

Takotsubo Cardiomyopathy Induced by Dobutamine Infusion During Hypertensive Therapy for Symptomatic Vasospasm After Subarachnoid Hemorrhage

—Case Report—

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Abstract

A 65-year-old female with subarachnoid hemorrhage (SAH) developed takotsubo cardiomyopathy induced by dobutamine infusion for vasospasm 9 days after onset of SAH. She underwent neck clipping of the ruptured cerebral aneurysm on day 1. Course after surgery was uneventful, but she developed motor aphasia on day 9. Hypertensive therapy was carried out under the diagnosis of symptomatic vasospasm. Half an hour after initiation of dobutamine infusion at 6 $\mu\text{g}/\text{kg}/\text{min}$, sudden symptoms of takotsubo cardiomyopathy developed. Fortunately, her symptoms recovered in a few days with supportive therapy without any consequences. Takotsubo cardiomyopathy is one pattern of cardiac dysfunction occasionally encountered after SAH. Possible mechanisms of this disorder include epicardial catecholamine cardiotoxicity. Therefore, generally, cardiac function is worst at the early stage of SAH, when sympathetic activity is highest, and recovers thereafter. Dobutamine infusion seems to have triggered the takotsubo cardiomyopathy in the present patient even 9 days after onset of SAH. Inotropic agents including dobutamine are often used during the course of SAH, and since takotsubo cardiomyopathy can occur in patients with SAH, this complication must be considered.

Key words: subarachnoid hemorrhage, vasospasm, dobutamine, takotsubo cardiomyopathy

Introduction

Cardiac dysfunction after subarachnoid hemorrhage (SAH) is a well-recognized phenomenon. Electrocardiographical changes such as QT elongation and ST-T changes are observed in as many as 90% of cases.³⁾ Left ventricular systolic dysfunction occurs in approx. 10% of patients with SAH.^{2,6,8)} Although the pathophysiology of cardiac injury after SAH is still not clear, the most likely cause of cardiac dysfunction after SAH is excessive catecholamine release within the myocardium.^{4,5)}

We report a case of SAH associated with takotsubo cardiomyopathy which manifested after dobutamine infusion during hypertensive therapy for symptomatic vasospasm 9 days after onset of SAH.

Case Report

A 65-year-old female with history of smoking and moderate obesity suffered sudden onset of severe headache. Her consciousness was almost alert without limb paresis during ambulance transportation to our hospital and immediately after arrival she suffered another attack. Her con-

sciousness level deteriorated to Glasgow Coma Scale (GCS) 4 (E1V1M2). Brain computed tomography (CT) revealed SAH (Fig. 1A). After admission, her consciousness gradually recovered. Three-dimensional CT angiography demonstrated an anterior communicating artery aneurysm (Fig. 1B), which was successfully clipped on the next day with consciousness level at GCS 12 (E2V4M6) (Fig. 1C). The postoperative course was uneventful until 9 days after onset.

She developed motor aphasia on day 9. Cerebral angiography performed a day before revealed vasospasm in the left carotid and left middle cerebral arteries (Fig. 1D). Hypertensive therapy was carried out with the diagnosis of symptomatic vasospasm. Half an hour after initiation of dobutamine infusion at 6 $\mu\text{g}/\text{kg}/\text{min}$, sudden symptoms of heart failure developed. Electrocardiography showed marked ST elevation in leads I, II, aVL, and V2-V6 (Fig. 2). Emergency coronary angiography was performed suspecting acute myocardial infarction, but was negative (Fig. 3A, B). However, left ventriculography showed apical akinesis and basal hyperkinesis indicating takotsubo cardiomyopathy (Fig. 3C, D). Hypertensive therapy was stopped at this point. She was observed in the coronary care unit for 3 days, her heart failure did not worsen and gradually recovered. Her motor aphasia also recovered in

