Broken heart syndrome
Síndrome do coração partido

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STRESS CARDIOMYOPATHY
With several other denominations such as: Broken Heart Syndrome, Apical Balooning Syndrome, Takotsubo Syndrome and Stress Cardiomyopathy, it represents a novel clinical entity characterized by an acute ventricular dysfunction that fully mimics acute myocardial infarction, including ST-T alterations, alterations of ventricular repolarization, enzyme alterations, and apical ballooning.

However, some peculiarities distinguish this syndrome from conventional infarction:
1. Normal coronary arteries
2. Rapidly reversible
3. Triggered by profound psychological stress (hours, exceptionally days)
4. Incidence among women, 95 to 100% at 25-80 years of age, mean age of 65 years.

First described by Dote et al.\(^1\) in Japan, 1991, who named the Tako-Tsubo syndrome because of the octopus-shaped appearance of the left ventricle (narrow neck and round base). Further, Tsuchihashi et al.\(^2\) collected 135 cases in the 1990’s, whose incidence represented 1% of the hospitalizations for suspected myocardial infarction. What drew attention was the sudden onset and fast resolution of the syndrome, and since it had been described in Japan it was initially considered a unique disease, geographically confined to Asians.

In the past four years, the syndrome has been demonstrated in the white population of Europe, as well as in the United States, and in Latin America, Brazil, more specifically.

From 1999 to 2003, Sharkey et al.\(^3\) published 22 consecutive cases of the syndrome, the largest series known in the United States, and Wittstein et al.\(^4\), from
Johns Hopkins, simultaneously published a series of 19 cases. These authors studied the syndrome from a neurohumoral standpoint, and using magnetic resonance imaging (MRI), electrocardiography, echocardiography, coronary angiography and ventriculography, and endomyocardial biopsy.

The syndrome is triggered 6 to 12 hours following profound emotional stress (unexpected death of a dear one, significant material losses, robbery, catastrophic medical diagnosis, and others), and the findings demonstrate an acute release of catecholamines, such as epinephrine, norepinephrine, and dopamine and its metabolites metanephrine, normetanephrine, neuropeptide Y stored with catecholamines in the synapses of sympathetic nerves and chromophilic cells of the adrenal which are released during stress, as well as the brain natriuretic peptide (BNP) and serotonin. This release would result from the activation of the adrenomedullary hormonal system and chromophilic system. The levels of these catecholamines in the syndrome are three-fold higher than the levels found in myocardial infarction, and seven-fold higher than placebo.

The mechanism through which the activation of these neurohumoral substances work in the heart, especially in the apical region, remains unknown. The hypothesis of epicardial coronary artery spasm was raised, but not confirmed. Microvascular spasm was an alternative considered, and had already been cited in the past. A possible explanation would be a direct local toxic action on myocytes producing what we call myocardial stunning.

High levels of catecholamines are known to reduce myocyte viability through cyclic AMP and calcium overload. Catecholamines are also known to be potential sources of free radicals, and in animal models they produce myocyte lesion. Stunning is understood as a situation where acute ischemia of any causes and not very prolonged does not produce necrosis but rather a transient ventricular dysfunction. It is important to report that in Sharkey et al. series, 37% of cases required hemodynamic support with vasopressor agents, including intraaortic balloon. In 95% of patients, MRI demonstrated contractility changes in several myocardial segments.

However, some questions on the syndrome remain to be answered:
1. Why does the syndrome affect middle-aged women?
2. How and why does profound psychological stress trigger the phenomenon?
3. Why is the apical region so vulnerable to ballooning?

Recent studies have attempted to explain the topographic preference for apical ballooning. The ventricle is known to be formed of three interlaced fiber bundles. However, the left ventricular apex would lack these three bundles. The apex would behave as a boundary area which would lose its elasticity if the vascular supply were affected, thus resulting in ballooning [figure 1].

Focal myocarditis was suggested, however myocardial biopsy ruled out this possibility. In only one case an area of necrosis was verified in biopsy.

Finally, the key question: is this syndrome a novel disease, or would it already exist without being recognized?

It is hard to admit this hypothesis because coronary angiography and ventriculography in the acute phase of myocardial infarction has been performed for more than 10 years.

Despite the absolute female preponderance of the syndrome, in all studies suggesting a biological susceptibility to stress leading to left ventricular dysfunction, the grounds for such predisposition remain unknown. Sexual hormones seem to have a significant influence on the sympathetic-neurohumoral axis, as well as on coronary vasoreactivity. Differences in the responses to catecholamine metabolism related to gender are very little known. For instance, men have higher baseline levels of sympathetic activity and higher plasma levels of catecholamines in response to emotional stress, and they are more sensitive to vasoconstriction. However, women seem to be more vulnerable to ventricular dysfunction, to sympathetic-induced stunning, as evidenced by the increase in catecholamine production, and left ventricular dysfunction following subarachnoid hemorrhage and/or brain trauma.

For the moment, what we should bear in mind is that although the syndrome is not very frequent, it does exist; and we should consider this possibility when we treat a female patient with acute stress.

According to some authors, recurrence is 10%, which would be a formal indication to maintain these patients on beta-blockers and converting enzyme inhibitors.

REFERENCES