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SUDDEN CARDIAC DEATH
A CASE WITH TWO DISTINCT AND UNRELATED CAUSES

Abstract: Cardiovascular diseases are the most frequent causes of Sudden Death in the adult. The authors report the case of a 44-year-old man who died sudden and unexpectedly when driving from Lisbon to Coimbra. A forensic *postmortem* examination revealed not only hypertensive and ischemic cardiopathy but also hypersensitivity non-illicit drug-induced myocarditis, with morphological evidence of both mechanical and arrhythmic mechanisms leading to death. It highlights the relevance of histological examination in the investigation of sudden death and emphasizes the etiologic complexity underlying cardiac sudden, unexpected deaths.
Keywords: Sudden death; myocardial infarction; drug-induced myocarditis.

Introduction

Sudden Death is a worldwide important problem, not only due to its non-suspected nature, but also in virtue of the multiplicity of possible underlying causes. Cardiovascular disorders account for the highest rate (90%).[1]

Case report

The present case refers to a 44-year-old male with family history of diabetes mellitus and personal antecedents of systemic hypertension, who died suddenly when driving from Lisbon to Coimbra. He was found parked at the side of the motorway without evidence of trauma / accident. The family reported that lately he was living under a great professional stress, for what he used to take benzodiazepines and that he complained of a muscular / osteo-articular pain on the shoulder, for which he self-medicated with a non-steroid anti-inflammatory analgesic. Four month earlier, he had an episode of syncope, which he neglected.

Death circumstances required a forensic *postmortem* examination.

The autopsy presented minor alterations of the other organs, being the heart the target-diseaded organ. It weighed 600g; had concentric hypertrophy of the left ventricle, whose myocardium showed anomalous grey and bright foci; and the three

coronary arteries contained major occlusive atherosclerotic plaques, some complicated with thrombosis. Microscopic examination confirmed the aforementioned lesions and characterized them as myocardial hypertrophy, severe and complicated (with erosion, thrombosis and lumen occlusion from 50% to ≥75%) coronary atherosclerosis – type VI of the "American Heart Association" classification – (Figures 1, 2, 3), as well as acute myocardial infarction with an evolution of 7-10 days (that is, in the phase of late granulation tissue and recent, still cellular fibrotic scar tissue – Figure 4) in the setting of hypertensive and ischemic cardiopathy. Yet, microscopy also disclosed unexpected pathology, consisting in hypersensitivity myocarditis (since it presents interstitial œdema and eosinophils-rich inflammatory infiltrate, inducing focal myocardial fibers' necrosis or contraction bands – Figures 5, 6).

Toxicology was negative for alcohol and illicit drugs, but positive (within therapeutic concentrations) for benzodiazepines and metabolites – bromazepan, nordiazepan, diazepam –, as well as for the non-steroid anti-inflammatory analgesic ibuprofen (traces).

Discussion

Sudden Death is defined as a non-traumatic fatal event, occurring instantaneously or within one hour after the onset of complaints[2] and, if unwitnessed, when the deceased was in good health 24 hours before death happens.[3] The incidence of the underlying causes varies with age group[4], and if cardiac, coronary heart disease is the major cause in adults (60%).[1] Yet, other causes attain different ages in a more uniform way, like for example myocarditis.[5] The causes may act *per se* or in a combined manner, each contributing with its pathological share to the mechanism which will lead to the final outcome. Ultimately, the lethal mechanism is either mechanical, arrhythmic or both.[5] Death, in the case here reported, results of a combination between those two mechanisms. In one hand, they are underlain by hypertensive and ischemic cardiopathy – with its increased myocardial mass, scarring / remodeling areas and decreased coronary blood flow. On the other hand, there is the drug-induced hypersensitivity myocarditis – with its inflammatory / immunological alterations. Increased myocardial mass requires additional contraction effort and higher blood flow, leading to a mechanical burden. Scaring / remodeling areas may contribute to the mechanical burden due to its non-contractile nature, which creates an obstacle to the normal heart dynamics. Furthermore, this obstacle is also rhythmic, since the granulation / fibrotic tissue is not conductive. Atherothrombotic decreased coronary blood flow leads to further ischemia of an hypertrophic myocardium with already altered functional reserve, favoring mechanical and arrhythmic distress. Myocarditis inflammatory constituents comprise interstitial œdema and inflammatory cells. The former enlarges the myocardium interstitial compartment and compresses the muscle fibers, disturbing both mechanical and conduction function. The presence of inflammatory cells – lymphocytes, macrophages, plasma cells and eosinophils – not only further enlarges the interstitium and directly induce muscle fibers hypercontraction and/or focal myocyte destruction / necrosis, but also lead to indirect myocardial hypercontraction / destruction / necrosis due to the production and release of immunological reaction mediator factors, like for example cytokines, conditioning arrhythmic events and mechanical instability. Hypersensitivity

myocarditis occurred despite drug concentrations being therapeutic and/or in a trace amount. Evidence of ventricular arrhythmia is demonstrated by the contraction bands. In this case, arrhythmia is *cum materia*, meaning that it is caused by pathology with morphological lesions partially recognized on macroscopic examination of the heart and partially through histology.

Conclusions

This case (1) highlights the importance of systematic microscopic examination in the investigation of Sudden Death; (2) emphasizes the fact that multiple noxa may converge and contribute to the final event; and (3) shows the complexity of the interactions among potential causes of death and the challenge of knowing the real influence of each contribution. It also draws attention to the individual immunological answer to different drug concentrations, to the meaning and interpretation of the toxicological results and to their integration with the morphological lesions (4).

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