

Transient Left Ventricular Apical Ballooning Syndrome and Cardiac Dysfunction after Subarachnoid Hemorrhage: Similar Clinical Entities?

Giuseppe Andò*, Olimpia Trio and Cesare de Gregorio

Department of Medicine and Pharmacology, Cardiology Section, Policlinico "G. Martino", Messina University, Italy

Abstract: Universally accepted diagnostic criteria for transient left ventricular apical ballooning syndrome are not yet available and the cardiac dysfunction complicating subarachnoid hemorrhage drops several hints of discussion about the clinical and pathophysiological similarities with the "typical" transient left ventricular apical ballooning syndrome.

We suggest that, in the light of clinical and pathophysiological evidences, transient left ventricular apical ballooning syndrome should no longer be considered an exclusively "apical" myocardial abnormality and this diagnosis should not be excluded in patients experiencing acute brain injury and cerebrovascular events. Each kind of reversible cardiac dysfunction, mediated by the central nervous system and initiated by acute brain injury, both physical, like cerebrovascular accidents or head traumas, and psychical, like sudden emotional stress, should be encompassed in a unifying definition with the widest inclusion criteria, such as "Acute Ballooning Cardiomyopathy" (ABC), that is likely to be more representative of the real needs in the clinical setting.

INTRODUCTION

Takotsubo-like or transient left ventricular apical ballooning syndrome (TLVABS) is an increasingly reported acute cardiac syndrome. It predominantly occurs in postmenopausal women and is noteworthy for the absence of obstructive coronary artery disease (CAD) and the typical precipitation by intense psychological or emotional stress [1, 2]. Transient ST elevation or deep T-wave inversions are seen on the electrocardiogram (ECG), whereas the apical left ventricular (LV) ballooning is characteristically found on ventriculography or echocardiography [1, 2]. Despite the presence of myocardial damage expressed by the release of cardiac biomarkers, and the possibility of hemodynamic complications, almost all patients recover completely and wall motion normalizes within few weeks [1, 2].

Universally accepted diagnostic criteria for TLVABS are not yet available; the diagnosis is frequently made in the cardiac catheterization laboratory because the patients are referred for urgent coronary angiography, therefore, there is a general consensus that early coronary angiography is mandatory, since organic stenosis or acute plaque rupture with subsequent thrombosis have to be ruled out [1-3].

We recently observed two cases of transient LV dysfunction complicating subarachnoid hemorrhage (SAH) that dropped several hints of discussion about the clinical and pathophysiological similarities with the "typical" TLVABS.

THE CLINICAL PICTURE

Despite the fact that the neurological status is substantially different, from the cardiological standpoint patients with "typical" TLVABS are not likely to differ from those

with cardiac dysfunction complicating subarachnoid hemorrhage. According to the timing of clinical observation, ECG can show either mild ST-segment elevation or diffuse deep T-wave inversion with QT-interval prolongation; mild increases of cardiac troponins can be sampled. Transthoracic echocardiography can demonstrate LV wall motion abnormalities, often having the typical pattern of apical ballooning, and ejection fraction may be severely depressed. Potent antiplatelet agents are obviously contraindicated, and patients should be managed conservatively, unless hemodynamic compromise is present. If coronary angiography is performed during hospitalization, and it could be used simultaneously with diagnostic or interventional cerebral angiography, no atherosclerotic obstructive coronary disease is found, unless patients have either a high coronary risk profile or known coronary artery disease.

DISCUSSION

Pathophysiological Insights

A great body of literature about the cardiovascular complications of SAH has been generated. Evolving ECG changes, apparently consistent with myocardial ischemia, were classically reported almost five decades ago [4]; however, early autopsy-based studies showed that SAH-related ECG changes did not correlate with CAD or with gross myocardial damage [5]. Release of cardiac biomarkers, consistent with such damage and reversible LV wall motion abnormalities and systolic dysfunction, were later reported, not only in patients with SAH, but in all patients with cerebrovascular events and even in those with other forms of brain injury [6]. Importantly, in patients with ischemic stroke the ECG changes are often supposed to result from underlying CAD [7]; coronary angiography in patients with SAH, however, constantly demonstrates that LV dysfunction usually occurs in the absence of stenosis or obstructions [8].

Even though this phenomenon, generally known as neurogenic stunned myocardium [8], has been well documented,

*Address correspondence to this author at the Department of Medicine and Pharmacology, Cardiology Section, Policlinico "G. Martino", Messina University, Via Ugo Bassi 144, 98123 Messina, Italy; Tel: +39 090 2939471; Fax: +39 090 2923957; E-mail: giuseppe.ando@tiscali.it

its pathogenesis still remains controversial, although experimental data indicate that SAH results in catecholamine-mediated cardio-toxicity [9], and clinical and genetic human studies [10-12] have suggested that the cardiac dysfunction is probably due to the catecholamine surge accompanying SAH. Thus, SAH-related damage to discrete sites within cerebral cortex, hypothalamus and brainstem promotes a neuroendocrine and autonomic disequilibrium that leads, in turn, to both cardiac and other organ dysfunction [13]. Accordingly, cardiac injury after SAH should be regarded as a catecholamine-mediated event, likely predicted by the degree of neurological impairment [14].

