G108 Please, Don't Get Angry! Two Fatal Cases of Emotional Stress-Related Death in Left Ventricular Apical Ballooning Syndrome (Tako Tsubo Cardiomyopathy)

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The goal of this presentation is to present two cases of death due to Tako Tsubo cardiomyopathy. The growing interest of the scientific community in understanding physiopathology, still far from a complete definition and the amazing of videos presented, makes the presentation absolutely peculiar.

This presentation will impact the forensic science community by highlighting characteristics of syndrome and the importance of a complete postmortem examination in rare fatal cases. This presentation demonstrates the typical histological signs of catecholamine toxicity (CBN), but further studies are still needed for further in-depth knowledge of TTC and stress-related cardiac physiopathology. In particular structural alteration of the contractile and cytoskeletal proteins could also be investigated.

Tako-tsubo cardiomyopathy (TTC) is also known as stress-induced cardiomyopathy (SICMP) or left ventricular apical ballooning syndrome (LVABS), broken heart syndrome, and ampulla cardiomyopathy. It was first described in the early 1990s in Japan in which patients (generally postmenopausal women) complained of chest pain and dyspnea, mimicking a coronary arterial disease. The name of "tako-tsubo" cardiomyopathy is derived from a pot with a short neck and a round bottom used for octopus fishing in the Japanese sea, as this resembles the left ventriculogram during the acute phase of the disease. It is characterized by a transient akinesia of the apex and compensatory basal hyperkinesis, triggered by marked psychological or physiological stress in the absence of significant epicardial coronary artery disease. TTC has been recently classified as primary, acquired cardiomyopathy and diagnostic criteria have been proposed: reversible akinesis or dyskinesis of the left ventricular apical and midventricular segments, with apical ballooning extending beyond a single epicardial vascular territory, new ECG ST-segment or T-wave abnormalities mimicking AMI, absence of exclusion criteria, including obstructive coronary disease or angiographic evidence of acute coronary plaque rupture, recent significant head trauma, etc. Although precipitating stress is not always identifiable, the stressful trigger could be emotional or physical. Multivessel epicardial spasm, myocardial dysfunction triggered by excess of cathecolamine levels, microvascular coronary spasm or dysfunction and neurologically mediated myocardial stunning have been proposed to explain TTC. Generally the prognosis is good but complications including death have been reported with an extremely low mortality rates. Deaths in these cases generally occur as a consequence of fatal ventricular arrhythmia (VF) or cardiogenic shock due to stress- related sudden severe ventricular dysfunction. Two fatal cases of TTC will be presented.

Case 1: A 52-year-old woman complained of thoracic pain and dyspnea after a quarrel with colleagues at the workplace. She had complained of the same symptoms a few months prior. Clinical examination on ED showed moderate high BP (160/90); pulse (90 bpm) and oxygen saturation (96%) were normal. A 12 lead ECG registration was immediately performed showing ST segment reduction mimicking myocardial infarction. Cardiac markers were elevated on lab test (CK 220, troponin 5.173). A severe ventricular failure was observed on echocardiography (EF < 30%). Cardiac catheterization was unremarkable for coronary obstruction. TTC was suspected, and confirmed at ventriculogram, where a typical systolic dysfunction involving left ventricular apex was recorded. Beta-blocker therapy was introduced but few hours after charge on cardiology department, death suddenly occurred in spite of resuscitation maneuvers.

Case 2: A young 30-year-old suddenly collapsed after a violent altercation with colleagues at the workplace and immediately presented to the emergency department of the local hospital. ECG was performed, showing ventricular fibrillation. The patient died few minutes after presentation. One week before, the young man complained thoracic pain and a 12 lead ECG was performed, showing ST segment reduction mimicking myocardial infarction. A complete postmortem examination was performed few days after death, in both cases. External examination was unremarkable. Internal examination showed mild cerebral edema and heavy lungs presenting white foam on the main bronchi, in both cases. Hearts were fixed in formalin. Cardiac sizes were normal, with conical shape. Macroscopic study (cut in cross-section 3 mm intervals) of coronary arteries were unremarkable, in both cases. Histological examination revealed polyvisceral stasis, mild cerebral edema; massive pulmonary edema was also detected. The pathological myocardial picture included multiple foci of contraction band necrosis; a few areas of patch interstitial fibrosis were also detected. Cardiac microscopic study was completed by means of immunohistochemistry by means of beta2 adrenergic receptor antibodies, showing expression on myocyte membranes in both cases. Confocal laser 3D scans of myocytes was also performed. No signs of cell death (apoptosis) was detected (TUNEL). Dosage of catecholamines and their metabolites on a blood and urine samples was performed, showing high levels of catecholamines, metanephrine and vanillyl-mandelic acid. Toxicological examination was negative. Clinical data, autopsy findings, data collected from immunoistochemical and CLSM study of myocytes and laboratory

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analysis, led us to conclude that cardiogenic shock after intense emotional stress complicated by malignant arrhythmia (VF) in Tako- tsubo cardiomyopathy was the main cause of death in both cases.

This research demonstrates typical histological signs of catecholamine toxicity (CBN) but further studies are still needed for further in-depth knowledge of TTC and stress-related cardiac physiopathology. In particular, structural alteration of the contractile and cytoskeletal proteins could be also be investigated.

Tako Tsubo Cardiomyopathy, Emotional Stress-Related Death, Cathecolamine Toxicity

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