Population Genetics, Genetic Epidemiology, Statistics, Bioinformatics

AB050. Later onset Fabry disease, cardiac damage progress in silence-experience with a highly prevalent mutation

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Background: Recently, several studies revealed a much higher prevalence of later onset Fabry disease (FD) than previously expected. It suggested that later onset FD might present as an important hidden health issue in certain ethnic or demographic populations in the world. However, the natural history of its phenotype has not been systemically investigated, especially the cardiac involvement. The study analyzed a large-scale newborn screening program for FD to understand the natural course of later onset FD.

Methods: To date, 916,383 newborns have been screened for FD in Taiwan, including more than 1,200 individuals with the common, later onset IVS4 + 919G > A (IVS4) mutation. Echocardiography was performed in 620 adults with the IVS4 mutation to analyze the prevalence of left ventricular hypertrophy (LVH), and gadolinium-enhanced cardiac magnetic resonance imaging was performed in 129 patients with FD, including 100 IVS4 adults.

Results: LVH was observed in 67% of men and 32% of women older than 40 years. Imaging evidenced significant late gadolinium enhancement in 38.1% of IVS4 men and 16.7% of IVS4 women with the IVS4 mutation but without LVH. Seventeen patients underwent endomyocardial biopsies, which revealed significant globotriaosylceramide substrate accumulation in their cardiomyocytes.

Conclusions: Significant cardiomyocyte substrate accumulation in IVS4 patients led to severe and irreversible cardiac fibrosis before development of LVH or other significant cardiac manifestations. Thus, it might be too late to start enzyme replacement therapy after the occurrence of LVH or other significant cardiac manifestations in patients with later onset FD. This study also indicated the importance of newborn screening for early detection of the insidious, ongoing, irreversible cardiac damage in patients with later onset FD.

Keywords: Cardiac fibrosis; IVS4 + 919G > A; late gadolinium enhancement; newborn screening

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