

Bronchial asthma as a trigger of tako-tsubo-like cardiomyopathy in elderly women

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To the Editor

Tako-tsubo cardiomyopathy (TTC) is clinically characterized by acute onset of chest pain and/or dyspnea associated with ST-segment elevation or deep negative T waves, slight rise of myocardial injury biomarkers and apical or midventricular left ventricular ballooning in the absence of significant coronary artery lesions.^{1,2} The syndrome is prevalent in women, typically of postmenopausal age.² A typical feature of TTC is the occurrence of an emotionally or physically stressful event preceding the clinical syndrome. Among the stressors described, some case reports point out a possible role of acute asthma.^{3–6} Here we describe our experience in TTC, which seems to confirm a role of acute bronchial asthma as a trigger of the syndrome.

From January 2006 to December 2012, we observed 25 patients in whom the clinical, electrocardiographic, biohumoral and angiographic findings were consistent with the diagnosis of TTC. The mean age was 75 ± 16 years and 23 of them were women. Emotional stress preceded the disease in 14 cases. In one patient, TTC developed during acute anemia due to gastroenteric hemorrhage, in another after hip fracture and in four patients a true trigger could not be identified. In five patients (Table 1), all elderly women with a mean age 81 ± 9 years, the disease occurred during an episode of acute asthmatic bronchitis. In three out of five cases, asthmatic attack represented an exacerbation of chronic obstructive lung disease, whereas in the remaining two no signs or symptoms of chronic obstructive airway disease were previously present. On admission, all five patients were severely dyspneic, without chest pain. In all cases physical examination revealed severe bronchospasm. Electrocardiogram (ECG) showed anterior ST elevation in two cases and deep anterior negative T wave in three cases. The echocardiogram showed apical

akinesia/dyskinesia in all patients; in one patient with basal septal hypertrophy, a transient dynamic intraventricular obstruction due to systolic anterior movement of the anterior mitral leaflet was documented. Troponin was slightly increased in all the cases (mean peak value: 1.6 ± 0.86 ng/ml). Coronary angiography was performed in four out of five patients (one patient refused consent) and showed the absence of clinically significant coronary lesions, while ventriculography confirmed the presence of apical ballooning. Serial ECG recordings showed regression of ST elevation on admission, when present, and evidence of deep negative T waves and QT lengthening in all cases. The short-term outcome was good in all five cases.

In keeping with previous reports, our experience shows that asthmatic attacks with severe bronchospasm may precipitate TTC. It is therefore time to think about a possible pathophysiological link between the two diseases. The myocardial histological changes in TTC include, among others; a contraction band that typically reflects the consequences of high intracellular concentration of Ca^{2+} , as seen during catecholamine cardiotoxicity, in particular during epinephrine-induced toxicity.^{2,4} Furthermore, it is now proved that the mammalian left ventricle contains an apical–basal gradient of β -adrenergic receptors, with the apex characterized by the widest population of β -receptors (on which medulla-secreted epinephrine acts) and the lowest sympathetic nerve density.⁷ Thus, myocardial responsiveness to adrenergic stimulation during a massive release by the adrenal medulla (as during acute stress) is far more pronounced in the apex. Furthermore, a switch in cardiomyocyte intracellular signaling after a massive occupation of β -adreno-receptors, from Gs protein to Gi protein coupling, may occur, with impairment of contractility and possibly histologic changes.⁷ Usually, the trigger for massive adrenal medulla epinephrine release is a psychological or physical stressor. Histamine, a chemical mediator delivered during anaphylaxis and asthma, is also a main stimulus for epinephrine release, by a direct action on the adrenal medullary cells.⁸ In addition, during acute asthma, massive degranulation of mast-cells may occur, with delivery of negative inotropic factors, including α tumor necrosis factor and β interleukin-1.⁹ Moreover, during acute asthma serious impairment of blood gas balance, with

Table 1 Main clinical and instrumental findings of the case series

Case	1 (A.Q.)	2 (S.D.)	3 (D.D.M.)	4 (I.G.)	5 (V.R.)
Age	67	92	88	73	86
Sex	F	F	F	F	F
Emotional trigger	—	—	—	—	—
Symptoms at onset:					
Chest pain	—	—	—	—	—
Dyspnea with bronchospasm	+	+	+	+	+
Predominant aspect of ST-T changes at arrival:					
ST elevation	—	+	—	—	+
T wave inversion	+	—	+	+	—
ECG during in-hospital stay:					
T wave inversion	+	+	+	+	+
Long QT	+	+	+	+	+
Typical LV morphology at TTE	+	+	+	+	+
Peak of troponin (ng/ml)	1.10	1.32	2.05	1.90	1.63
Significant coronary artery disease	—	NA	—	—	—
Discharged alive	+	+	+	+	+

F, female; LV, left ventricular; NA, not available; TTE, transthoracic echocardiography.

hypoxia and/or hypercapnia, is frequent, and this may produce acute neuro-hormonal activation, with further catecholamine release.¹⁰ Finally, therapeutic use of β -mimetic drugs may further amplify the adrenergic ‘attack’ on the left ventricular apex. All our patients were elderly women with mean age older than the mean age reported in TTC series (perhaps the very low estrogen levels may enhance vulnerability to acute epinephrine hypersecretion during acute asthmatic bronchitis).

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