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Short communication

Intra-arterial vasodilator therapy for parainfectious cerebral vasospasm☆,☆☆

Ather Taqui, Lauren Koffman, Ferdinand Hui, Joao Gomes, M. Shazam Hussain, Mark Bain, Gabor Toth *

Cerebrovascular Center, Cleveland Clinic, Cleveland, OH, USA

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ABSTRACT

Cerebrovascular complications of bacterial meningitis may include vasculitis, vasospasm or vasoconstriction, delayed cerebral infarction, venous and arterial thrombosis, intracranial aneurysm formation. The role of invasive endovascular therapies has not been well studied for infectious vasospasm, which can lead to dire neurologic consequences. We present 2 patients who were diagnosed with bacterial meningitis. Brain MRI showed areas of acute ischemia. Neurologic worsening was seen in both patients despite aggressive medical management. Follow-up imaging demonstrated significant narrowing of the intracranial vessels with associated new scattered infarcts. Both patients underwent targeted intra-arterial vasodilator infusion with angiographically improved vessel caliber and distal flow. The neurological exam subsequently stabilized in both cases. Follow-up radiographic images demonstrated no further ischemia in one of the 2 patients. Vasculopathy and vasospasm causing delayed ischemic neurologic deficit is a rare, but severe complication of acute meningitis. It can be a significant predictor of poor prognosis, and the disease may progress despite aggressive medical therapy. Although frequently used in subarachnoid hemorrhage-related vasospasm, to our knowledge, this is the first report of endovascular vasodilator treatment as adjunctive intervention in patients with meningitis associated vasculopathy.

1. Introduction

Acute community acquired bacterial meningitis is associated with high mortality and morbidity. The mortality rate remains up to 20% in the US for the last 15 years [15]. Cerebrovascular complications in acute bacterial meningitis are frequent. Parainfectious vasculopathy may include vasculitis, vasospasm, venous and arterial thrombosis and intracranial aneurysm formation, among others [10]. Arterial vascular complications have been shown to be relatively common when studied with Transcranial Doppler (TCD) [9], or cerebral angiography [11,12]. Cerebrovascular complications in acute bacterial meningitis are significant predictors of worse prognosis [9,11,14]. The exact etiology of vascular narrowing or vasospasm in bacterial meningitis is still not fully understood, but inflammatory cytokines, CSF leukocytes and vasospasm-inducing free radicals have been shown to play an important role in the pathomechanism [5,6].

Given that presence of vascular changes may lead to ischemic stroke and worse prognosis, early identification and treatment may be a key target in patients with acute bacterial meningitis. We present two cases of pneumococcal meningitis with cerebral vascular changes and ischemic strokes that were successfully treated with intra-arterial vasodilator therapy.

2. Case reports

2.1. Patient 1

A 38-year-old male with a history of recurrent ear infections presented with depressed mental status and fever inquiring intubation. He was found to have left mastoiditis, severe Streptococcus Pneumoniae meningitis, ventriculitis, diffuse cerebral edema and hydrocephalus. He was administered antibiotics, steroids and seizure prophylaxis. An extraventricular drain was placed, and the patient underwent mastoidectomy. MRI brain on day 4 showed acute infarcts in bilateral inferior cerebellar hemispheres (Fig. 1A). Magnetic resonance venography (MRV) on day 6 showed patent venous sinuses. Noninvasive magnetic resonance angiography (MRA) study on day 6 was suggestive of mild vasoconstriction in bilateral supraclinoid internal carotid arteries. On day 9, the patient developed bradycardia, worsened mental status and

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* Corresponding author at: Cerebrovascular Center, Mail Code S80, Cleveland Clinic, Cleveland, OH 44195, USA. Tel.: +1 216 636 5860; fax: +1 216 636 2061.
E-mail address: tothg@ccf.org (G. Toth).

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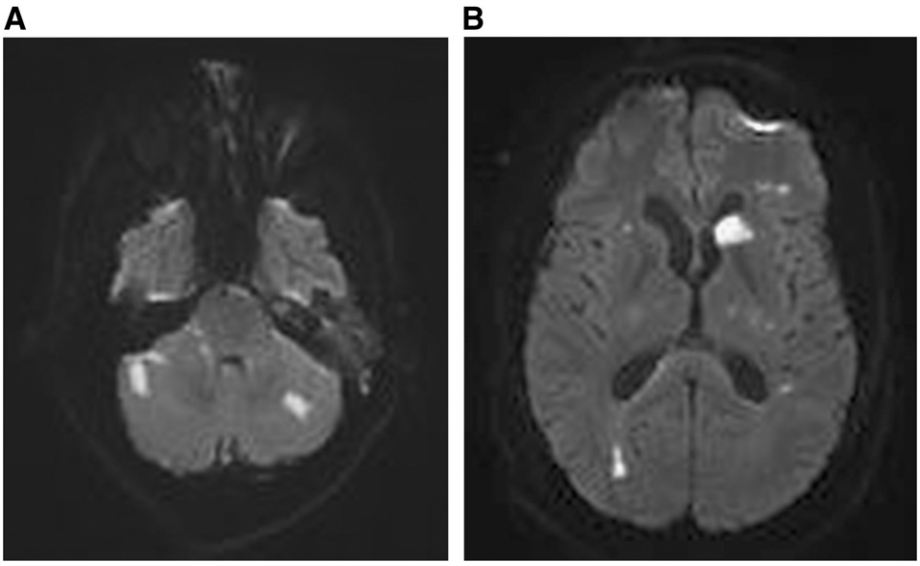

