References

1. Wilairatana P. Acute viral hepatitis A: a cause of jaundice in typhoid fever. *Southeast Asian J Trop Med Public Health* 1996;**27**:406–7.
2. Phaddke AY, Desai HG. Hepatitis E virus and Salmonella paratyphi A coinfection. *Indian J Gastroenterol* 1997;**16**:115–6.
3. Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. *Bull World Health Organ* 2004;**8**:346–53.
4. Acharya SK, Madan K, Dattagupta S, Panda SK. Viral hepatitis in India. *Natl Med J India* 2006;**19**:203–17.
5. Nasrallah SM, Nassar VH. Enteric fever: a clinicopathologic study of 104 cases. *Am J Gastroenterol* 1978;**69**:63–9.
6. Khosla SN, Singh R, Singh GP, Trehan VK. The spectrum of hepatic injury in enteric fever. *Am J Gastroenterol* 1988;**83**: 413–6.
7. El-Newihi HM, Alamy ME, Reynolds TB. Salmonella hepatitis: analysis of 27 cases and comparison with acute viral hepatitis. *Hepatology* 1996;**24**:516–9.

Saqib Ahmad
Rayid Abdulqawi*
Department of Medicine, Princess Royal Hospital, Apley Castle, Telford TF1 6TF, UK

Khaled Ashawesh
Diabetes and Endocrinology Department, Walsgrave Hospital, University Hospitals, Coventry and Warwickshire NHS Trust, Coventry, UK

*Corresponding author. Tel.: +44 (0)1952 641222
E-mail address: rayid_abdulqawi@hotmail.com (R. Abdulqawi)

Corresponding Editor: Craig Lee, Ottawa, Canada

17 November 2007

doi:10.1016/j.ijid.2008.01.005

Cerebellar hemorrhage as an atypical complication of meningococcal meningitis

Cerebrovascular phenomena have been well documented in traditional reviews of bacterial meningitis in children and adults alike.[1–6] However, this is the first documented case of cerebellar hemorrhage linked to *Neisseria meningitidis* serogroup B in a child.

A previously healthy 5-year-old boy presented with a 36-h history of muscle tenderness, fever, and headache. In the preceding 3 h, the patient had developed petechiae on his skin and mucosal surfaces. Upon examination, he presented neck stiffness, and his Glasgow Coma Scale score was 14. His vital signs were as follows: axillary temperature 37.5 °C, pulse 150 bpm, respiration 30 breaths/min, and blood pressure 100/60 mmHg. The preliminary diagnosis was meningococcal meningitis with sepsis. Therefore, we initiated antibiotic treatment with intravenous ceftriaxone (100 mg/kg/day for seven days) and dexamethasone (0.6 mg/kg/day for four days). His white blood cell (WBC) count was 18.5×10^9/l and platelet count was 52×10^9 cells/l. Coagulation studies demonstrated an international normalized ratio (INR) of 2.0 and an activated partial thromboplastin time of 60 s. A computed tomography (CT) scan of the brain was normal, and a lumbar puncture was performed after transfusion of fresh-frozen plasma and platelets. The cerebrospinal fluid (CSF) contained 940×10^6 WBC/l and 269 mg/dl of protein, and the CSF glucose/blood glucose ratio was 0.10. Gram stain of the CSF showed Gram-negative diplococci. The results of the latex agglutination test and counterimmunoelectrophoresis of the CSF were positive for *N. meningitidis* serogroup B, as were those of the CSF culture.

The patient demonstrated clinical and hemostatic improvement during the first 24 h. However, on the second day of hospitalization, his level of consciousness deteriorated rapidly. A second CT scan of the brain revealed a high-density area in the right cerebellar hemisphere, suggesting cerebellar hemorrhage (Figure 1). The platelet count was 82×10^9 cells/l and coagulation studies demonstrated an INR of 1.6. Transesophageal echocardiogram and extracranial carotid Doppler study results were within normal limits. One week after the hemorrhagic phenomenon, a neurological examination showed a nearly complete clinical recovery and a CT scan revealed virtually total absorption of the hematoma (Figure 2). In a routine follow-up examination, performed 9 months later, the patient reported no further problems.

