Delayed Recurrent Ischemic Stroke after Initial Good Recovery from Pneumococcal Meningitis

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Abstract

We describe unusual delayed recurrent episodes of ischemic stroke in a patient with initial good recovery from pneumococcal meningitis due to progressive arterial stenosis for over 3 months. We postulate that any of the following may have been responsible for his condition: widespread cerebral vasculopathy due to the effects of purulent material bathing the base of the brain, an immune-mediated para-infectious condition, or a rebound effect of the primary inflammatory reaction that was initially suppressed by dexamethasone. This case demonstrates that progressive arterial stenosis can evolve months after bacterial meningitis and should be recognized as a potential vascular complication.

Key words: cerebral infarction, pneumococcal meningitis, vasculopathy, steroid therapy

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Introduction

Cerebrovascular complications are common in bacterial meningitis (1, 2). Cerebral infarction is especially common in patients with pneumococcal meningitis and it typically develops within the first few days of the disease when the central nervous system inflammation is most severe (3, 4). Delayed cerebral vasculopathy is a rare complication (5-7). Herein, we describe delayed recurrent episodes of ischemic stroke due to cerebral vasculopathy evolving for over 3 months after initial good recovery.

Case Report

A 52-year-old healthy man without cardiovascular risk factors or any immunodeficiency presented with headache, fever and altered consciousness. A neurological examination revealed neck stiffness and disturbed consciousness. Community-acquired bacterial meningitis was suspected and he was immediately started on 2 g of meropenem three times daily, 2 g of ceftriaxone twice daily, and 4 mg of dexamethasone four times daily. The combination treatment was continued for 30 days and gradually tapered. The clinical course of the patient is shown in Fig. 1. On admission, cranial magnetic resonance imaging (MRI) revealed lateral ventriculitis (Fig. 2A) and angiography (MRA) revealed no abnormality, except for the presence of a microaneurysm of the left anterior cerebral artery (Fig. 2B). At the onset of treatment, an examination of the cerebrospinal fluid (CSF) revealed 1,374 leukocytes/mm³ accompanied by high protein (648 mg/dL) and low glucose levels (4 mg/dL). Cultures of the CSF yielded Streptococcus pneumonia sensitive to penicillin. The patient improved clinically over the next few days. An examination of the CSF on day 16 revealed 30 leukocytes/mm³ and CSF gram stain and cultures yielded no bacteria. However, on day 20, he suddenly started to lapse into unconsciousness under dexamethasone. He was started on antiplatelet therapy (intravenous ozagrel and oral clopidogrel) because cranial MRI revealed infarction of the bilateral thalami (Fig. 2C) and MRA revealed slightly indistinct peripheral flow of the anterior and middle cerebral arteries (Fig. 2D), probably due to vasculitis or vasospasm. After 2 weeks, he showed excellent recovery and was fit for discharge. The fever and headache recurred on day 40, when the CSF contained 41 leukocytes/mm³, elevated protein (648 mg/dL) and almost normal glucose levels (39 mg/dL). Although meropenem and dexamethasone were restarted for 7

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weeks, no clinical improvement occurred. Repeated MRI on day 46 revealed pus around the brain surface (Fig. 2E) and MRA revealed a more indistinct flow than previous examinations (Fig. 2F). Meropenem therapy was stopped on day 89 and linezolid (600 mg p.o. twice a day) was started. Although linezolid was effective for the fever, the patient developed hemianopsia on day 102. Cranial MRI showed recurrent cerebral infarctions in both hemispheres (Fig. 2G) and MRA showed progressive narrowed or occluded multiple cerebral arteries (Fig. 2H). Dexamethasone was increased but the patient deteriorated into abulia. Cranial MRI on day 109 showed widespread infarcts (Fig. 2I) and progression of the vascular stenosis or occlusion was evident on 3D-CT angiograms on day 110 (Fig. 2J). Dexamethasone was discontinued, and oral prednisolone was started at a dose of 50 mg and then gradually tapered (Fig. 1). Improvement of the vascular lesions in a repeated MRA on day 124 suggested that the effects were due not only to vasculitis, but also to vasospasm (Fig. 2K). Brain perfusion single-photon emission computed tomography (SPECT) with $^{99m}$Tc-ECD revealed hypoperfusion in the frontal lobes as well as the occipital lobes (Fig. 2L). These findings explained the abulia. His condition stabilized and his level of consciousness slowly improved. He was discharged to a rehabilitation facility on day 160. After several months of rehabilitation, he was able to return home. Currently, he is ambulatory but unable to resume his previous occupation.

Discussion

We present a patient with delayed recurrent episodes of ischemic stroke complicating pneumococcal meningitis due to the progressive narrowing of cerebral arteries for over 3 months after initial good recovery. In the present case, repeated examination of CSF showed a substantial reduction of white blood cell counts and recovery of the low glucose level. All but the initial CSF sample had negative bacterial cultures. These findings suggest a mechanism of persistent or recurrent inflammation without bacterial infection. Inflammatory infiltration (i.e., vasculitis) and reactive vasospasm with residual organic stenosis have been reported (8, 9). The etiology of the ischemic stroke of the present patient is unknown, although infection could trigger an autoimmune process towards the cerebral blood vessels.

We postulate that any of the following could have been responsible for his condition: widespread cerebral vasculopathy due to the effects of the basal exudate of bacterial meningitis, an immune-mediated para-infectious condition, or a rebound effect of the primary inflammatory reaction that was initially suppressed by dexamethasone.

We came across only one similar report describing progressive arterial stenosis evolving over months in an adult patient with initial excellent recovery from bacterial meningitis (5). In that report, a 51-year-old woman was described with a headache 2 months after treatment for *Haemophilus influenza* type C meningitis. Initial angiography showed no abnormality; a second angiogram 7 months later showed progressive multifocal intracranial stenosis affecting mainly the internal carotid arteries. She had no episodes of ischemic stroke and was treated with steroids after clinical deterioration. Findings from a pathologic examination disclosed diffuse collagenosis consistent with chronic vascular injury from meningitis. The arterial lesions stabilized, and the patient remained asymptomatic.

To our knowledge, no information concerning the natural history of this vasculopathy is available. This process would probably not have been identified in this patient because of the early benign clinical course. It is likely that late-
Figure 2. Axial diffusion-weighted MRI shows lateral ventriculitis (arrowheads) on admission (A), bilateral thalamic infarcts on day 20 (C), pus around the brain surface on day 46 (E), infarcts of the left cingulate gyrus and the right frontal and occipital lobes on day 102 (G), and additional infarcts involving the contralateral cingulate gyrus and occipital lobe on day 109 (I). MRA shows no abnormalities, except for the presence of a microaneurysm in the left anterior cerebral artery on admission (B), progressive cerebral vasculopathy on days 20 (D), 46 (F) and 102 (H). 3-D CT angiography shows multiple sites of cerebral vasculopathy with arterial narrowing and occlusion (J). Repeated MRA on day 124 reveals mild improvement of the vascular lesions (K). ⁹⁹mTc-ECD SPCT shows hypoperfusion in not only the ischemic lesions, but also the frontal lobes (L).
developing intracranial arterial stenosis following severe pyogenic meningitis may be a more frequent occurrence than currently acknowledged, and it should be recognized as a potential vascular complication.

The authors state that they have no Conflict of Interest (COI).

References