Case Report

Repeated Hypotensive Episodes with Fluctuating Symptoms in a Patient with Acute Pontomedullary Infarction

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Dysfunction of cardiovascular regulation, including arterial hypotension, is a rare complication of acute ischemic stroke. We report a patient with an acute pontomedullary infarction who frequently had severe hypotensive episodes. A 78-year-old diabetic man suddenly developed faintness and left hemiparesis. MRI revealed a fresh infarct at the right pontomedullary region, including (or adjacent to) the rostral ventrolateral medulla. During the initial few weeks, urination and head-up tilts frequently induced hypotensive episodes accompanied by systolic blood pressure drops of up to 60 mmHg that were accompanied by fluctuating symptoms. In conclusion, pontomedullary stroke should be considered as a possible cause of hypotension accompanied by fluctuation of neurological symptoms during acute stroke. (*Hypertens Res* 2008; 31: 1829–1831)

***Key Words*: stroke, blood pressure, pontomedullary infarction, hypotension, rostral ventrolateral medulla**

Introduction

A brain lesion can potentially produce arterial hypotension, as well as hypertension (*1*). Because the medulla oblongata contains vasomotor centers that control peripheral vascular tone and blood pressure (BP), damage to the medulla oblongata due to ischemia, tumor, demyelination, extrinsic compression, and other causes may produce a failure of cardiovascular regulation, including paroxysmal neurogenic hypertension (*2*). In the present report, we describe a patient with an acute pontomedullary infarction, which appeared to cause frequent, severe, paroxysmal hypotensive episodes that were accompanied by progression of the stroke syndrome.

Case Report

A 78-year-old man with a 10-year history of diabetes mellitus and a single episode of syncope 10 years earlier suddenly developed faintness followed by left motor weakness. On admission to our hospital, his BP was 180/90 mmHg, and his heart rate was regular (66 beats/min). He was alert, dysarthric, and had mild left hemiparesis. On emergent diffusion-weighted MRI, a high intensity lesion was seen in the right pontomedullary region (Fig. 1A). On MR angiography, as well as catheter angiography, the right vertebral artery was occluded. The basilar artery and the left vertebral artery were intact. Nerve conduction measurements of the right median nerve, right tibial nerve, and right sural nerve were normal. He did not have cardiac diseases, including cardiac conduc-