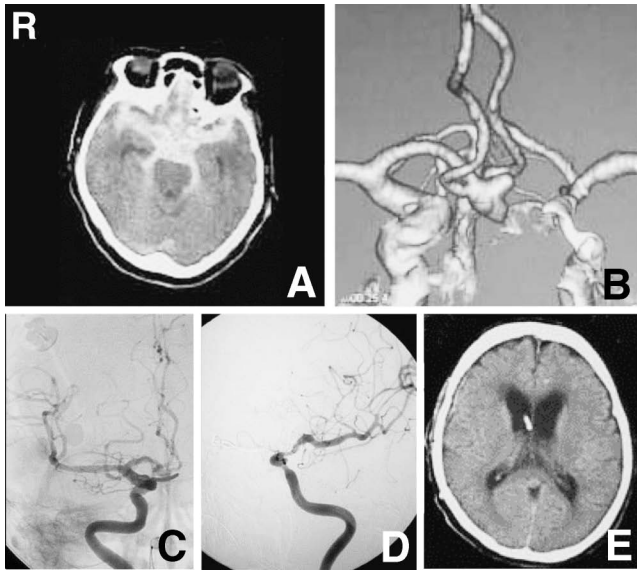


Fig. 1 A: Brain computed tomography (CT) scan obtained on admission. B: Three-dimensional CT angiogram (anteroposterior view) revealing an anterior communicating artery aneurysm. C, D: Digital subtraction angiograms performed on day 8 revealing complete clipping of the aneurysm (C: right carotid angiography, anteroposterior view) and multiple moderate to severe vasospasm (D: left carotid angiography, oblique view). E: Brain CT scan obtained just before the patient was discharged to local hospital for further rehabilitation.

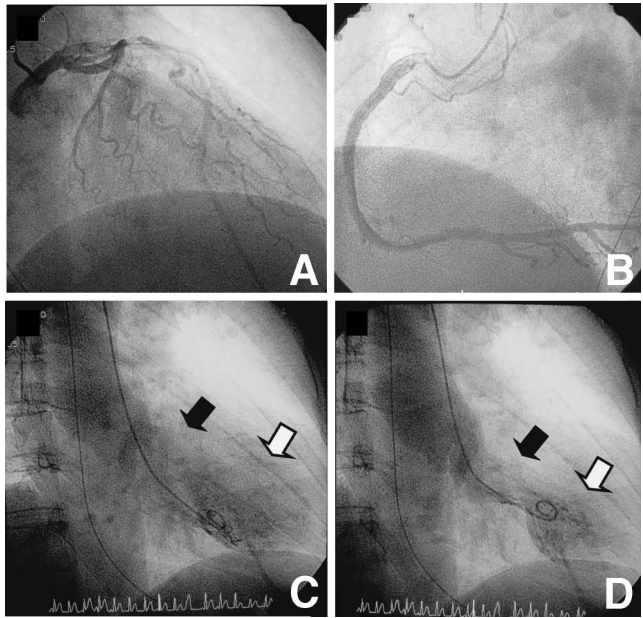


Fig. 3 A, B: Left (A) and right (B) coronary angiograms showing no obstruction or significant stenosis. C, D: Left ventriculograms (C: diastolic phase, D: systolic phase) showing apical akinesis (white arrow) and basal hyperkinesis (black arrow) indicating takotsubo cardiomyopathy.

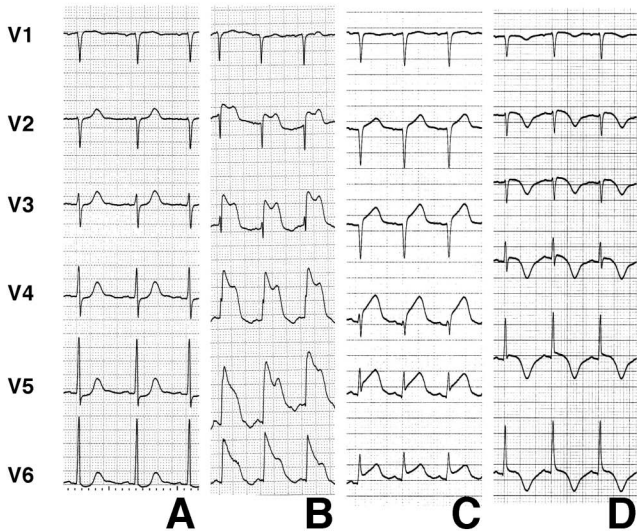


Fig. 2 Electrocardiograms obtained on admission (A), just after manifestation of takotsubo cardiomyopathy (B), after emergency coronary angiography (C), and a day after onset of takotsubo cardiomyopathy (D).

a few days. After placement of a ventriculoperitoneal shunt, she was discharged to another hospital for further rehabilitation (Fig. 1E).

