

## CASE REPORT

# Moyamoya syndrome after bacterial meningitis

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## INTRODUCTION

Bacterial meningitis (BM) is a serious disease for children, and many patients have various complications and sequelae even after receiving antibacterial treatments. Moyamoya disease (MMD) is a cerebrovascular disease characterized by bilateral stenosis/occlusion of the terminal portion of the internal carotid artery (ICA) and its main branches and by moyamoya vessels (abnormal vascular net) in the base of the brain. The etiology of MMD is unknown. Patients having similar cerebral vasculopathy with underlying diseases are described using the term moyamoya syndrome (MMS).<sup>1</sup> Onset of MMS after BM is rare. Here, we report the case of a patient diagnosed with MMS 22 weeks after the onset of *Streptococcus pneumoniae* meningitis. This is the first reported pediatric case of MMS diagnosed after pneumococcal meningitis.

## CASE REPORT

A previously healthy girl aged 1 year and 8 months was sent to our department after suffering from fever for 5 days and experiencing a convulsion once on the fifth day of fever. Physical examination of the patient revealed a stiff neck and bilateral positive Babinski sign. A routine blood test found a white blood cell count of  $24.6 \times 10^9$  cells/L, with 88.3% neutrophils, and a routine cerebrospinal fluid (CSF) test yielded a white blood cell count of  $12800 \times 10^6$  cells/L, with 90% polykaryocytes. Furthermore,

a CSF biochemistry test revealed a chloride concentration of 108 mmol/L, glucose concentration of 0.38 mmol/L, and protein concentration of 3,350 mg/L. Culture of the CSF showed *Streptococcus pneumoniae*, which was sensitive to ceftriaxone (mean inhibitory concentration [MIC]: 0.25 mg/L) and vancomycin (KB: 21 mm) and was intermediately resistant to penicillin (MIC: 0.125 mg/L).

Following treatment with an antibiotic (intravenous ceftriaxone, 100 mg/kg per day), dexamethasone, and mannitol, the patient's fever and neural symptoms disappeared, her CSF white blood cell count decreased to  $12 \times 10^6$  cells/L, her protein concentration decreased to 600 mg/L, and her glucose concentration increased to 2.78 mg/L. Magnetic resonance angiography (MRA) results were normal (Figure 1A). Four weeks after admission, the patient fully recovered and was discharged from the hospital.

The patient had no neural symptoms after being discharged from the hospital, and her growth and development were normal for her age. About 16 weeks after the initial hospitalization, when the patient returned to our hospital for a routine follow-up visit, computer tomography (CT) images of her head showed plaque-like low-density lesions in the right temporal and occipital lobes and cerebral malacia foci with focal cerebral atrophy in the left occipital lobe and right caudal nucleus. The patient's parents refused any more therapy based on the patient's otherwise well condition and economic factors.

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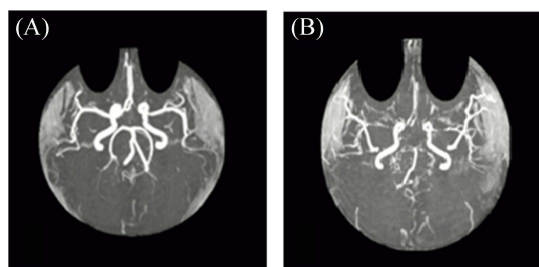
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Twenty-one weeks after the initial hospitalization, the patient was again sent to the emergency department of our hospital for fever, a coma for 2 days, and intermittent convulsions for 1 day. Physical examination revealed that the patient was unconscious and in a superficial coma. A routine blood test found a white blood cell count of  $11.60 \times 10^9$  cells/L, with 79.4% neutrophils. The C-reactive protein level was elevated to 507 mg/L. A routine CSF test found a white blood cell count of  $100 \times 10^6$  cells/L, with 10% polykaryocytes, and a biochemistry test of the CSF revealed a chloride concentration of 130 mmol/L, glucose concentration of 2.24 mmol/L, and protein concentration of 2 090 mg/L. Acid-fast staining and Gram staining of the CSF were negative. No spores or hyphae were found in the CSF, nor were any bacteria cultured in the CSF. Considering a possible recurrence of bacterial meningitis, cefepime was applied for anti-infection; however, the patient's consciousness and convulsions did not improve.

Twenty-two weeks after the onset of BM, the patient's Magnetic Resonance Imaging (MRI) showed prior infarction and subacute hemorrhage (Figure 2). MRA results showed stenosis/occlusion on the bilateral distal internal carotid arteries, middle cerebral arteries, and posterior cerebral arteries. Numerous small collateral blood vessels were found within the base of the brain and distal middle cerebral arteries (Figure 1B). Moreover, no evidence of autoimmune diseases, immune deficiency, tuberculous meningitis, sickle cell diseases, Down syndrome, or other reported related medical conditions was found.<sup>1</sup> Thus, the patient was diagnosed with MMS. Twenty-two weeks and 4 days after the initial hospitalization, the patient's parents gave up additional therapy for economic reasons.

The patient had no history of allergies or family history of MMS or other vascular diseases.



