Cardiomyocyte steatosis and defective washout of iodine-123-β-methyl iodophenyl-pentadecanoic acid in genetic deficiency of adipose triglyceride lipase

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Long-chain fatty acid (LCFA) is a major energy source for the heart. LCFA is taken up through CD36 and transported to mitochondria for β-oxidation to produce ATP. Therefore, in contrast to adipocytes where LCFA is stored as triglyceride (TG) in cytoplasmic lipid droplets, cardiomyocytes usually do not have lipid droplets.

We previously reported a novel phenotype called ‘Triglyceride deposit cardiomyovasculopathy’ (TGCV) in a cardiac transplant (CTx) recipient (Case 1). TGCV is characterized by the massive accumulation of TG in both myocardium and coronary arteries. Case 1 was homozygous for a rare genetic deficiency of adipose triglyceride lipase (ATGL) which is essential to hydrolyze intracellular TG to release LCFA as energy source.

The macro-, micro-, and electron microscopic examination of specimens from explanted heart at CTx and endomyocardial biopsy showed severe cardiomyocyte steatosis accompanied by severely vacuolar degeneration with lipid droplets in cytoplasm, suggesting impaired LCFA metabolism (Panels A–D). To evaluate LCFA metabolism in the heart, we performed myocardial scintigraphy with iodine-123-β-methyl iodophenyl-pentadecanoic acid (BMIPP), a radioactive analogue for LCFA, in other three patients with different ATGL mutations (see Supplementary material online, Table). Although Bull’s eye SPECT images varied between individuals, depending on severity of TGCV, BMIPP washout was defective in all cases (Panel E) (see Supplementary material online, figure).

Because BMIPP is incorporated into the TG pool in cardiomyocytes and oxidized for the decay, these observations indicate severe impairment of LCFA metabolism in TGCV. In addition, BMIPP may be useful to detect cardiomyocytes steatosis with abnormal LCFA metabolism.

Panels A and B. Gross examination of the explanted heart in Case 1 revealed excessive adipose tissue-like appearance of the epicardium (A) and myocardium (B). The line of demarcation between the epicardium and the myocardium was not well defined on cross section of the heart (arrow in B). The letters A, L, R, P denotes anterior, left, right and posterior, respectively.

Panels C and D. Numerous cardiomyocytes showed severely vacuolar degeneration with vesicular appearance (C) (Case 1) and were filled with lipid droplets in cytoplasm (arrows in D) (Case 3), which explains the above macroscopic appearance (A and B).

Panel E. Bull’s eye images for BMIPP scintigrams for Cases 3 and 4. Patients were injected with 123I-BMIPP and then scanned twice by myocardial SPECT using the same imaging settings. The first scan at 30 min after post-injection was obtained to determine early BMIPP uptake and the second scan after 4 h was taken to study delayed uptake. Washout rate was calculated between early and delayed images by Heart View software (Reference value 19.4 ± 3.2%).

Supplementary material is available at European Heart Journal online.

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