

Case Report

Takotsubo Cardiomyopathy in a Patient with Chronic Inflammatory Demyelinating Polyneuropathy

Amit Kandel, MBBS;^{1*} Marilou Ching, MD, MPH;¹ Osman Farooq, MD;¹
Rohit Gokhale, MBBS;² Carina Alfaro-Franco, MD, MS, FACC;² Ping Li, MD¹

¹ Department of Neurology, University at Buffalo, SUNY-Buffalo, NY

² Department of Cardiology, University at Buffalo, SUNY-Buffalo, NY

Takotsubo cardiomyopathy is an acute non-ischemic cardiomyopathy and may be triggered by physical, emotional stress or following excessive catecholamines in the body. It has been associated with many neurologic conditions. We report a patient with chronic inflammatory demyelinating polyneuropathy (CIDP) who developed acute transient cardiomyopathy after an episode of hypoxia. To our knowledge, this is the first reported case of takotsubo cardiomyopathy associated with CIDP.

[*N A J Med Sci.* 2015;8(2):100-104. DOI: 10.7156/najms.2015.0802100]

Key Words: CIDP, cardiomyopathy, takotsubo cardiomyopathy, neurogenic cardiomyopathy

INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy (CIDP) is defined as a progressive or relapsing autoimmune condition that develops over at least two months.¹ CIDP is predominantly a motor neuropathy with sensory symptoms, however sensory dysfunction can occur in CIDP variants.² In CIDP, autonomic dysfunction is common but is usually mild, predominantly sudomotor impairment,³⁻⁶ whereas in acute inflammatory demyelinating polyneuropathy (AIDP), autonomic dysfunction can be severe.⁷

Takotsubo cardiomyopathy is an acute nonischemic cardiomyopathy that may be triggered by emotional stress or following excessive catecholamines in the body.^{8,9} Takotsubo cardiomyopathy has been associated with subarachnoid hemorrhage,^{10,11} ischemic stroke,¹² myasthenia gravis crisis,¹³ amyotrophic lateral sclerosis (ALS),¹⁴ top of the basilar syndrome,¹⁵ status epilepticus,¹⁶ seizure¹⁷ and Guillain-Barre syndrome.¹⁸ However, to our knowledge, this is the first case reported of takotsubo cardiomyopathy associated with CIDP.

CASE REPORT

We report the case of a 64-year-old Caucasian woman with history of diabetes mellitus that developed weakness and pain in her lower extremities. She has no family history of hereditary neuropathy. The weakness gradually progressed to involve her upper extremities within 4-5 weeks. She ultimately became wheelchair bound by 5 to 6 months. In addition to her weakness, she developed paresthesia in her hands and pain in her lower back. Her memory, language and

speech remained intact during this time. On examination she displayed weakness in her all extremities, proximal greater than distal and relative sparing of bilateral distal leg muscle and mild weakness of neck flexors. Sensory examination demonstrated bilaterally asymmetric decreased sensation to pinprick right side more than left side. The deep tendon reflexes were absent.

Evaluation of her cerebrospinal fluid (CSF) revealed an elevated protein of 92 mg/dl (15-45 mg/dl) with normal glucose and cytology. Electrophysiological studies of the right extremities showed absent sensory nerve conduction responses in the Ulnar, Median, Radial, Sural and Superficial Peroneal nerves. In addition, prolonged distal latencies, decreased response amplitudes and slow conduction in the Ulnar, Median, Peroneal, and Tibial nerves were seen, with normal Tibial response amplitude. F-responses were absent in Ulnar, Median, and Tibial nerves. Tibial H-reflexes recording in Soleus were also absent bilaterally. The clinical and electrophysiological data met the American Academy of Neurology (AAN) task force and European Federation of Neurological Societies and the Peripheral Nerve Society (EFNS/PNS) criteria for CIDP diagnosis.^{19,20} As the patient's clinical presentations involved all four extremities in a subacute to chronic fashion, the diagnosis was more consistent with CIDP and less with diabetic amyotrophy with generalized polyneuropathy.

Given the diagnosis of CIDP, she was admitted for intravenous immunoglobulin (IVIG). During her hospital stay she developed sudden acute respiratory distress even before start of IVIG. Upon evaluation, she displayed orthopnea and tachypnea, arterial blood gas revealed respiratory acidosis. Further examination revealed profound

Received: 03/06/2015; Revised: 04/13/2015; Accepted: 04/16/2015

*Corresponding Author: Department of Neurology, Erie County Medical Center, Buffalo, NY. Tel: 716-898-3638, Fax: 716-898-5602.