Fig. 1. Initial MRI brain axial diffusion weighted (DWI) sequences showing scattered infarcts prompting vascular imaging, aggressive medical therapy, and subsequent endovascular treatment in Patient #1 (A) and Patient #2 (B).

motor deficits. A computed tomography angiogram (CTA) of the brain demonstrated significant narrowing of the vertebrobasilar system with associated new scattered infarcts on magnetic resonance imaging (MRI). He was started on nimodipine and hemodynamic triple-H therapy with only mild improvement on exam. An angiogram the same day confirmed severe vasospasm in the distal vertebral arteries, basilar artery, posterior cerebral arteries (PCAs), and moderate to severe vasospasm in bilateral supraclinoid internal carotid arteries (Fig. 2A and C). After intra-arterial (IA) verapamil infusion (5–10 mg per treated vessel, infused over 3–4 min), mild-to-moderately improved target vessel caliber and distal flow were seen(Fig. 2B and D). The patient's neurological exam improved after the intervention, but not to his baseline. A follow-up angiogram on day 14 revealed mildly increased spasm that responded well to repeat IA vasodilator therapy. The patient had no further neurologic decline. Final follow-up MRI on day 31 showed no evidence of new ischemia. Marked improvement on clinic follow-up 2 months later was seen, with residual ataxia and dysarthria, and a National Institute of Health Stroke Scale (NIHSS) of 6.

2.2. Patient 2

A 57 year old man was admitted with a two-day history of altered mental status and reported seizure activity, requiring intubation for respiratory failure. Initial CT showed obstructive hydrocephalus and cerebral edema, and an EVD was placed. Blood and CSF cultures confirmed the diagnosis of streptococcus pneumoniae bacteremia and meningitis. Transesophageal echocardiogram also showed 3 mm posterior mitral valve lesion concerning for endocarditis. MRI performed after admission revealed multiple infarcts consistent with septic emboli (Fig. 1B). An MRA showed diffuse vessel narrowing. After receiving antibiotics, hyperdynamic therapy, steroids and oral nimodipine, there was radiographic evidence of new infarcts and increased TCD velocities). On day 10, cerebral angiogram showed severe narrowing of bilateral ICAs (Fig. 3B), M1 and A1 segments with improvement in caliber and flow after IA nicardipine (5–10 mg per treated vessel, infused over 4–5 min) administration (Fig. 3C). No significant vasospasm of the posterior circulation was seen. A decline in neurologic exam on day 13 prompted reimaging, which showed new ischemic infarcts. Repeat angiogram confirmed diffuse bilateral anterior circulation vasospasm and IA nicardipine led to further mild improvement in vessel narrowing. TCD velocities demonstrated decreasing values after IA treatments (Fig. 3A). No further angiogram was performed. The patient eventually also received intrathecal nicardipine, which we occasionally consider as adjuvant therapy on a case-by-case basis for subarachnoid hemorrhage patients with severe and/or refractory vasospasm. The clinical exam subsequently remained stable, but the final follow-up MRI on day 21 did show interval development of a few new ischemic areas. Fortunately, there was interval resolution of abnormal hyperintensities previously seen in the cerebral convexities and basilar cisterns, presumably representing infectious proteinaceous material. The patient did require tracheostomy placement before discharge.

3. Discussion

Neurovascular complications, including ischemic stroke, may occur secondary to a number of possible mechanisms in acute bacterial meningitis: cerebral venous thrombosis, endocarditis related septic emboli, hypercoagulable state mediated by underlying inflammatory condition, vasculitis/vasculopathy, and cerebral vasoconstriction. Pfister et al. [11] showed in their study that 48.1% of 27 patients with acute bacterial meningitis who underwent cerebral angiograms had pathological changes in their cerebral arteries, major sinuses and cortical veins [11,12]. Moreover, 69.2% of the patients with angiographic cerebrovascular abnormalities had infarctions during the course of their disease. Out of the 13 patients with cerebrovascular complications, 6 died, one was in a vegetative state, and 4 suffered moderate to slight disability.

Cerebral vasoconstrictive disease may occur due to vasculitis, vasospasm or stenosis secondary to intimal thickening and smooth muscle proliferation. Histopathological studies have shown that arterial narrowing may be secondary to local pressure on vessels by inflammatory exudate or infiltration of the vessel wall by cells leading to wall edema and intimal thickening, such as seen in vasculitis [2,11,13]. Inflammatory cytokines, CSF leukocytes and vasospasm-inducing free radicals have been shown to play an important role in the pathomechanism [5,6], despite early histopathological studies suggesting no inflammatory correlate at the regions of arteriopathy [4]. Our two fulminant meningitis cases with obvious significant underlying inflammatory response also support the importance of inflammation in mediating vasospasm. Another possible contributor to the vessel narrowing is a reflex active vascular response to the infectious process. It may be important to make this distinction, as hypothetically