

# Cushing's Triad in Pneumococcal Meningitis Due to Brainstem Ischemia: Early Detection by Diffusion-Weighted MRI

Eric G. Haarman, MD, PhD\*,
R. Jeroen Vermeulen, MD, PhD<sup>†</sup>,
A. Marceline van Furth, MD, PhD<sup>‡</sup>,
Jonathan I.M.L. Verbeke, MD<sup>§</sup>,
and Frans B. Plötz, MD, PhD<sup>¶</sup>

An infant with pneumococcal meningitis developed signs of raised intracranial pressure during the progression of the disease, including loss of consciousness, hypertension, bradycardia, and respiratory depression. However, both the emergency computed tomography scan findings and intracranial pressure measured by lumbar puncture were normal. Diffusion-weighted magnetic resonance imaging identified multiple lesions with restricted diffusion suggestive of ischemia in the brainstem, explaining the signs observed in the patient. These lesions could not be identified on  $T_2$ -weighted images at that time. © 2008 by Elsevier Inc. All rights reserved.

Haarman EG, Vermeulen RJ, van Furth AM, Verbeke JIML, Plötz FB. Cushing's triad in pneumococcal meningitis due to brainstem ischemia: Early detection by diffusion-weighted MRI. Pediatr Neurol 2008;38:276-278.

#### \*From the Department of Pediatrics, <sup>†</sup>Department of Pediatric Neurology, <sup>§</sup>Department of Pediatrics and Infectious Diseases, <sup>§</sup>Department of Radiology, and <sup>¶</sup>Department of Pediatric Intensive Care, Vrije Universiteit University Medical Center, Amsterdam, The Netherlands.

# Introduction

Increased intracranial pressure is a severe complication of pneumococcal meningitis. Its signs vary from headache and vomiting (early) to cranial-nerve palsies, reduced consciousness, hypertension, bradycardia, and respiratory depression. The constellation of the latter three signs, also known as Cushing's triad, constitutes a late and often preterminal event. The present case report describes a patient with pneumococcal meningitis, in whom Cushing's triad was observed during the progression of the disease, without evidence for increased intracranial pressure at that time.

# **Case Report**

An 8-month-old girl was admitted to the Intensive Care Unit of the VU University Medical Center with pneumococcal meningitis complicated by generalized convulsions necessitating intubation, ventilation, and anticonvulsive and antibiotic therapy. After initiation of treatment, her condition improved gradually. After 5 days, she was transferred to the Department of Pediatrics. Shortly afterward, she deteriorated, with loss of consciousness, fever, a right-sided nonresponsive dilated pupil, a low pulse of 60 beats per minute, hypertension, and respiratory failure attributable to bradypnea. Although raised intracranial pressure was clinically suspected, an emergency computed tomography scan and lumbar puncture (intracranial pressure + 10 cm H<sub>2</sub>O) did not provide evidence for this. The electroencephalogram did not detect any epileptiform activity. A conventional magnetic resonance imaging scan did not reveal any abnormalities (Fig 1A). However, using diffusion-weighted magnetic resonance imaging, multiple lesions with markedly restricted diffusion suggestive of ischemia were visualized in the basal nuclei left, in the thalamus on both the left and right sides, in the mesencephalon, and in the brainstem (Fig 1B), explaining the signs observed in the patient.

The clinical condition of the patient did not improve during the next 2 weeks. A repeated magnetic resonance imaging scan after 2 weeks showed extensive areas of increased signal intensity on  $T_2$ -weighted images in the areas previously identified by reduced diffusion (Fig 1C). The somatosensory-evoked and brainstem-evoked potentials were negative. Based on the patient's clinical condition and the electrophysiologic and magnetic resonance imaging findings, and after consultation with the parents, treatment was discontinued. Shortly afterward, the patient died.

### Discussion

Both increased intracranial pressure and focal infarction of brain tissue are common complications in pneumococcal meningitis. Though the clinical signs of these conditions differ, similar signs can be observed in cases of brainstem infarction. Using conventional imaging tech-

Communications should be addressed to:

Dr. Haarman; Department of Pediatrics, Vrije Universiteit University Medical Center; De Boelelaan 1117; 1081 HV Amsterdam, The Netherlands.

E-mail: EG.Haarman@vumc.nl

Received September 19, 2007; accepted October 29, 2007.



Figure 1.  $T_2$ -weighted (TR/TE = 3000/120 ms) (A) and diffusion-weighted (TR/TE = 3400/122 ms) (B) magnetic resonance imaging performed early during the progression of pneumococcal meningitis, clearly demonstrating ischemic changes on diffusion-weighted magnetic resonance images, but not on  $T_2$ -weighted images. After 2 weeks,  $T_2$ -images (C) indicated infarctions in areas previously identified by diffusion-weighted magnetic resonance imaging.

niques, it is difficult to establish the correct diagnosis at an early stage, as this case report illustrates.

Increased intracranial pressure in bacterial meningitis is caused by a combination of cytotoxic edema (because of cell death), vasogenic edema (cytokine-induced increased capillary permeability), obstruction of cerebrospinal fluid flow from the ventricles (because of fibrosis, gliosis, or edema of the surrounding tissues of the aqueduct of Sylvius), and obstructed reabsorption of cerebrospinal fluid in the arachnoid villus. If the increased intracranial pressure is not dispersed equally between the supratentorial and infratentorial compartment, transtentorial herniation of the upper brainstem and brainstem dysfunction ensue. Clinically, this condition can be recognized by cranial nerve palsies, reduced consciousness, systemic hypertension, bradycardia, and respiratory depression. Signs of herniation occur in about 6% of cases of bacterial meningitis [1].