(Email: akandel@buffalo.edu)

neck flexor weakness, asymmetrical sensory loss, and quadriparesis with right greater than left sided weakness and relative sparing of distal leg muscles. Deep tendon reflexes were absent. Speech and language were intact. Electrocardiogram (ECG) showed ST elevation in V1-V3, symmetrical T wave inversion in anterolateral leads as well as leads I and II, and a QTc interval of 437 milliseconds, which was different from her baseline ECG (Figures 1A and 1B). Cardiac enzymes also revealed elevated troponin T, CK-MB and Brain Natriuretic Peptide (BNP) of 0.38, 121 and 885 respectively. Immediate bedside transthoracic echocardiogram (TTE) showed severely reduced left ventricular ejection fraction (EF) of 25-30%, apical dilation with mid and distal anteroseptal, apical, and anterolateral akinetic segments (Figures 2A and 2B). In comparison, she had a normal ejection fraction of 65-70% without any wall

motion abnormalities in a TTE done 3 months prior to the admission.

The patient rapidly became hypotensive and an emergent cardiac catheterization was performed to evaluate for an anteroseptal myocardial infarction. Left ventriculography showed a large area of akinesis involving the anterior, anteroapical, and inferoapical segments with severe left ventricular systolic dysfunction. Her estimated ejection fraction was 20%. Angiography revealed 80-90% narrowing of the right proximal coronary artery while the remainder of her coronary arteries were unremarkable (Figures 3A and 3B). Coronary intervention was not performed. Mild troponin elevation was considered to be the result of demand ischemia. She subsequently required mechanical ventilation because of respiratory distress. Patient received Beta-blocker, ACE inhibitor, and diuretics for her cardiac condition.

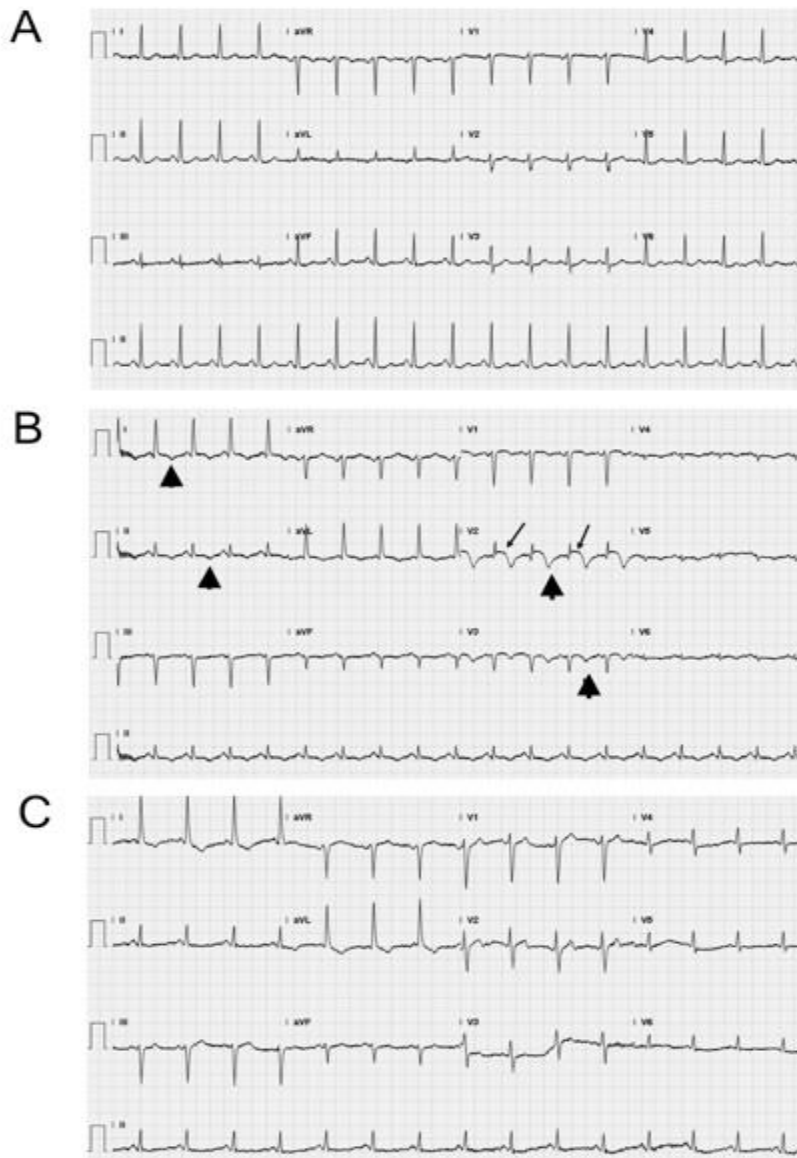


Figure 1. 1A: ECG 3 months before the admission, 1B: ECG on the day of the event (arrow head: T inversion, thin arrow: ST elevation), 1C: ECG on 22nd days after the event.