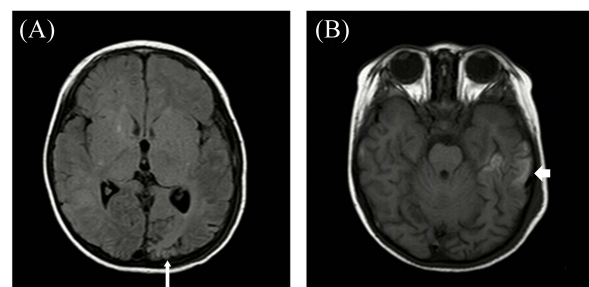
**FIGURE 1** MRA images. A, MRA on Day 8 after BM onset; B, MRA images at 22 weeks after BM onset.

## DISCUSSION

The diagnosis of MMS in this case was confirmed by the patient's history of BM and the characteristic MRA findings. However, we found no other factors associated with MMS. Data about the treatment and prognosis for

MMS after BM are rare. To our knowledge, this is the first reported case of MMS following pneumococcal meningitis in a child. A PubMed search uncovered three reported adult cases of MMS after BM (Table 1). All three of those patients were diagnosed with MMS at 3 to 9 months after BM onset, indicating that MMS is a delayed vasculopathy of BM.

The base pathophysiology of MMS is stenosis/occlusion in the terminal portions of the internal carotid artery and its main branches, where the stenosis or occlusion of arteries leads to reduced blood flow in the anterior circulation of the brain and the subsequent development of compensatory collateral vessels. Therefore, the symptoms of MMS can be classified into two categories: brain ischemia (i.e., stroke, transient ischemic attacks [TIAs], and seizures) and compensatory collateral vessels (i.e., hemorrhage).<sup>2</sup> Among pediatric MMS patients, 70%–80% present with brain ischemia.<sup>1</sup> For our patient, both infarction and hemorrhage were observed using MRI (Figure 2). For the three adult MMS patients we reviewed (Table 1), hemiplegia and headache were the most frequent neurological manifestations. Case 1 and case 2 improved, but case 3 died.



**FIGURE 2** MRI images at 22 weeks after BM onset. A, Local atrophy in bilateral occipital lobes suggests prior infarction (arrow). B, Abnormal hyperintensity on T1-weighted image W1 on the left temporal-parietal lobe, right temporal lobe, and anterior part of right basal ganglia suggest subacute hemorrhage (arrow).

The pathogenesis of the stenosis or occlusion of the arteries is unknown. One report showed that MMS after tuberculous meningitis is attributed to vasculitis due to inflammatory exudant.<sup>3</sup> Here, our patient's first CSF assessment showed a very high white blood cell count ( $12\,800 \times 10^6$  cells/L) and protein concentration (3 350 mg/L). The CSF detection results indicated that she had severe inflammation and massive quantities of inflammatory exudant in the intracalvarium. Thus, similar pathologic changes may have occurred in our patient. According to the literature, other possible pathogeneses for post-infective vasculopathy include reactive vasospasm and residual organic stenosis due to infection,<sup>3</sup> autoimmune processes,<sup>4</sup> and host susceptibility to autoimmune diseases.<sup>5</sup>

**TABLE 1** Information about three previously reported MMS cases

Case Number	Pathogen	Gender/ Age (years)	Progression of clinical manifestation	Progression of vasculopathy	Follow-up time/Outcomes
Case 1 <sup>6</sup>	<i>H. influenzae</i>	F/51	6 weeks: headache, episode of left-side numbness; 2 months: severe headache; 7 months: headache improved	2 months: normal in angiography; 7 months: stenosis in bilateral; supraclinoid segment of the ICA, bilateral M1, left intracranial VA, right P1; 9 months: primary stenosis progressing, proliferation of lenticulostriate collateral vessels	3 years/ no headache, improvement in the degree of stenosis and persistence of collateral vessels
Case 2 <sup>7</sup>	<i>S. pneumoniae</i>	M/55	3 months: headache, hemiplegia	3 months: stenosis-occlusion in bilateral supraclinoid segment of the ICA, bilateral A1, M1, VA-BA system, appearance of collateral vessels lenticulostriate collaterals	0.5 years / hemiplegic symptom improved, no relapses had occurred, motor improvement
Case 3 <sup>4</sup>	<i>S. pneumoniae</i>	F/20	9 days: hemiplegia 48 days: headache, and CT shows evolution of the previously noted infarcts 118 days: language problem 139 days: cortical Blindness and MRI shows new occipital infarction 260 days: a large left basal ganglion hemorrhage and died	12 days: moderate stenosis of distal bilateral VA and BA, mild stenosis of left M1, left A1 150 days: severe stenosis in the BA and VA, progressing of left M1, new stenosis of the A1, appearance of lenticulostriate collaterals. 237 days: proliferation of posterior penetrating vessels, further proliferation of lenticulostriate collaterals	0.7 years / a large left basal ganglion hemorrhage and died

In conclusion, MMS is a rare but serious delayed manifestation of BM vasculopathy. We suggest that clinicians consider MMS as a possible late complication in BM patients and recheck their MRA if the patients have symptoms of brain ischemia.

## CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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