

# Pontine Warning Syndrome

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**Background:** Little is known about stroke mechanisms in patients with fluctuating symptoms and the role of branch atherosclerotic disease.

**Objective:** To report a novel stroke presentation associated with a paramedian pontine infarct due to branch disease with a fluctuating course.

**Design:** Case report.

**Setting:** Academic research.

**Patient:** A 63-year-old man with hypertension, diabetes mellitus, and dyslipidemia was seen with fluctuating right-sided weakness and dysarthria. He had had 2 episodes of complete bilateral horizontal conjugate gaze palsy with unimpaired consciousness lasting for 5 minutes each. His pupils were 4 mm and were equal and reactive to light. Vertical gaze and convergence were preserved. His neurologic status fluctuated between 3 and 15 on the National Institutes of Health Stroke Scale.

**Main Outcome Measures:** Results of computed tomographic angiography, perfusion, and magnetic resonance imaging.

**Results:** Intravenous tissue plasminogen activator was administered within a 3-hour window. Fluctuations in motor weakness persisted for 12 hours after receiving thrombolytic therapy. Neuroimaging showed an acute left paramedian pontine infarct with a patent basilar artery.

**Conclusions:** Branch disease is a common mechanism in pontine infarctions. We coined the term "pontine warning syndrome" to characterize recurrent stereotyped episodes of motor or sensory dysfunction, dysarthria, or ophthalmoplegia associated with a high risk of imminent basilar artery branch infarction and a permanent deficit resembling those of capsular warning syndrome.

*Arch Neurol.* 2008;65(10):1375-1377

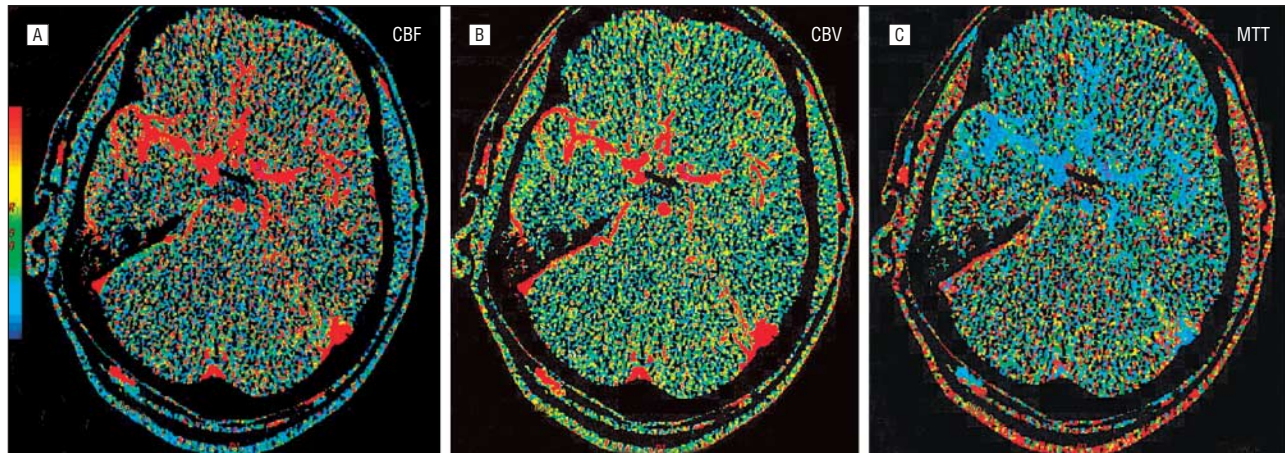
**S**MALL-VESEL BRAIN DISEASE IS a common and potentially devastating disorder. It constitutes one of the most common causes of isolated pontine strokes, particularly among patients with hypertension and diabetes mellitus.<sup>1</sup> Unfortunately, we know little about stroke mechanisms in patients with fluctuating symptoms and about the role of branch atherosclerotic disease. This is a case report of fluctuating pontine stroke with bilateral complete ophthalmoplegia due to branch atherosclerotic disease.

