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Malfunction of endothelial progenitor cells and endothelial function in patients with Fabry disease


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Introduction:

Fabry disease is an X-linked lysosomal storage disorder caused by a deficiency of the enzyme alpha-galactosidase resulting in progressive intracellular accumulation of glycosphingolipids. Deposition of glycosphingolipids in the vascular system may lead to alterations in vascular function and endothelial progenitor cells (EPC).

Materials and Methods:

In patients with Fabry disease (n=23; 38.9±12.4 years) and in healthy age-matched controls (n=21; 40.8±8.9 years), vascular function was assessed by peripheral arterial tonometry (PAT) based on finger plethysmography. Vascular function was defined as the ratio of pulse wave amplitude (PWA) during reactive hyperemia relative to baseline. In addition, the duration of increased PWA until return to baseline levels was determined as an additional marker for vasodilatory capacity. The augmentation index was calculated by an automatized determination of the reflected pulse wave as a marker for arterial stiffness. Left ventricular wall thickness was assessed by echocardiography. Vasoregenerative capacity was estimated by investigating number and function of circulating EPC.

Results:

Patients with Fabry disease had an increased PAT hyperemia ratio (2.44±0.13 vs 1.96±0.1; p=0.008), whereas the duration of increased PWA during hyperemia was significantly reduced compared with healthy controls (222.4s±54.3s vs 300.5s±52.2s; p<0.01). Fabry patients had a significant increase in arterial stiffness with increasing age, whereas this was not observed in healthy controls. Duration of increased PWA was inversely correlated with increased left ventricular end-diastolic posterior wall thickness (standardized coefficient -0.58, p=0.029). In contrast, PAT hyperemia ratio, basic blood parameters, glomerular filtration rate, gender and age were not correlated with left ventricular hypertrophy. Finally, migratory potential of circulating EPC was impaired by 46±12% (p<0.05) in Fabry patients compared with healthy age-matched controls. Underlying molecular mechanisms and therapeutic options are currently investigated.
Discussion and Conclusions:

The present data point to an early pathologic involvement of the vascular system including impairment of the vasoregenerative reserve in Fabry disease. This was may aid our understanding of the progressive development of cardiovascular disease in patients with Fabry disease.