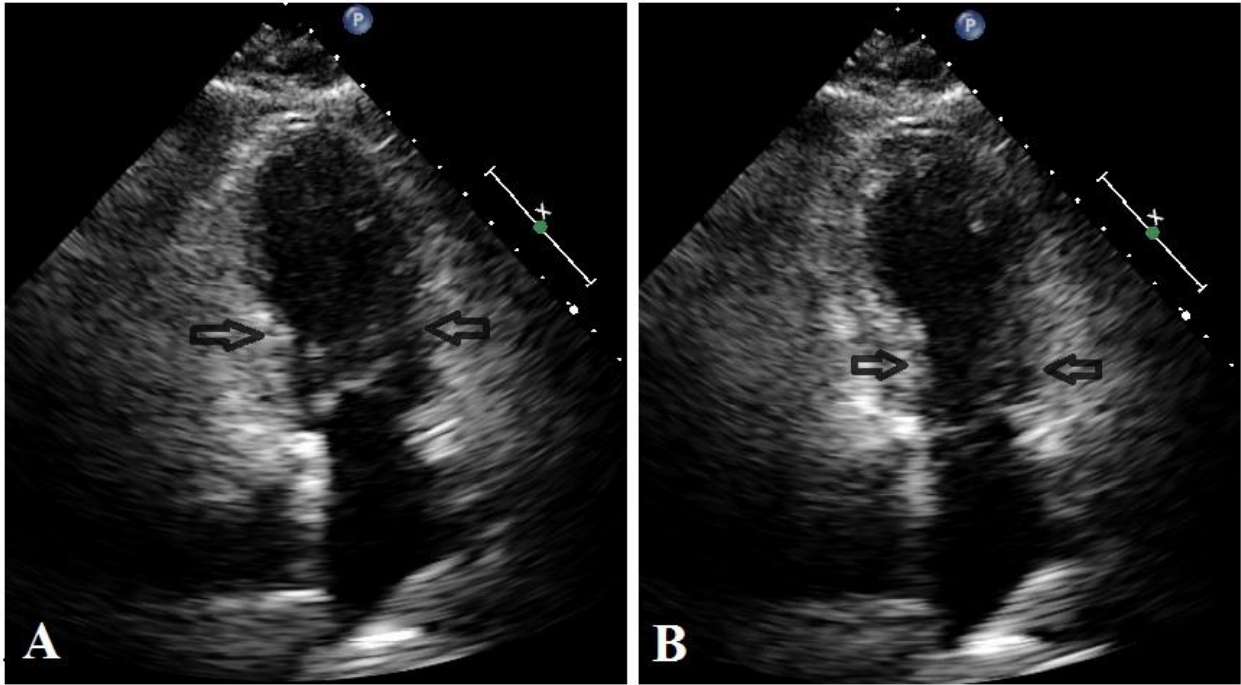


Figure 2. 2A: In diastole with arrow showing the basal wall in echocardiogram, **2B:** In systole with arrows showing basal wall in end systolic phase and relative lack of contraction in the apical and midventricular zone in echocardiogram.