Ischemia in bacterial meningitis results from a combination of reduced perfusion of the brain because of systemic hypotension, increased intracranial pressure, the loss of autoregulation of cerebral blood flow [2,3], and the occlusion of small blood vessels because of septic embolism or vasculitis after direct invasion by microorganisms [4,5]. Most often, the frontal lobes are affected [6], but focal thalamic, pontine, and upper spinal-cord infarcts were reported [7,8]. Multiple infarcts in the brainstem can mimic the signs of raised intracranial pressure, as described in atherosclerotic disease of the basilar artery in adults [9]. However, to our knowledge, this is the first description of a child with pneumococcal meningitis with signs of increased intracranial pressure because of brainstem infarcts.

The early detection of focal ischemic lesions in meningitis, though of major clinical importance, is difficult. Vasculitis of small vessels can produce small areas of active ischemic change not detectable on computed tomography scans, conventional magnetic resonance imaging, or angiography [10]. Diffusion-weighted magnetic resonance imaging is a more sensitive tool for visualizing these lesions. Diffusion-weighted magnetic resonance imaging reveals the diffusion of water molecules, and is used to detect cytotoxic edema. After an episode of ischemia, the diffusion of water is highly restricted because of the shift of fluid into the intracellular compartment, and is indicated as areas with increased signal intensity.

Only a few studies were published regarding diffusionweighted magnetic resonance imaging findings in bacterial meningitis in children [6,11,12]. Jan et al., describing diffusion-weighted magnetic resonance imaging findings in 13 infants with bacterial meningitis of various etiologies, emphasized that, insofar as the white matter in the brain of an infant is not yet myelinated, the identification of cortical infarcts can be extremely difficult using conventional magnetic resonance imaging [6]. Early ischemic changes in these areas were more easily identified by diffusion-weighted magnetic resonance imaging. Peng et al. argued that, after studying eight children with bacterial meningoencephalitis, diffusion-weighted magnetic resonance imaging was more sensitive for the detection of cerebral lesions than T<sub>2</sub>-weighted or fast fluid attenuated inversion recovery images [11]. Another advantage of diffusion-weighted magnetic resonance imaging was demonstrated by Wong et al. [12]. They demonstrated that diffusion-weighted magnetic resonance imaging could discern purulent leptomeningeal empyemas from reactive effusions in children with bacterial meningitis. Because of the increased protein content, the diffusion of water is hindered in empyemas, resulting in increased signal intensity.

In conclusion, this report described a child with pneumococcal meningitis with ischemic lesions in the brainstem mimicking the signs of increased intracranial pressure. This case also illustrates the importance of diffusion-weighted magnetic resonance imaging in the early detection of ischemia.

#### References

[1] Horwitz SJ, Boxerbaum B, O'Bell J. Cerebral herniation in bacterial meningitis in childhood. Ann Neurol 1980;7:524-8.

[2] Tureen JH, Dworkin RJ, Kennedy SL, Sachdeva M, Sande MA. Loss of cerebrovascular autoregulation in experimental meningitis in rabbits. J Clin Invest 1990;85:577-81.

[3] Ashwal S, Tomasi L, Schneider S, Perkin R, Thompson J. Bacterial meningitis in children: Pathophysiology and treatment. Neurology 1992;42:739-48.

[4] **DiNubile** MJ, Boom WH, Southwick FS. Septic cortical thrombophlebitis. J Infect Dis 1990;161:1216-20.

[5] Dodge PR, Swartz MN. Bacterial meningitis—A review of selected aspects. II. Special neurological problems, postmeningitic com-

plications and clinicopathological considerations. N Engl J Med 1965;272:954-60.

[6] Jan W, Zimmerman RA, Bilaniuk LT, Hunter JV, Simon EM, Haselgrove J. Diffusion-weighted imaging in acute bacterial meningitis in infancy. Neuroradiology 2003;45:634-9.

[7] Perry JR, Bilbao JM, Gray T. Fatal basilar vasculopathy complicating bacterial meningitis. Stroke 1992;23:1175-8.

[8] Garg BP, DeMyer WE. Ischemic thalamic infarction in children: Clinical presentation, etiology, and outcome. Pediatr Neurol 1995;13: 46-9.

[9] Plum F, Posner JB. The diagnosis of stupor and coma, 3rd ed. Philadelphia: F.A. Davis Co., 1980:161-2.

**[10] Yuh** WT, Ueda T, Maley JE. Perfusion and diffusion imaging: A potential tool for improved diagnosis of CNS vasculitis. AJNR 1999;20:87-9.

[11] **Peng** SS, Tseng WY, Liu HM, Li YW, Huang KM. Diffusionweighted images in children with meningoencephalitis. Clin Imag 2003; 27:5-10.

[12] Wong AM, Zimmerman RA, Simon EM, Pollock AN, Bilaniuk LT. Diffusion-weighted MR imaging of subdural empyemas in children. AJNR 2004;25:1016-21.