Recognition of the Apical Ballooning Syndrome in the United States

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The apical ballooning syndrome is characterized by the abrupt onset of angina-like chest pain, ECG changes that typically demonstrate ST-segment elevation, diffuse T-wave inversions and abnormal QS-wave development, discrete wall motion abnormalities involving the lower anterior wall and apex on echocardiography or left ventriculography, and limited myocardial enzyme release relative to the extent of ventricular akinesia. The clinical presentation mimics acute myocardial infarction but always occurs in patients without evidence for hemodynamically significant coronary arterial stenoses by angiography. It was first described in the Japanese literature in 1991 by Dote and colleagues, who proposed the term “tako-tsubo” (Japanese for octopus trap) cardiomyopathy on the basis of the peculiar appearance of a rounded bottom and narrow neck on the end-systolic left ventriculogram. The clinical features and outcomes of the syndrome have been well characterized in Asian populations in studies by Kurisu et al (n=30 patients) and Abe et al (n=17 patients) and in an important multicenter observational study of 88 patients by Tsuchihashi et al. The “tako-tsubo” syndrome has been reported to account for 1% of admissions for suspected acute myocardial infarction in Japan during the past decade. A striking hallmark of the disease is its extremely rapid resolution after sudden onset despite markedly impaired ventricular systolic function. Its predilection for Japanese patients in the published literature initially suggested a unique geographical or racial distribution to the disorder. However, the apical ballooning syndrome has now been reported in white populations in Europe and the United States during the past 3 years.

The study by Sharkey and colleagues adds substantially to our knowledge of this unusual clinical syndrome by providing the largest and most comprehensive observational study of the apical ballooning syndrome in the United States. The authors collected a consecutive series of 22 patients who were prospectively identified in a community-based cardiology practice during a period of less than 36 months. Acute myocardial infarction or an acute coronary syndrome was suspected in each case on the basis of a clinical presentation of typical chest pain and ECG changes that demonstrated ST-segment elevation (13 patients), T-wave inversions in the anterolateral leads (5 patients), or serial evolution of T-wave inversions (3 patients). Conventional coronary risk factors such as smoking, hypertension, and hyperlipidemia did not differ from those in the general population. Serum troponin levels were mildly to moderately elevated, either at initial presentation or during the first 48 hours of hospitalization, in 82% of patients. All patients experienced a particularly stressful incident, either psychological or physical, within minutes to hours of onset of symptoms. Hemodynamic compromise requiring either vasopressor support or intra-aortic balloon counterpulsation occurred in more than one third of subjects. Despite the severity of hemodynamic compromise, including 1 patient who sustained a cardiac arrest, left ventricular systolic dysfunction and the associated marked apical regional wall motion abnormalities rapidly improved over a 7- to 30-day time period. All patients survived their index hospitalization and demonstrated normalization of resting left ventricular ejection fraction (mean initial left ventricular ejection fraction, 29±9% to 63±6%). The authors confirm key features of this unusual disease as reported in the Japanese literature, the most salient of which are the striking female predominance (100% in this series), convincing myocardial infarction mimicry despite the absence of fixed epicardial coronary artery disease, the pivotal role of intense psychological stress as a precipitating factor, and its rapid resolution. The study provides 2 new insights into this disease: first, cardiac MRI data are provided for the first time in all patients and help clarify potential pathophysiological mechanisms. MRI identified abnormal regional wall motion beyond any single vascular territory in 95% of patients. Gadolinium contrast enhancement failed to show...
evidence for increased myocardial edema; furthermore, delayed hyperenhancement indicative of myocardial infarction was absent in all but 1 patient, who demonstrated a small apical region of scar formation. Second was the important recognition that up to 10% of patients may experience a second recurrence of the disorder.

