Newborn Screening, Inborn Errors of Metabolism

AB077. Identification of lysosomal and extralysosomal globotriaosylceramide (Gb3) accumulation in endomyocardial biopsies before the occurrence of typical pathological changes of Fabry disease

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Background: Early initiation of enzyme replacement therapy (ERT) could be effective in stabilizing the progression of Fabry disease (FD), and potentially preventing irreversible organ damage. Certain late-onset cardiac FD treatment guidelines suggest performing an endomyocardial biopsy to confirm typical FD histopathological changes as a prerequisite for the initiation of ERT. However, the sensitivity of routine histological examinations for FD has neither been discussed nor investigated before. The objective of this study is to evaluate the sensitivity of routine histological examinations with immunofluorescence (IF) staining of endomyocardial biopsies in FD patients.

Methods: IF staining of globotriaosylceramide (Gb3) and lysosomal-associated membrane protein 1 (LAMP-1) was performed on endomyocardial biopsies of patients who were suspected of Fabry cardiomyopathy, yet had negative or only slight Gb3 accumulation determined by routine histological examinations (hematoxylin and eosin, H & E) staining, toluidine blue staining, and electron microscopy examination.

Results: The IF staining results revealed that all patients had abundant Gb3 accumulation in their cardiomyocytes, while extralysosomal Gb3 accumulation were found in some patients.

Conclusions: Current routine histopathological examinations for FD cardiac biopsies mainly focus on the existence of Gb3 inclusion bodies. However, before the formation of Gb3 inclusion bodies, significant Gb3 had already accumulated in the cardiac tissues. Moreover, the presence of significant extralysosomal Gb3 suggested the irreversible damages of cardiomyocytes might have occurred. We propose that Gb3 IF staining to be performed as a re-evaluation method when no typical FD pathological findings are observed in the biopsies of patients who are highly suspected to have Fabry cardiomyopathy.

Keywords: Fabry disease (FD); cardiomyopathy; globotriaosylceramide; immunofluorescent staining

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