Discussion

Takotsubo cardiomyopathy is one pattern of cardiac dysfunction occasionally found after SAH,¹³ characterized by transient left ventricular apical wall motion abnormality with electrocardiographic changes and minimal myocardial enzymatic release mimicking acute myocardial infarction, but without significant coronary artery disease.^{7,16,17} Several possible mechanisms have been proposed for takotsubo cardiomyopathy including epicardial catecholamine cardiotoxicity. Most reported cases of takotsubo cardiomyopathy have shown simple clinical courses after onset. Usually cardiac function is worst at the early stage of SAH, when sympathetic activity is highest, and recovers thereafter. However, in our case, dobutamine infusion 9 days after onset of SAH triggered the manifestation of takotsubo cardiomyopathy. Although the precise mechanism still remains unclear, sympathetic overactivation may be important in takotsubo cardiomyopathy in patients with SAH.^{11,18} Excess sympathetic nervous activation occurs after SAH, with increased plasma norepinephrine level within 48 hours that persists during the 1st week after hemorrhage.^{10,12,14} Therefore, in many cases, ejection fraction is worst during the early stage of SAH and recovers afterward.¹¹ A previous patient with SAH had takotsubo cardiomyopathy which worsened in the late phase of vasospasm.¹⁵ However, the takotsubo cardiomyopathy was present at disease onset. In our patient, electrocardiography on admission did not show any evidence of takotsubo cardiomyopathy. Therefore, the onset of takotsubo cardiomyopathy in our case was un-

usual.

Dobutamine infusion seems to have triggered the cardiac dysfunction in the present case. Direct release of toxic levels of catecholamines into the myocardium by the cardiac sympathetic nerve terminals is indicated as a more likely cause of neurocardiogenic injury than adrenal release of catecholamines into the systemic circulation in animal models.¹³⁾ No significant association was found between serum levels of either norepinephrine or epinephrine and cardiac troponin I release that indicate myocardial necrosis in patients with SAH.¹⁸⁾ However, a case of takotsubo cardiomyopathy resulting from dobutamine infusion was reproducible in the catheterization laboratory, suggesting that catecholamine-induced microvascular dysfunction may be the predominant etiological factor in takotsubo cardiomyopathy.¹⁾ A case of takotsubo cardiomyopathy precipitated by dobutamine stress testing was also reported in a morbidly obese woman who underwent a dobutamine nuclear stress test as preoperative screening before bariatric surgery.¹⁶⁾ In the present case, known preceding psychological stressor was absent, so dobutamine may have been the precipitant.

Treatment of takotsubo cardiomyopathy in a patient with symptomatic cerebral vasospasm is complicated. Hemodynamic augmentation, consisting of increasing intravascular volume and blood pressure parameters, is difficult to attain.¹¹⁾ Cardiac output may need support with dobutamine or milrinone, especially if the blood pressure remains low. However, use of pressor could have resulted in unfavorable outcome in our patient. We only could maintain the systolic blood pressure at 100–120 mmHg, which may not have been high enough during the phase of cerebral vasospasm. Fortunately, motor aphasia observed in our patient disappeared without any consequences. One study demonstrated acute improvements in electrocardiographic and ventriculographic abnormalities with intravenous propranolol infusion.⁹⁾ Such new evidence may be a help for future management of similar cases. Inotropic agents including dobutamine are often used during the course of SAH, and since takotsubo cardiomyopathy can occur in patients with SAH, the complication encountered in the present case must be considered.

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