What mechanism(s) could account for these acute but rapidly reversible wall motion abnormalities? Coronary vasospasm may play a pathophysiological role in some cases: diffuse multivessel vasospasm was observed in a single patient in the present study and has been reported in up to 15% of reported Japanese patients when provocative testing was performed in the catheterization laboratory. Acute lymphocytic myocarditis may also mimic acute myocardial infarction, with ECG changes that extend beyond a single coronary arterial territory, marked segmental wall motion abnormalities that resolve rapidly, and mild-to-modest biomarker evidence for myocardial necrosis. However, the unique apical ballooning pattern of segmental dysfunction has not been described in biopsy-proven cases of myocarditis. Furthermore, endomyocardial biopsy, when performed in a limited number of cases, has uniformly failed to demonstrate histopathological evidence for myocarditis. Most convincingly, gadolinium-enhanced MRI in the present study failed to detect regional T2 enhancement, which has been convincingly shown to detect myocardial inflammation and necrosis in biopsy-proven lymphocytic myocarditis. Although microvascular ischemia is theoretically appealing, it has not yet been demonstrated in the limited number of physiological studies in this population that have used Doppler flow-wire measurements or contrast echocardiographic techniques. It is tempting to speculate that excessive sympathetic activation because of profound psychological or medical stress may be playing a key pathophysiological role. Transient regional left ventricular stunning has been well recognized during acute subarachnoid hemorrhage and the endocrine crisis of pheochromocytoma. Supporting this hypothesis, the distal left ventricular apical wall has been shown to be particularly vulnerable to a selective form of myocardial stunning in catecholamine-mediated toxicity. Unfortunately, the findings of normal or mildly elevated plasma norepinephrine levels and the absence of characteristic catecholamine-induced myocardial changes on endomyocardial biopsy argue against this hypothesis. However, it must be noted that each of these potential pathogenic mechanisms has been studied in a very limited number of patients; thus, a unifying mechanistic explanation is still lacking.

A number of unanswered questions persist regarding this reversible form of cardiomyopathy. (1) Why do middle-aged/elderly women appear particularly susceptible to this disorder? (2) Exactly how does profound psychological stress trigger its sudden onset? (3) Why is the left ventricular apex selectively vulnerable to regional ballooning? Several recent observations may provide at least a partial explanation. It is now recognized that several anatomic and physiological factors may contribute to disease localization. The left ventricular apex does not have the usual 3-layered myocardial structure that is present in other regions of the ventricle; the apex behaves as a border zone when myocardial blood flow is impaired, and the apical region appears to more easily lose its elasticity after excessive expansion. Perhaps most intriguing, fatty acid metabolism, as quantified by $^{123}$I $\beta$-iodophenyl-pentadecanoic acid ($^{123}$I-BMIPP) cardiac uptake, has been shown to be more severely impaired than myocardial perfusion as assessed by $^{201}$Tl imaging in the akinetic apical regions during the early phase of this syndrome and to gradually return to normal during the recovery phase. (4) Is this really a new disease with increasing incidence, or has it previously been unrecognized? The lack of any published description despite decades of left ventriculographic studies before the early 1990s suggests that it may be a relatively recent phenomenon. (5) Should pharmacological therapy as initiated during the acute phase of the disease, particularly $\beta$-adrenergic blockade and ACE inhibition, be continued indefinitely? Reports of several late recurrences raise the possibility that lifetime treatment with antiadrenergic and neurohormonal antagonists may be necessary. Finally, might these patients continue to have a subclinical form of cardiomyopathy? An increased risk of sudden death was recently reported among patients who had apparently completely recovered by echocardiographic criteria from tachycardia-induced cardiomyopathy. Whether ultrastructural abnormalities of the interstitial matrix or myocytes may persist and predispose these patients to the late development of systolic left ventricular dysfunction and/or sudden cardiac death will require long-term follow-up.

What is the clinical relevance of this uncommon syndrome in day-to-day practice? Although rarely encountered, the apical ballooning syndrome must now be considered by cardiologists and emergency department physicians in their differential diagnosis of the patient who presents with a suspected acute coronary syndrome or ST-segment elevation myocardial infarction. It should be considered especially when the extent of ischemic ECG abnormalities exceeds the biomarker evidence for myocardial necrosis and coronary angiography confirms noncritical atherosclerotic disease. Its prompt recognition and aggressive treatment with pharmacological agents and/or mechanical circulatory support are indicated, because complete recovery of systolic function and restoration of normal functional capacity can be expected for these patients by the time of hospital discharge. The most effective long-term management of this syndrome remains to be defined.

References


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