

Morphologic and molecular pathway of cushing syndrome cardiomyopathy

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Dear Sir,

With the present letter we would like to draw your attention to some major statements of the editorial by Vassiliadi DA and Tsagarakis S titled “Cardiac hypertrophy in Cushing’s syndrome: if not hypertension then what”, published recently in *Endocrine* (2017; 56:453–455).

Specifically, in their report, the authors declare that the mechanisms of human Cushing cardiomyopathy are still unknown. With this statement they miss two recent publications based on endomyocardial biopsy studies of patients affected by Cushing cardiomyopathy where both histologic and molecular investigations have been obtained [1, 2]. Here it is demonstrated in a small number of patients (eight patients with Cushing cardiomyopathy, before and after cortisol normalization) that the increased plasma cortisol levels affecting Cushing disease cause, through activation of FOXO (Forkhead box) transcription factor, a 28 times increase of atrogin 1 and ubiquitin. This mechanism promotes proteasome proteolysis and then myofibrilolysis and cell death. Reduction of myofibrillar content of myocardiocytes is, however, a reversible event, as documented by a control biopsy at 1 year from adrenalectomy and normalization of plasma cortisol levels. Indeed, myofibrilolysis cell area reduced from 61 to 22%, and was paralleled by recovery of cardiac dimension and function.

Clinical implications from these observations are that chronic administration of steroids because of hematologic, allergic or autoimmune diseases can be followed by a toxic

cardiomyopathy that, if recognized, can be potentially reverted by drug discontinuation.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

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