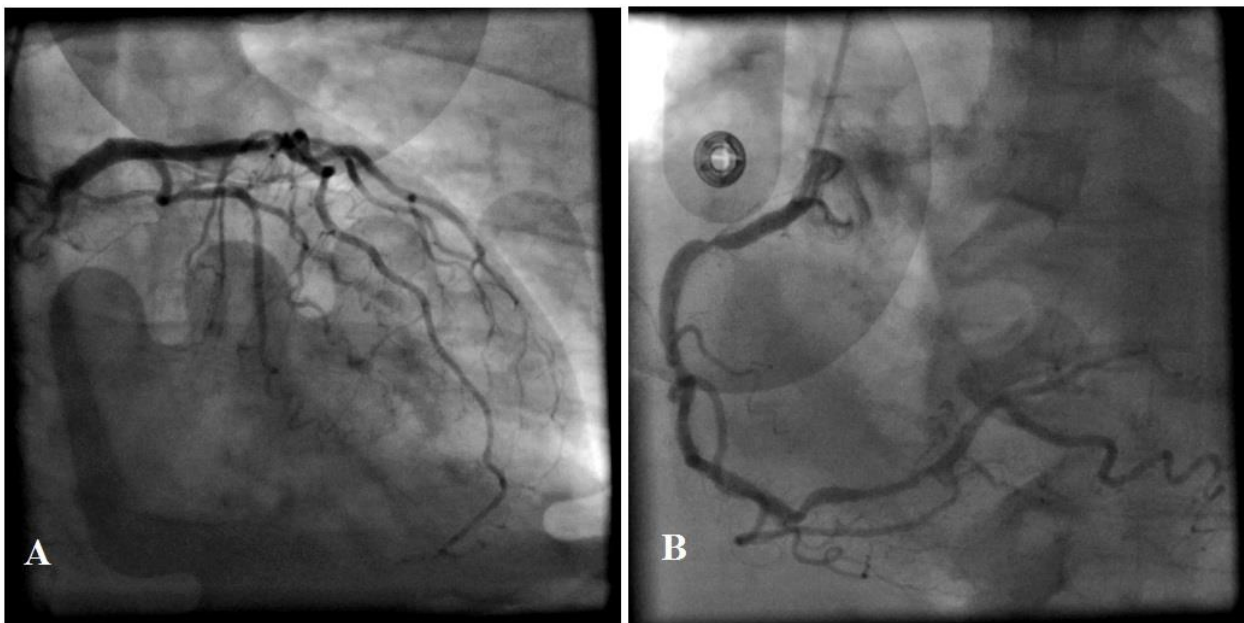


Figure 3. 3A: coronary angiogram showing left coronary artery with left circumflex branch and left anterior descending branch, and **3B:** coronary angiogram showing right coronary artery with 80-90% stenosis.

Due to medically refractory hypotension, an intra-aortic balloon pump was placed for hemodynamic support for three days. She was subsequently treated with IVIG for CIDP for 5 days and successfully extubated. At that time a repeat ECG revealed sinus rhythm and slight ST and T wave abnormalities. A TTE performed four days later revealed improvement in the ejection fraction to 30-35% with

resolution of apical dilatation. Her neurological examination showed findings similar to preadmission examination, which was consistent with diagnosis of CIDP. She was discharged to acute medical rehabilitation unit. A follow up TTE, 24 days later showed a return to baseline ejection fraction (>55%) devoid of any wall motion abnormalities. Neurological examination showed slight improvement in

motor evaluation from the time of respiratory event but she continued to have motor and sensory impairments as similar to her exam during admission.

DISCUSSION

Various unique presentations were noted in this case. First, this was an acute transient cardiomyopathy with typical apical and mid-ventricular hypokinesia. Second, it occurred in a female patient in her mid-60s who developed electrocardiographic and echocardiographic abnormalities in the setting of a neurological condition without evidence of significant coronary artery disease to explain the presentation. Third, this acute transient cardiomyopathy occurred in the patient with the diagnosis of CIDP.

A review of literature revealed several case reports of a transient non-ischemic cardiac syndrome with apical and mid-ventricular hypokinesia. The apical ballooning resembles the shape of an “octopus trap” or “takotsubo” in Japanese.²¹⁻²⁴ The transient systolic dysfunction of the apical and mid segments of the left ventricle mimics that seen in acute myocardial infarction. The exact pathophysiology is unknown, however it is hypothesized that acute stressors trigger this condition.^{25,26} Takotsubo cardiomyopathy is also known as stress induced cardiomyopathy,²⁶ broken heart syndrome²⁷ and transient left ventricular apical ballooning.²² It typically occurs in women with a median age of 65 years and has a remarkable recovery of symptoms and echocardiogram features in 6+/-3 days.²⁵ Even though there are reported cases of recurrent takotsubo cardiomyopathy with myotonic dysfunction, pheochromocytoma, stress, myasthenia gravis, but risk of recurrence is dependent on the primary condition and resultant stress.