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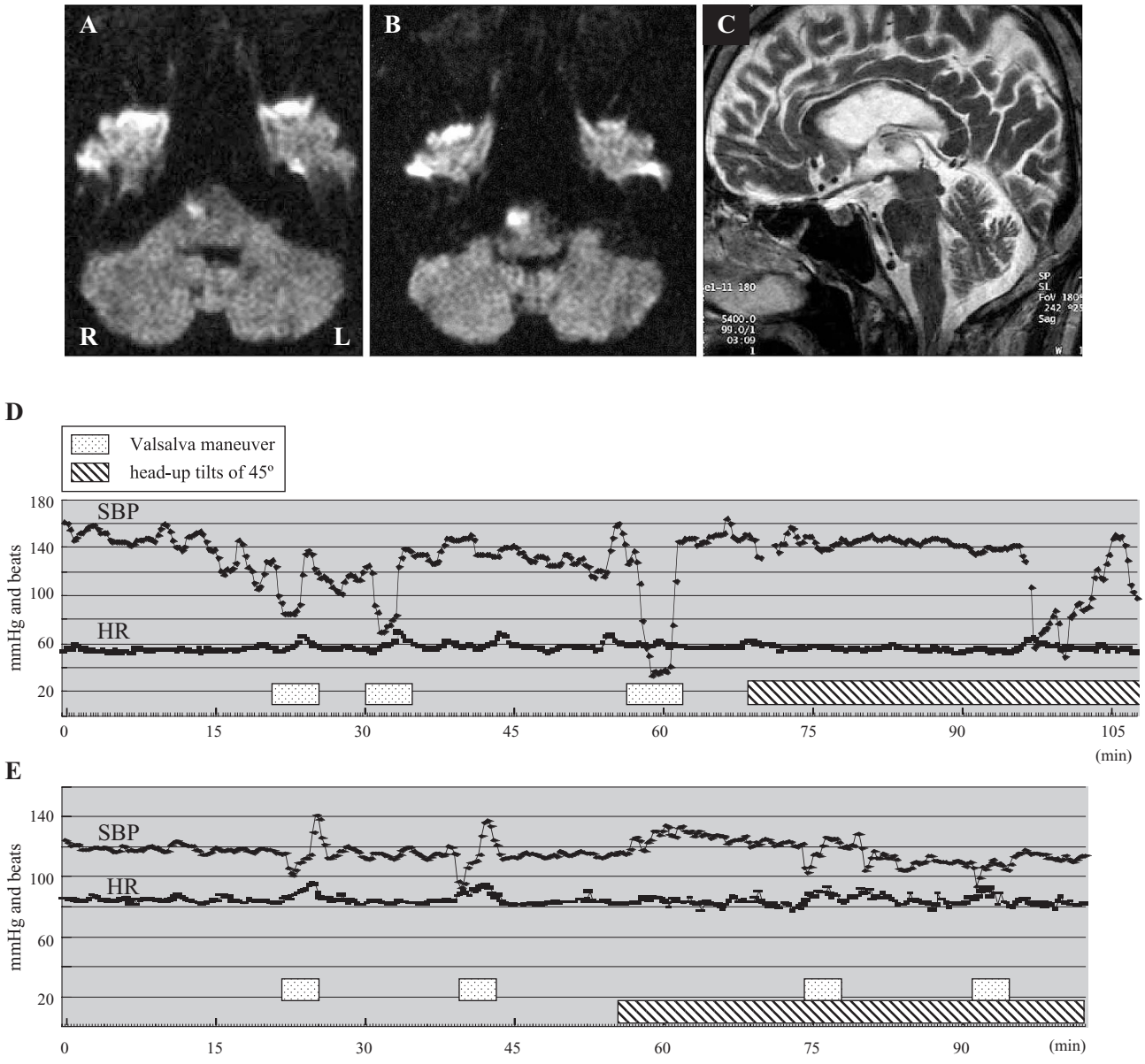

Fig. 1. *A–C: A pontomedullary infarct on MRI. Diffusion-weighted image (b value=1,000) on day 1 shows high intensity in the pontomedullary junction including or adjacent to the rostral ventrolateral medulla (A), which can be seen to have expanded dorsally on day 16 (B: diffusion-weighted image; C: T_2-weighted image). D, E: Changes in systolic blood pressure (SBP) and heart rate (HR). On day 14 (D), severe hypotension with a 60-mmHg drop in SBP was recorded during the Valsalva maneuver and during 30-min head-up tilts of 45°. On day 40 (E), the SBP drop during the Valsalva maneuver or head-up tilts was less (< 20 mmHg). The HR can be seen to have increased from ~60 beats/min on day 14 to ~80 beats/min on day 40.*

tion abnormality. Thyroidal function was intact. With a diagnosis of fresh pontomedullary infarction, oral aspirin, 200 mg/d, and intravenous argatroban, an antithrombin agent that has been approved in Japan for the treatment of acute ischemic stroke, were administered immediately. However, on days 2, 4, and 8, he suffered repeated hypotensive episodes with an approximately 60 mmHg drop in systolic BP accompanied by deterioration of his left hemiparesis and dysarthria immediately after urination in the supine position. He also had repeated severe drops in BP (up to 60 mmHg) during Valsalva maneuvers or during short-duration head-up tilts to 45° (Fig. 1D). His hemiparesis and dysarthria deteriorated at the same time as the hypotension on day 7. He wore elastic stockings to prevent hypotensive attack. Oral antihypotensive drugs, including dihydroergotamine mesilate (3 mg/d), droxydopa (200 mg/d), and fluorocortisone acetate (0.05

mg/d), were not effective in preventing the hypotensive episodes. Following the frequent fluctuations in his symptoms, the pontomedullary infarct was seen to have expanded dorsally on the follow-up MRI (Fig. 1B, C). On day 13, in addition to aspirin, he was started on oral cilostazol (100 mg/d), an antiplatelet agent that often increases the heart rate. Following this treatment, his basal heart rate increased and the hypotensive attacks became infrequent (Fig. 1E). His serum noradrenaline level increased from 196 pg/mL on day 5 to 507 pg/mL on day 38. His uric noradrenaline level increased from 30.1 μg/d to 57.3 μg/d. No further episodes of faintness occurred. The patient's hemiparesis improved, and he could walk with a cane.

