Expression of Peroxisome Proliferators Activated Receptor Gamma in the Heart Tissue of Patients with Arrhythmogenic Right Ventricular Cardiomyopathy.

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Peroxisome proliferators activated receptor gamma (PPARgamma) is a ligand-activated transcription factor of the nuclear receptor family which regulates cell proliferation, fat metabolism and inflammatory process [1,2]. Recently it has been reported that PPARgamma expressed in the heart tissue with various cardiac diseases [3,4]. Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a heart muscle disease of unknown etiology and may lead severe ventricular arrhythmia [5]. In this study, we investigated whether expression of PPARgamma is augmented in the heart tissue of ARVC.

Endomyocardial biopsy was performed in 12 patients (10 males and 2 females, mean age: 43.1) with ARVC. Three patients suspected to have cardiomyopathy but had no significant pathologic findings at biopsy were used as control subjects. The heart tissue specimens were fixed with 10% buffered formalin, embedded in paraffin and cut into 4 micrometer thick sections for histology and immunohistochemistry. Histological sections were stained with hematoxylin and eosin. Immunohistochemical staining was performed using monoclonal antibody for PPARgamma (Santa Cruz Biotechnology, CA, USA) in paraffin sections of the tissue. The EnVision detection system and DAB (diaminobenzidine) were used according to the manufacturer's protocol for immune complex detection.

Histopathological aspects of the heart tissue with the disease showed various degree of fibrosis and fatty replacement with degeneration and hypertrophy of cardiomyocytes (FIG.1, A,C). Immunonohistochemical staining for PPARgamma disclosed positive reactivity in the nuclei of some cardiomyocytes as well as fat cells and vascular smooth muscle cells (FIG.1, B,D). No positive immunoreactivity was detected in the control heart tissue.

In the present study, we first demonstrated by immunohistochemistry that expression of PPARgamma is augmented in the heart tissue of ARVC. Our results suggest that intrinsic increase of PPARgamma in the myocardium may be involved in the pathogenesis of this disease.

References

- [1] G. Chinetti, et al., Inflamm. Res. 49 (2000) 497.
- [2] M. Ricote, et al., J. Leukoc. Biol. 66 (1999) 733.
- [3] P.M. Barger and D.P. Kelly, Trends. Cardiovasc. Med. 10 (2000) 238.
- [4] M.R. Mehrabi, et al., Eur. J. Heart Fail. 5 (2003) 733.
- [5] C. Gemayel, et al., J. Am. Coll. Cardiol. 38 (2001) 1773.

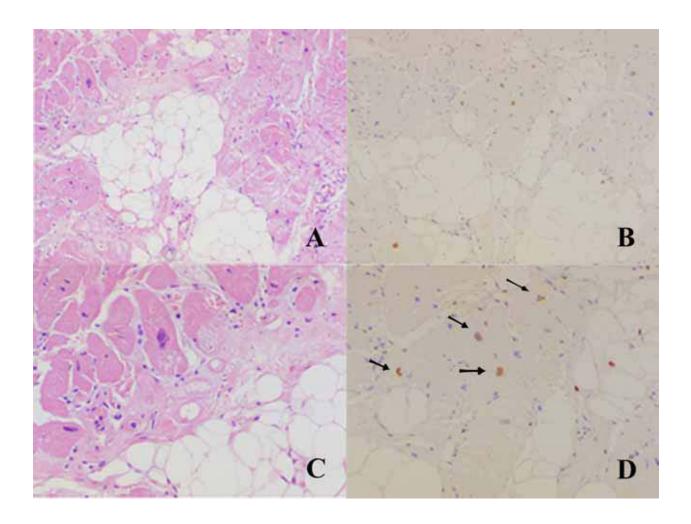


FIG.1 – Histopathological findings of endomyocardial biopsy from patients with arrhythmogenic right ventricular cardiomyopathy showing fibrosis and fatty replacement with degeneration and hypertrophy of cardiomyocytes (A:x100, C:x200). Immunohistochemical staining for peroxisome proliferators activated receptor gamma discloses distinctively positive in the nuclei of cardiomyocytes (arrows), fat cells and vascular smooth muscle cells (B:x100, D:x200).