When the Worst Headache Becomes the Worst Heartache!

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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.4–7 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 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 ejec-
tion 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 refer-
cence 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 dys-
function affecting the apical region and no significant coro-
nary 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 tran-
sient LVAB. Because of its association with emotional or
physical stress, catecholamine-mediated multivessel epicar-
dial spasm, microvascular coronary spasm, or possible direct
catecholamine-mediated myocyte injury have been advocated
as possible pathophysiologic mechanisms.9–11 Like neuro-
genic 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.12–15 This theory has also been supported by the association of transient LVAB with syndromes that involve excessive catecholamine release, such as pheochromocytomas.10,11 Furthermore, several studies have demonstrated that patients with transient LVAB often have a long wrap-around artery.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.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.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.22

The association of transient LVAB syndrome with SAH represents only a small fraction of the cardiac complications seen with SAH.12–15 A recent study by Banki et al7 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 RWMAs, 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.11 The largest series of Takotsubo cardiomyopathy associated with SAH has been documented by Lee et al.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 RWMAs 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.10,11 Whereas it carries a favorable prognosis generally, this pattern of cardiac dysfunction in SAH has been associated with increased overall morbidity.12–15 It may be reasonable to consider Transthoracic echocardiography 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.

Figure 2. a, TTE showing apical ballooning during systole. Akinesis of the apical region with normokinesia of the base gives the characteristic apical ballooning or Takotsubo like appearance. b, Resolution to normal systolic function within 5 days. Note the uniform contraction of both the apex and the base during systole.

of catecholamine assays have varied widely, calling the causal relationship between catecholamines and transient LVAB into question.10,11 Another postulation is spontaneous multivessel epicardial spasm—with ergonovine or acetylcholine infusion, it was described in <30% of patients.11,18

Another etiologic theory holds that transient LVAB could be related to perfusion problems in a single coronary artery, specifically a long wrap-around left anterior descending artery that supplies not only the anterior LV wall but also the LV apex. Several studies have demonstrated that patients with transient LVAB often have a long wrap-around artery.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.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.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.22

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Disclosures
None.

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