The primary pathologic feature in takotsubo cardiomyopathy is myocytolysis,²⁶ which is characterized histopathologically by contraction band necrosis, early mineralization of the myofibril and mononuclear cellular infiltrates. These pathologic changes are entirely different from the coagulative necrosis seen in myocardial infarction. Similar clinical and pathologic changes have been reported in other neurological conditions such as subarachnoid hemorrhage (SAH), intracerebral hemorrhage, ischemic stroke.^{11,12,28} Elevated cardiac markers as well as electrocardiographic changes such as QTc prolongation, T wave inversion, abnormal U waves and repolarization changes have all been observed in the aforementioned disorders.^{11,29-31}

Interestingly, takotsubo cardiomyopathy has been reported in patients with pheochromocytoma as well as in animal studies after norepinephrine infusions.^{8,32,33} The release of catecholamines during stress is hypothesized to result in cardiac injury.^{34,35} Increased catecholamine level isn't required for the diagnosis of takotsubo cardiomyopathy. Its level is measured to rule out pheochromocytoma as an etiology. Firstly, the resultant apical and midventricular hypokinesia, with relative sparing of the basal segment of myocardium, is likely related to these myocytes being more sensitive to catecholamines. Secondly, there is also an apex-

to-base perfusion gradient as the apical region is more perfused than the basal segment of the heart.^{26,36}

In summary, takotsubo cardiomyopathy may occur in the context of various medical and neurologic conditions, however to our knowledge this is the first reported case of takotsubo cardiomyopathy associated with CIDP. The postulated mechanism appears to be stunned myocardium secondary to stress-induced catecholamine release. CIDP is associated with mild autonomic instability.^{4,5} Mild autonomic instability, orthopnea, neck flexor weakness in the reported case may have caused subsequent hypoxia and respiratory acidosis. These consequences could have resulted in an elevation of stress-induced catecholamine release and subsequent neurogenic cardiac injury. Multiple medical issues along with CIDP may have contributed to severe autonomic dysfunction. This case shows the possibility of occurrence of sympathetic overstimulation in patients with CIDP. It could be related to primary autonomic dysfunction or secondary autonomic manifestation because of stress due to hypoxia or weakness and CIDP.

The diagnosis of takotsubo cardiomyopathy should be suspected in postmenopausal women who present with an acute coronary syndrome in the context of acute physical, neurological or emotional stress in whom the clinical and ECG manifestations are out of proportion to the degree of elevation in cardiac biomarkers.

CONFLICT OF INTEREST

There is no commercial, financial or other association that poses a conflict of interest in connection with the article.

ETHICAL APPROVAL

This work meets all the ethical guidelines.

ACKNOWLEDGEMENTS

All the work was done in Millard Fillmore Gates Hospital. Dr. Maxim Mokin assisted in preparation of final figures.

REFERENCES

1. Sander HW, Latov N. Research criteria for defining patients with CIDP. *Neurology*. 2003;60:S8-15.
2. Lewis RA. Chronic inflammatory demyelinating polyneuropathy. *Neurol Clin*. 2007;25:71-87.
3. Ingall TJ, McLeod JG, Tamura N. Autonomic function and unmyelinated fibers in chronic inflammatory demyelinating polyradiculoneuropathy. *Muscle Nerve*. 1990;13:70-76.
4. Lyu RK, Tang LM, Wu YR, et al. Cardiovascular autonomic function and sympathetic skin response in chronic inflammatory demyelinating polyradiculoneuropathy. *Muscle Nerve*. 2002;26:669-672.
5. Stamboulis E, Katsaros N, Koutsis G, et al. Clinical and subclinical autonomic dysfunction in chronic inflammatory demyelinating polyradiculoneuropathy. *Muscle Nerve*. 2006;33:78-84.
6. Figueroa JJ, Dyck PJ, Laughlin RS, et al. Autonomic dysfunction in chronic inflammatory demyelinating polyradiculoneuropathy. *Neurology*. 2012;78:702-708.
7. Zochodne DW. Autonomic involvement in Guillain-Barré syndrome: A review. *Muscle Nerve*. 1994;17:1145-1155.
8. Samuels MA. 'Voodoo' death revisited: the modern lessons of neurocardiology. *Cleve Clin J Med*. 2007;74:S8.
9. Nef H, Mollmann H, Akashi Y, et al. Mechanisms of stress (Takotsubo) cardiomyopathy. *Nat Rev Cardiol*. 2010;7:187-193.
10. Lee V, Connolly H, Fulgham J, et al. Tako-tsubo cardiomyopathy in aneurysmal subarachnoid hemorrhage: an underappreciated ventricular dysfunction. *J Neurosurg*. 2006;105:264-270.

