When the Worst Headache Becomes the Worst Heartache!

Abdul Hakeem, MD; Adam D. Marks, MPH; Sabha Bhatti, MD; Su Min Chang, MD

**Background and Purpose**—Although a great deal of literature has been generated regarding left ventricular wall abnormalities, ECG changes and cardiac enzyme leaks associated with subarachnoid hemorrhage (SAH), there have been only a few reports of true transient left ventricular apical ballooning syndrome in patients with SAH. Several pathophysiological mechanisms have been proposed to explain the unusual features of this syndrome, such as multivessel coronary vasospasm, abnormalities in coronary microvascular function, and catecholamine-mediated cardiotoxicity.

**Summary of Case**—A previously healthy 64-year-old woman with no history of vascular disease was found unresponsive at home. She was taken to the emergency room where a CT head revealed an SAH due to a ruptured aneurysm of the posterior communicating artery. On admission, an ECG showed deeply inverted T-waves and QT prolongation, typical of SAH. Cardiac troponin was measured at 1.2 ng/mL, and later increased to 3.7 ng/mL. A transthoracic echocardiogram on the next day revealed a large left ventricular wall abnormality, characteristic of apical ballooning with an ejection fraction of 25% to 30%. The patient remained hemodynamically stable and was started on low dose β-blocker and angiotensin-converting enzyme inhibitor. She had an uneventful cardiac recovery within 5 days at which time a repeat transthoracic echocardiogram revealed a normal ejection fraction with no wall motion abnormality.

**Conclusions**—This report adds to the growing list of “stressors” for Takotsubo cardiomyopathy. Clinicians should be aware of the existence and the typical clinical manifestations of this syndrome, which is increasingly recognized in various populations. In particular, neurologists should consider this syndrome in the differential diagnosis of ECG changes and apical wall motion abnormalities in patients with SAH. Prognosis is generally very good with full recovery in most patients; however, there may be increased morbidity associated in patients with SAH. (Stroke. 2007;38:3292-3295.)

**Key Words:** Broken Heart Syndrome • subarachnoid hemorrhage • Takotsubo cardiomyopathy

The neurocardiogenic spectrum of subarachnoid hemorrhage (SAH) spans from ECG abnormalities in almost 50% to 100% patients1,2 (deep T-wave inversions, QT prolongation, and torsades de pointes) to myocardial enzyme release in 20% to 40%3–5 and regional wall motion abnormalities (RWMA) in 10% of patients.6,7 These cardiac phenotypes have been attributed largely to the catecholamine surge accompanying SAH.4,5,7 The extent of troponin I elevation and RWMA have been strongly associated with poor outcomes.3–7 Moreover, the degree of neurological injury has been independently associated with myocardial necrosis.5,7 Pathologically, this form of myocardial injury is characterized by subendocardial contraction band necrosis, which is thought to result from excessive release of norepinephrine from the cardiac sympathetic nerves.4,5,7

Takotsubo cardiomyopathy, also known as transient left ventricular apical ballooning (LVAB) syndrome has recently been an increasingly recognized entity characterized by transient, virtually global LV dysfunction consisting of akinesia of the LV apex in response to sudden emotional or physical stress, predominantly in postmenopausal women as seen in our case.8–11 It is associated with minimal cardiac enzyme release and has characteristically normal coronary arteries on angiography in contrast to acute coronary syndromes (ACS).9,10 Recently, reports have emerged linking transient LVAB with SAH.13–16 With a unifying pathophysiology of excessive sympathetic discharge, transient LVAB may represent a variant of RWMA's associated with SAH.12–15

**Clinical Summary**
A previously healthy 64-year-old woman with no history of vascular disease was found unresponsive at home. She was taken to the emergency room where a CT head revealed an SAH due to a ruptured aneurysm of the posterior communicating artery. On admission, an ECG showed deeply inverted T waves and QT prolongation, typical of SAH (Figure 1). Cardiac troponin was measured at 1.2 ng/mL, and later increased to 3.7 ng/mL. A transthoracic echocardiogram (TTE) on the next day revealed a large LV wall abnormality,
characteristic of apical ballooning (Figure 2a) with an ejection fraction (EF) of 25% to 30%. The patient remained hemodynamically stable and was started on low dose β-blocker and ACE inhibitor. She had an uneventful cardiac recovery within 5 days at which time a repeat TTE revealed a normal EF with no wall motion abnormality (Figure 2b).

Discussion

A great deal of literature has been generated concerning left ventricular wall abnormalities associated with SAH, and the phenomenon of neurogenic stunned myocardium has been well documented.3–7 However, to the best of our knowledge, there have only been a handful of reports of true transient LVAB in patients with SAH.12–15 Also called Takotsubo cardiomyopathy, this syndrome was first described in 1991 in Japan16 and named Takotsubo-like LV dysfunction in reference to the associated LV morphological features consisting of akinesia predominately of the apex and midventricle with relative sparing of the basal segment, creating a highly characteristic configuration during systole8–11 (Figure 2a; Takotsubo is a pot with a round bottom and narrow neck used for trapping octopuses in Japan).9–16

Also called Human Stress Cardiomyopathy and Broken Heart Syndrome,9 this constellation of findings includes sudden onset of chest symptoms, ECG changes consistent with myocardial ischemia, characteristic transient LV dysfunction affecting the apical region and no significant coronary stenosis on angiography.