## REPORT OF A CASE

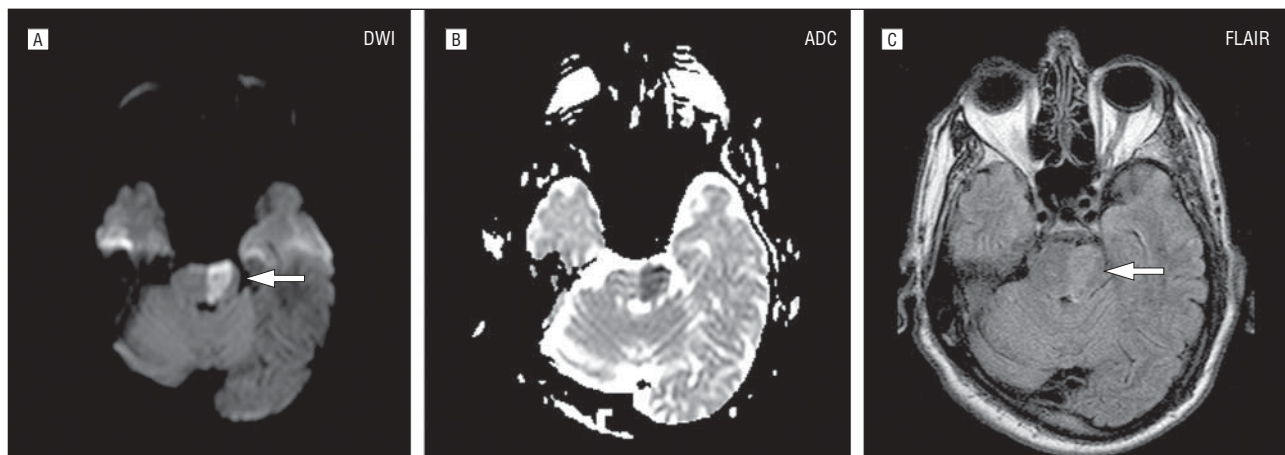
A 63-year-old man with hypertension, diabetes mellitus, and dyslipidemia was seen with fluctuating right-sided weakness and dysarthria. He denied previous episodes of transient ischemic attack or stroke. His general physical examination revealed a blood pressure of 167/92 mm Hg, but the find-

ings were otherwise unremarkable. On neurologic examination, he was alert with moderate dysarthria, reduced sensation in the right arm, and right-sided hemiparesis more pronounced in the distal upper limb (Medical Research Council scale grade 2) than in the lower limb (grade 4). He had had 2 witnessed episodes of complete bilateral horizontal conjugate gaze palsy with unimpaired consciousness lasting for 5 minutes each. His pupils were 4 mm and were equal and reactive to light. Vertical gaze and convergence were preserved. His neurologic status fluctuated at least 7 times between 3 and 15 on the National Institutes of Health Stroke Scale (NIHSS). Computed tomography of the head, computed tomographic angiography, and computed tomographic perfusion (**Figure 1**) showed no significant abnormalities. Intravenous tissue plasminogen activator was administered at 150 minutes after the onset of symptoms. Magnetic resonance imaging of the head showed an acute left-sided paramedian

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**Figure 1.** Computed tomographic perfusion shows no decrease in cerebral blood flow (A), cerebral blood volume (B), or prolonged mean transient time (C).



**Figure 2.** Magnetic resonance imaging performed 13 hours after computed tomography of the head. A, Axial fluid-attenuated inversion recovery (FLAIR) image shows well-delineated increased signal in the left aspect of the paramedian pontine tegmentum (arrow) involving the nucleus raphe interpositus, medial longitudinal fasciculus, and fascicles of abducens nuclei. The same area exhibits restricted diffusion with high signal (arrow) on the diffusion-weighted image (DWI) sequence (B) and low signal on the apparent diffusion coefficient (ADC) map (C).

pontine infarct (**Figure 2**). The basilar artery was patent on magnetic resonance angiography. A transthoracic echocardiogram revealed no cardiac source of embolism. Fluctuations in motor weakness persisted for 12 hours after receiving thrombolytic therapy. By the next 24 hours, his neurologic deficit remained unchanged. The patient was discharged with severe right arm weakness, dysarthria, and bilateral horizontal gaze ophthalmoplegia (12 on the NIHSS).