11. Jung JH, Min PK, Rim SJ, et al. Are Electrocardiographic Changes in Patients with Acute Subarachnoid Hemorrhage Associated with Takotsubo Cardiomyopathy? *Cardiology*. 2010;115:98-106.
12. Yoshimura S, Toyoda K, Ohara T, et al. Takotsubo cardiomyopathy in acute ischemic stroke. *Ann Neurol*. 2008;64:547-554.
13. Bansal V, Kansal MM, Rowin J. Broken heart syndrome in myasthenia gravis. *Muscle Nerve*. 2011;44:990-993.
14. Mitani M, Funakawa I, Jinnai K. [Transient left ventricular apical ballooning, "Takotsubo" cardiomyopathy, in an amyotrophic lateral sclerosis patient on long-term respiratory support]. *Rinsho shinkeigaku = Clinical neurology*. 2005;45:740-743.
15. Kato Y, Takeda H, Furuya D, et al. Takotsubo cardiomyopathy associated with top of the basilar artery syndrome. *J Neurol*. 2009;256:141-142.
16. Legriel S, Bruneel F, Dalle L, et al. Recurrent takotsubo cardiomyopathy triggered by convulsive status epilepticus. *Neurocrit Care*. 2008;9:118-121.
17. Stöllberger C, Wegner C, Finsterer J. Seizure-associated Takotsubo cardiomyopathy. *Epilepsia*. 2011;52:e160-e167.
18. Martins RP, Barbarot N, Coquerel N, et al. Takotsubo cardiomyopathy associated with Guillain-Barre syndrome: a differential diagnosis from dysautonomia not to be missed. *J Neurol Sci*. 2010;291:100-102.
19. Report from an Ad Hoc Subcommittee of the American Academy of Neurology ATF. Research criteria for diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP). *Neurology*. 1991;41:617-618.
20. Hughes RAC, Bouche P, Cornblath DR, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. *Eur J Neurol*. 2006;13:326-332.
21. Dote K, Sato H, Tateishi H, et al. Myocardial stunning due to simultaneous multivessel coronary spasms: a review of 5 cases. *J Cardiol*. 1991;21:203-214.
22. Tsuchihashi K, Ueshima K, Uchida T, et al. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. *Angina Pectoris-Myocardial Infarction Investigations in Japan*. *J Am Coll Cardiol*. 2001;38:11-18.
23. Owa M, Aizawa K, Urasawa N, et al. Emotional stress-induced 'ampulla cardiomyopathy': discrepancy between the metabolic and sympathetic innervation imaging performed during the recovery course. *Jpn Circ J*. 2001;65:349-352.
24. Kurisu S, Sato H, Kawagoe T, et al. Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: a novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J*. 2002;143:448-455.
25. Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and Reversible Cardiomyopathy Provoked by Stress in Women From the United States. *Circulation*. 2005;111:472-479.
26. Wittstein IS, Thiemann DR, Lima JAC, et al. Neurohumoral Features of Myocardial Stunning Due to Sudden Emotional Stress. *N Engl J Med*. 2005;352:539-548.
27. Wittstein IS. The broken heart syndrome. *Cleve Clin J Med*. 2007;74:S17.
28. Connor RCR. Heart Damage Associated with Intracranial Lesions. *Br Med J*. 1968;3:8-1,29-31.
29. Tung P, Kopelnik A, Banki N, et al. Predictors of Neurocardiogenic Injury After Subarachnoid Hemorrhage. *Stroke*. 2004;35:548-551.
30. Kerr G, Ray G, Wu O, et al. Elevated Troponin after Stroke: A Systematic Review. *Cerebrovasc Dis*. 2009;28:220-226.
31. Khechinashvili G, Asplund K. Electrocardiographic Changes in Patients with Acute Stroke: A Systematic Review. *Cerebrovasc Dis*. 2002;14:67-76.
32. Samuels MA. The Brain-Heart Connection. *Circulation*. 2007;116:77-84.
33. Schenk EA, Moss AJ. Cardiovascular Effects of Sustained Norepinephrine Infusions. II. Morphology. *Circ Res*. 1966;18:605-615.
34. Lacy CR, Contrada RJ, Robbins ML, et al. Coronary vasoconstriction induced by mental stress (simulated public speaking). *Am J Cardiol*. 1995;75:503-505.
35. Mann DL, Kent RL, Parsons B, et al. Adrenergic effects on the biology of the adult mammalian cardiocyte. *Circulation*. 1992;85:790-804.
36. Hernandez-Pampaloni M, Keng FY, Kudo T, et al. Abnormal longitudinal, base-to-apex myocardial perfusion gradient by quantitative blood flow measurements in patients with coronary risk factors. *Circulation*. 2001;104:527-532.