

Afferent baroreflex failure and tako-tsubo cardiomyopathy

Lucy J. Norcliffe-Kaufmann · Harmony R. Reynolds

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Tako-tsubo is a Japanese fisherman's octopus trapping pot. The word has become popular to describe a type of cardiomyopathy in which the left ventricle of the heart transiently balloons at the apex and mid portions and, with a little imagination, looks like a tako-tsubo [1]. Variant forms of transient left ventricular dysfunction in which the apex is not affected have also been described [2]. Additional names for this clinical syndrome are transient left ventricular dysfunction syndrome, stress cardiomyopathy or apical ballooning cardiomyopathy. Patients present similarly to those with myocardial infarction, typically with chest pain and dyspnea and with findings on electrocardiography which are characteristic of myocardial infarction such as ST segment elevation and T wave inversion [3–5]. However, elevation of cardiac biomarkers such as troponin is modest and, in addition, the coronary arteries show no flow-limiting stenosis on conventional angiography [3]. Tako-tsubo cardiomyopathy resolves spontaneously and nearly all patients completely recover within a few weeks [6]. Thus, tako-tsubo cardiomyopathy may be considered to represent myocardial “stunning” rather than a permanent injury.

What is so special about this peculiar ballooning of the heart? First, it affects women much more often than men, and perhaps most intriguingly, it occurs frequently after a catastrophic emotional stress, such as an earthquake [7] or

the unexpected death of a close friend or relative [3, 4]. Of course, events that occur after emotionally charged situations are always suspected to be caused by high levels of catecholamines, both norepinephrine, the neurotransmitter of the sympathetic nervous system, and epinephrine, the hormone that classically increases with stress. Indeed, patients with tako-tsubo cardiomyopathy have a 30-fold increase in their plasma levels of norepinephrine and epinephrine, which is substantially higher than the increase seen in patients with acute myocardial infarction [4]. Moreover, cases of tako-tsubo cardiomyopathy have been reported following intravenous infusion of epinephrine [8] or norepinephrine [9] as well as in patients with pheochromocytoma who have endogenous catecholamine surges [10–12]. Furthermore, microscopic analysis of myocardium in patients with tako-tsubo syndrome may show contraction band necrosis and focal inflammatory infiltrates, as seen in syndromes of catecholamine excess [13]. Recently, analysis of endomyocardial biopsies taken from patients who have tako-tsubo cardiomyopathy has shown alteration in expression of the sarcoplasmic reticulum calcium ATPase and dephosphorylation of phospholamban, changes which suggest overstimulation of myocardial beta adrenoceptors in this syndrome [14].

In this issue of clinical autonomic research Berganzo et al. suggest a possible link between afferent baroreflex dysfunction and tako-tsubo cardiomyopathy. This is not surprising. Normally, increases in sympathetic activity are restrained by the baroreflexes, which are classic negative feedback loops. Afferent baroreflex dysfunction (also called baroreflex failure to distinguish it from autonomic efferent failure) is a neuro-visceral disorder that selectively affects the relay of afferent baroreceptor information from the carotid sinus and aortic arch to the nucleus tractus solitarius (NTS) in the brainstem [15–17]. In patients with

L. J. Norcliffe-Kaufmann (✉)
Department of Physiology and Neuroscience, New York
University School of Medicine, New York, NY, USA
e-mail: lucynorcliffe@gmail.com

H. R. Reynolds
Cardiovascular Clinical Research Center, Leon H. Chamey
Division of Cardiology, Department of Medicine, New York
University School of Medicine, New York, USA

afferent baroreflex failure, cortical arousal evokes unrestrained surges in circulating catecholamines accompanied by profound hypertension and tachycardia and frequently severe headaches and flushing [15–17].

The case reported by Berganzo et al. features a 37-year-old woman who developed palpitations and shortness of breath while jogging. On admission to the emergency room, she had electrocardiographic ST changes and modestly elevated cardiac enzymes. Echocardiogram showed global hypokinesis of the left ventricle and coronary angiogram revealed no evidence of coronary artery disease. An MRI of the brain revealed bilateral lesions in the dorso-mediolateral region of the medulla, involving the NTS, presumably the result of an acute disseminated encephalomyelitis associated with her *Mycoplasma pneumoniae* infection. Although the pattern of left ventricular dysfunction was atypical for transient left ventricular dysfunction syndrome due to lack of preservation of contractile function at the base of the heart; there was, however, full recovery of normal function is as typical in this disorder.

If indeed this was tako-tsubo cardiomyopathy, the triggering stress that increased sympathetic activity in this case was exercise, which in a patient with afferent baroreflex failure can be particularly dangerous. In addition to the so-called central command, a CNS mechanism that increases sympathetic activity during exercise, mechanical and metabolic stimuli from the contracting muscles evoke a reflex increase in muscle sympathetic outflow [18]. Information from the contracting muscle is conveyed to the brain via the spinal cord in afferent nerve fibers with cell bodies in the dorsal root ganglia. By taking this route, this information bypasses the classic afferent baroreflex pathways, and increases efferent sympathetic outflow without directly involving the NTS. This case highlights the dangers of exercising without the normal inhibitory loop. It is tempting to speculate that patients with tako-tsubo cardiomyopathy have a subtle abnormality in their afferent baroreflex pathways that makes them susceptible to catecholamine-induced myocardial stunning.

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