Although originally reported in Japan, it is increasingly being recognized in Europe and North America.10,11 Almost 90% of reported patients are female and only few were younger than 50 years of age.10,11 Important influences of female hormones on sympathetic neuromodulation, coronary vasoreactivity and postmenopausal alteration in endothelial function have been proposed as possible mechanisms.10,17

Transient LVAB usually masquerades an acute coronary syndrome with a preceding physical or emotional stressor.9 Most patients present with chest pain or dyspnea.10,11 The ECG at presentation shows ST-segment elevation or T-wave inversion, and pathological Q waves are present in almost 40% of patients. Furthermore, cardiac biomarker levels are frequently raised, mimicking acute MI, and LV function is impaired with regional wall-motion abnormalities. However, coronary angiography is normal in most patients and may show mild, nonobstructive coronary lesions (50% luminal diameter stenosis).9–11 Differentiating transient LVAB from acute MI is hence important, because misdiagnosis may result in treatment with thrombolytic agents and may pose patients at unnecessary risk of bleeding.10,11

Several possible etiologies have been proposed for transient LVAB. Because of its association with emotional or physical stress, catecholamine-mediated multivessel epicardial spasm, microvascular coronary spasm, or possible direct catecholamine-mediated myocyte injury have been advocated as possible pathophysiological mechanisms.9–11 Like neurogenic stunned myocardium, excessive catecholamine release

Figure 1. ECG showing deep T-wave inversions and prolonged QT interval; mild ST-segment elevation is also noted in V1–V2.
is thought by many to play a key role in LVAB in patients with SAH.\textsuperscript{12–15} This theory has also been supported by the association of transient LVAB with syndromes that involve excessive catecholamine release, such as pheochromocytomas.\textsuperscript{10,11} Furthermore, several studies have demonstrated that patients with transient LVAB often have a long wrap-around artery.\textsuperscript{19} Other studies have suggested that a temporary intraventricular gradient may be the cause of transient LVAB. These studies draw from the fact that an elevated intraventricular pressure gradient is often observed in patients with transient LVAB, and that this gradient typically resolves when LV function returns.\textsuperscript{20}

Furthermore, there is some evidence suggesting that the apical myocardium may be more responsive to sympathetic stimulation and may be more vulnerable to sudden catecholamine surges.\textsuperscript{21} A longitudinal, base-to-apex decline in LV myocardial perfusion, as described in patients with coronary risk factors, was also proposed as a possible alternative explanation.\textsuperscript{22}

The association of transient LVAB syndrome with SAH represents only a small fraction of the cardiac complications seen with SAH.\textsuperscript{12–15} A recent study by Banki et al\textsuperscript{7} found that in a cohort of 173 patients with SAH, 15\% had a left ventricular EF <50\% by echocardiography, whereas 13\% were found to have a RWMA. Of the RWMA\s, the majority involves the basal and middle ventricular portions of the anteroseptal and anterior walls; rarely is the apex involved. Furthermore, only 66\% of individuals with left ventricular dysfunction were found to have recovered their EF, whereas past studies have found that >80\% of individuals with transient LVAB syndrome have full or near-full recovery of their LV function within days to weeks of onset.\textsuperscript{11} The largest series of Takotsubo cardiomyopathy associated with SAH has been documented by Lee et al.\textsuperscript{15} They identified 8 patients meeting echocardiographic criteria for Takotsubo cardiomyopathy. All 8 patients were women with severe grade SAH. Takotsubo cardiomyopathy was associated with pulmonary edema, prolonged intubation and cerebral vasospasm. Transient LVAB syndrome, then, may represent a subsection of RWMA\s with apical akinesia and sparing of the basal segments called Takotsubo cardiomyopathy.

Patients with transient LVAB syndrome have generally a benign prognosis. Only 1.1\% of reported patients died during the hospitalization period and almost all surviving patients’ recovered fully.\textsuperscript{10,11} Whereas it carries a favorable prognosis generally, this pattern of cardiac dysfunction in SAH has been associated with increased overall morbidity.\textsuperscript{12–15} It may be reasonable to consider TTE in patients with SAH, ECG abnormalities and cardiac enzyme leak for risk stratification and adequate hemodynamic management. Additional studies are warranted to better elucidate the pathomechanisms of this entity.
Disclosures
None.

References
When the Worst Headache Becomes the Worst Heartache!
Abdul Hakeem, Adam D. Marks, Sabha Bhatti and Su Min Chang

Stroke. 2007;38:3292-3295; originally published online October 18, 2007; doi: 10.1161/STROKEAHA.107.483578
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/38/12/3292

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/