Discussion

The major finding of this case is that an ischemic stroke in the pontomedullary region can induce severe hypotension accompanied by fluctuation of stroke symptoms during the acute phase.

BP control is supported by a descending sympathoexcitatory pathway from the rostral ventrolateral medulla to the intermediolateral cell column in the spinal cord, and damage to these areas can cause severe hypotension (*1*, *3*). Based on studies of anesthetized animals, the rostral ventrolateral medulla seems to play major roles in BP regulation (*4*). In the present case, a fresh infarct included (or was adjacent to) the rostral ventrolateral medulla. A few case reports have described hypotension and bradycardia due to autonomic dysfunction following a pontomedullary stroke (*5*), as well as paroxysmal apnea and BP instability following a medullary stroke (*6*). However, these episodes of cardiovascular dysregulation occurred in the chronic phase. This case is unique in that the dysregulation appeared during the acute stage of the stroke and affected the patient's neurological symptoms.

Although autonomic neuropathy due to diabetic mellitus might enhance hypotensive attacks, diabetes was not the main cause of this patient's hypotension because the nerve conduction study was normal and the attacks disappeared in the chronic stage. The mass effect of the pontomedullary infarct, including the surrounding edema, may have become less in the chronic stage, resulting in disappearance of the hypotensive episodes. The recovery of the noradrenaline levels during the chronic stage seems to support the temporary sympathetic nerve disorder during the acute stage. The tachycardic effect of cilostazol may also have provided protection against hypotension. Cilostazol may also improve cerebral vasomotor reactivity and increase cerebral blood flow (*7*, *8*). However, it is not certain if the recovery from hypotensive attacks was due to the effects of cilostazol or simply due to the natural time course for recovery.

A recent guideline for the early management of adults with ischemic stroke stated that arterial hypotension is associated with an increased likelihood of an unfavorable outcome, and the cause of arterial hypotension should be identified in patients with acute stroke (*9*). As potential causes of arterial hypotension, the guideline listed aortic dissection, volume depletion, blood loss, and decreased cardiac output secondary to myocardial ischemia or cardiac arrhythmias. Acute pontomedullary stroke should be considered as another possible cause of hypotension during the acute stage, and symptomatic progression due to hypotension should be prevented in patients with acute pontomedullary stroke.

References

1. Talman WT: Cardiovascular regulation and lesions of the central nervous system. *Ann Neurol* 1985; **18**: 1–12.
2. Benarroch EE: The central autonomic network: functional organization, dysfunction, and perspective. *Mayo Clin Proc* 1993; **68**: 988–1001.
3. Posner JB, Saper CB, Schiff ND, Plum F: Plum and Posner's Diagnosis of Stupor and Coma, 4 th ed. New York, Oxford University Press, 2007, pp 38–87.
4. Guyenet PG: The sympathetic control blood pressure. *Nat Rev Neurosci* 2006; **7**: 335–346.
5. Khurana RK: Autonomic dysfunction in pontomedulalry stroke. *Ann Neurol* 1982; **12**: 86 (Abstract).
6. Lassman AB, Mayer SA: Paroxysmal apnea and vasomotor instability following medullary infarction. *Arch Neurol* 2005; **62**: 1286–1288.
7. Tanaka K, Gotoh F, Fukuuchi Y, *et al*: Effects of a selective inhibitor of cyclic AMP phosphodiesterase on the pial microcirculation in feline cerebral ischemia. *Stroke* 1989; **20**: 668–673.
8. Ameriso SF, Lagos R, Ferreira LM, Fernández Cisneros L, La Mura AR: Cerebrovascular effects of cilostazol in patients with atherosclerotic disease. *J Stroke Cerebrovasc Dis* 2006; **15**: 273–276.
9. Adams HP Jr, del Zoppo G, Alberts MJ, *et al*: Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Stroke* 2007; **38**: 1655–1711.