Cerebrovascular accidents are determinants of unfavorable outcomes in bacterial meningitis, and they manifest clinically as focal neurological deficits or as a decrease in consciousness.[2,4,5] The impairment of cerebral vessels during meningitis has been demonstrated in histopathological

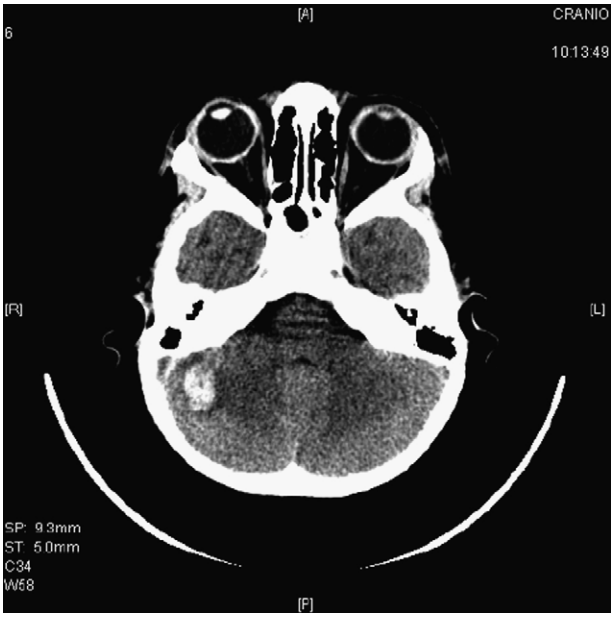

Figure 1 Brain CT image on the second day of hospitalization, revealing a high-density area in the right cerebellar hemisphere.

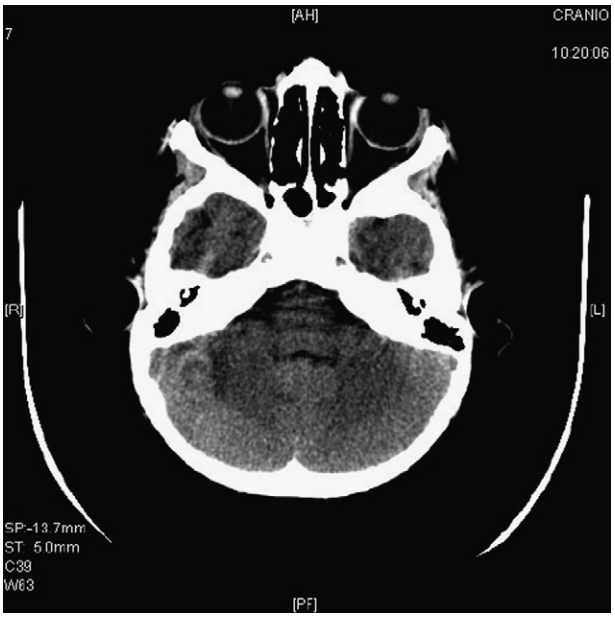

Figure 2 Brain CT image on the seventh day of hospitalization, showing a virtually total absorption of the hematoma.

studies in which arteritis, thrombophlebitis, and cerebral infarcts were detected,[4,6] as well as in reports of angiographic changes of cerebral arteries, including vessel wall irregularities, vasospasm, and focal dilatation.[1,4] In a prospective study of 86 adults with bacterial meningitis, it was reported that 13 (37.1%) developed cerebrovascular complications.[4] However, the authors isolated *N. meningitidis* in only one of the patients presenting a cerebrovascular accident. In patients with meningitis caused by *N. meningitidis*, mortality rates range from 3 to 13%, and morbidity rates range from 3 to 7%.[2] Although stroke caused by *N. meningitidis* affects adults[5,7,8] and children[9] alike, it is an atypical event[6] and has been linked to serogroups B,[5,9] C,[8] and Y.[7]