#### COMMENT

Pontine infarcts account for approximately 15% of acute vertebrobasilar ischemic strokes.<sup>2</sup> They can be classified according to the pathogenetic mechanism as follows: (1) small-artery disease, (2) atherosclerotic branch disease, (3) large-artery occlusive disease, or (4) cardioembolic; the corresponding underlying pathologic conditions are (1) lipohyalinosis, (2) microatheromatosis of the ostium or proximal portion of a small branch, (3) atherosclerosis of the large arterial wall, and (4) embolic.<sup>1</sup>

Complete bilateral horizontal gaze palsy is rare. Previously described patients had paraneoplastic brain-

stem encephalitis and multiple sclerosis.<sup>3,4</sup> Other authors reported complete bidirectional vertical gaze palsy in a patient with a unilateral midbrain infarct involving the rostral interstitial nucleus of the medial longitudinal fasciculus and the interstitial nucleus of Cajal.<sup>5</sup> Complete horizontal gaze palsy has not been described in acute ischemic stroke, to our knowledge.

The most common pontine structures responsible for horizontal gaze include the abducens nuclei, the medial longitudinal fasciculus, and the paramedian pontine reticular formation (PPRF). In patients with bilateral horizontal gaze palsy, small lesions affecting the medial longitudinal fasciculus and the median raphe have been involved.<sup>3</sup> In our patient, horizontal gaze palsy was explained by ischemia to the left PPRF and the adjacent median raphe. The disparity between complete gaze palsy with preserved consciousness could be anatomically explained by the sparing of the right PPRF and the caudal part of the left PPRF.<sup>5</sup>

The fluctuating course of stereotyped symptoms with a patent basilar artery suggested occlusion of the proximal portion or the ostium of a single basilar branch (branch disease).<sup>1,6</sup> This is one of the most common

mechanisms causing pontine strokes.<sup>7</sup> Basilar artery branch disease is particularly associated with large ventral infarcts, severe clinical symptoms, progressive or fluctuating course, and local recurrence.<sup>1,7</sup>

Unique features of this case include the clinical presentation with a fluctuating course and stereotyped symptoms, including complete bilateral horizontal conjugate gaze palsy with a patent basilar artery. We coined the term "pontine warning syndrome" to characterize recurrent stereotyped episodes of motor or sensory dysfunction, dysarthria, or ophthalmoplegia associated with a high risk of imminent basilar artery branch infarction and a permanent deficit resembling those of capsular warning syndrome described in the anterior circulation.<sup>8</sup> Early recognition of this clinical presentation and the accompanying stroke mechanism may guide the initial management and prognosis.

**Accepted for Publication:** May 13, 2008.

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**Author Contributions:** Dr Saposnik had full access to all the data in the study and had final responsibility for the decision to submit the manuscript for publication. *Study concept and design:* Saposnik. *Acquisition of data:* Saposnik. *Analysis and interpretation of data:* Saposnik, Noel de Tilly, and Caplan. *Drafting of the manuscript:* Saposnik and Noel de Tilly. *Critical revision of the manuscript for important intellectual content:* Saposnik and Caplan.

**Obtained funding:** Saposnik. **Administrative, technical, and material support:** Saposnik. **Study supervision:** Caplan.

**Financial Disclosure:** None reported.

**Funding/Support:** This study was supported by the Heart Stroke Foundation of Canada, Canadian Institutes for Health Research, Department of Research at St Michael's Hospital, and Connaught Foundation (University of Toronto) (Dr Saposnik).

**Role of the Sponsor:** None of the supporting agencies had a role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

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