the vasculopathy was unclear.

Several mechanisms have been proposed in the development of this vasculopathy. Inflammatory infiltration (ie, vasculitis) and reactive vasospasm with residual organic stenosis have been reported. Although postulated, intravascular thrombosis has not been a frequent finding and may be more the substrate of venous than arterial involvement. Electron microscopy has shown myonecrosis involving the vasaorum that may explain the structural abnormalities. Our patient’s biopsy specimen showed no signs of vasculitis or atherosclerosis, but a diffuse collagenosis involving the periadventitial tissue was consistent with chronic vascular injury.

REFERENCES