A complex web of cells and molecules has been implicated in meningococcal infection.[10,11] However, the pathogenesis of stroke in a patient with meningococcal meningitis has not been fully deciphered. It is believed to be a phenomenon with multiple molecular/cellular mechanisms and pathogenic pathways.[2,4,5,8,11] Cytokines play a pivotal role in the genesis of endothelial dysfunction and imbalance of hemostatic forces,[10,11] as reflected by coagulopathy, low platelet counts, and hemorrhagic skin lesions in our patient. Interestingly, we have reported a phenomenon of cytokine expression within the central nervous system of a patient with meningococcal infection complicated by ischemic stroke.[8] Concentrations of interleukin-6 were notably elevated in the cerebrospinal fluid of the patient.[8] Recently, reactive oxygen species and reactive nitrogen intermediates have also been identified as critical mediators of the pathogenesis of bacterial meningitis.[1] While cytokines and other mediators involved in the genesis of endothelial dysfunction and coagulopathy are released by several cell types within the central nervous system and vascular tree,[1,2,4,5,8,10,11] widespread endothelial breakdown can continue, even if the CSF has been sterilized through antibiotic therapy. Therefore, it is probable that, in meningococcal infection, strokes are related to both local (endothelial damage) as well as systemic (imbalance of hemostatic forces) mechanisms.

Conflict of interest: No conflict of interest to declare.

References

1. Weisfelt M, de Gans J, van der Poll T, van de Beek D. Pneumococcal meningitis in adults: new approaches to management and prevention. *Lancet Neurol* 2006;**5**:332–42.
2. van de Beek D, de Gans J, Tunkel AR, Wijdicks EF. Community-acquired bacterial meningitis in adults. *N Engl J Med* 2006;**354**:44–53.
3. Swartz MN. Bacterial meningitis: more involved than just the meninges. *N Engl J Med* 1984;**311**:912–4.
4. Pfister HW, Borasio GD, Dirnagl U, Bauer M, Einhaupl KM. Cerebrovascular complications of bacterial meningitis in adults. *Neurology* 1992;**42**:1497–504.
5. Gironell A, Domingo P, Mancebo J, Coll P, Marti-Vilalta JL. Hemorrhagic stroke as a complication of bacterial meningitis in adults: report of three cases and review. *Clin Infect Dis* 1995;**21**:1488–91.
6. Hardman JM, Earle KM. Meningococcal infections: a review of 200 fatal cases. *J Neuropathol Exp Neurol* 1967;**26**:119.
7. Hsu SS, Kim HS. Meningococcal meningitis presenting as stroke in an afebrile adult. *Ann Emerg Med* 1998;**32**:620–3.
8. de Souza AL, de Oliveira AC, Romano CC, Sztajnbok J, Duarte AJ, Seguro AC. Interleukin-6 activation in ischemic stroke caused by *Neisseria meningitidis* serogroup C. *Int J Cardiol* 2008;**127**:e160–3.
9. Mankhambo LA, Makwana NV, Carrol ED, Beare NA, Taylor T, Kampondeni S, et al. Persistent visual loss as a complication of meningococcal meningitis. *Pediatr Infect Dis J* 2006;**25**:566–7.
10. Hermans PW, Hibberd ML, Booy R, Daramola O, Hazelzet JA, de Groot R, et al. 4G/5G promoter polymorphism in the plasminogen-activator-inhibitor-1 gene and outcome of meningococcal disease. *Lancet* 1999;**354**:556–60.
11. Weisfelt M, Determann RM, de Gans J, van der Ende A, Levi M, van de Beek D, et al. Procoagulant and fibrinolytic activity in cerebrospinal fluid from adults with bacterial meningitis. *J Infect* 2007;**54**:545–50.

Alexandre Leite de Souza*
Jaques Sztajnbok
Antonio Carlos Seguro
Intensive Care Unit, Emílio Ribas Institute of Infectology, São Paulo, Brazil

Antonio Carlos Seguro
Department of Nephrology, Laboratory of Basic Research, University of São Paulo School of Medicine, São Paulo, Brazil

*Corresponding author. Tel.: +55 11 3066 7292; fax: +55 11 30882267
E-mail address: alexandrelsouza@gmail.com (A. L. de Souza)
Corresponding Editor: Craig Lee, Ottawa, Canada

17 December 2007

doi:10.1016/j.ijid.2008.01.007