In recent cohorts, cardiac complications have been reported in 39% to 63% of SAH patients and associated with adverse neurological outcomes [11]. Gender preference has not been well documented, yet female gender is an independent predictor for elevated troponin level after SAH [12] and neurogenic stunned myocardium after SAH shares with TLVABS the peculiar occurrence in postmenopausal women [1, 2]. Moreover, as in TLVABS, the LV dysfunctional region frequently centers around the apex and wall motion normalizes within few weeks after SAH [8]. Of note, isolated TLVABS generally carries a favorable prognosis [1, 2], whereas an increased overall morbidity has reported when TLVABS complicates SAH, but cerebral damage may play a key role in determining the outcome [14].

On the other hand, several possible etiologies have been proposed for TLVABS but, among all and especially because of its association with emotional or physical stress, excessive catecholamine release and direct myocyte injury have been advocated as the most plausible pathophysiological mechanisms, like in the setting of neurogenic stunned myocardium, provided the deleterious effect of an excess of catecholamines on the myocyte [15, 16]. This theory is also supported by the consistent association of TLVABS with humoral evidence of excessive catecholamine release [2, 15].

The Need of a Common Definition

Acute brain injury, including SAH, is considered a clear exclusion criterion from the mainstay of the TLVABS [3, 17]. In particular, the <<Mayo Criteria>> [1] rule out TLVABS syndrome in those patients with head trauma or intracranial bleeding, mainly because the distribution of wall-motion abnormalities in consecutive patients with different forms of brain injury varied significantly in the literature [18]. According to Others' [19] and our own clinical experience and because of the widely rising awareness of this syndrome, we strongly believe that the current diagnostic criteria needs an important revision.

It is noteworthy, indeed, that after the initial reports of the Takotsubo-like LV dysfunction syndrome in the Japanese population [20], new variants of ventricular ballooning have been described. The ballooning may spare the cardiac apex and affect different segments of the left ventricle [21] as well as the right ventricle [22]. Actually, the "typical" apical wall motion abnormality is seen in about two third of the patients [23]. We suggest, therefore, that TLVABS should no longer be regarded as an exclusively "apical" myocardial abnormality. Rather, it should be identified as a transient cardiac dysfunction with a pattern of wall motion abnormality consisting in a ventricular ballooning that pecu-

liarily extends beyond the distribution of a single epicardial coronary artery. Importantly, the term Takotsubo-like would then be used misleadingly, since the LV shape in systole would not necessarily resemble the typical Japanese octopus-trapping pot.

In the light of the experimental [7] and histological [24] similarities, of the clinical resemblance and, especially, of the reversibility [8], we are furthermore tempted to speculate that the cardiac dysfunction complicating SAH shares with TLVABS a similar pathogenesis as well and is not a different clinical entity. Therefore, acute brain injury should not be considered a differential diagnosis from TLVABS. It seems reasonable to consider SAH, due to its inherent catecholamines surge, as one of the possible stressors that typically precipitates TLVABS and, in turn, to consider TLVABS merely as one of the possible manifestations of the neurogenic stunned myocardium [7]. Moreover, each kind of reversible cardiac dysfunction mediated by the central nervous system and triggered by acute brain injury, both physical, like cerebrovascular accidents or head traumas, and psychological, like sudden emotional stress (even if due to a concurrent medical condition), should be encompassed in a unifying definition with the widest inclusion criteria.

Clinical Implications

Cardiologists should always consider TLVABS in the differential diagnosis of ECG changes and troponin leaks in patients with SAH. Importantly, it seems clinically unjustifiable to refer a patient for urgent coronary angiography in the first hours of SAH in order to exclude CAD, when the clinical course is typical of the neurogenic stunned myocardium and SAH is identified as the preceding stressful event. Nonetheless, unstable CAD has to be rule out because of its different management and prognostic implications. Making this differential diagnosis, especially outside the coronary care unit or the catheterization laboratory, would benefit physicians for a more suitable clinical approach to patients with multidisciplinary problems. It seems appropriate, therefore, to propose an early echocardiographic evaluation in all patients with SAH for the appropriate risk stratification and an adequate hemodynamic management. Yet, first of all, increased awareness of this intriguing clinical entity is mandatory.

CONCLUSIONS

Takotsubo-like syndrome or TLVABS should no longer be considered an exclusively "apical" myocardial abnormality and this diagnosis should not be excluded in patients experiencing acute brain injury and cerebrovascular events, including SAH. The term to identify this disease concept should, moreover, include both specific features and pathophysiological issues that, to the best of our knowledge, are still unresolved. The more generic definitions "stress-induced cardiomyopathy", or "neurogenic stunned myocardium", or simply "Acute Ballooning Cardiomyopathy" (ABC) may be more representative of the real needs in the clinical setting.

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Received: November 14, 2008

Revised: January 02, 2009

Accepted: January 02, 2009

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