

Fabry disease: Different clinical manifestations in two monozygous twin brothers

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Fabry disease is an X-linked inherited disorder that accumulates globotriaosylceramide (Gb3) in cells due to a deficiency of α -galactosidase A (α -GAL). It is caused by genetic mutations in the GLA gene located on the X chromosome. The skewed X-chromosome inactivation makes monozygotic twin sisters have heterozygous clinical manifestations, while almost all monozygous twin brothers manifested similar clinical expressions. We report a case of different clinical manifestations in monozygous twin brothers with Fabry disease. A 49-year-old man visited the hospital for proteinuria in April 2020. He was diagnosed with hypertension in 2006. The spot urine protein/Cr ratio (UPCR) was 799.7mg/g in 2019. Six months ago, his monozygous twin brother started hemodialysis due to renal failure of unknown cause. Laboratory findings were serum Cr 0.85mg/dL, MDRD eGFR 95.8/1.73m², UPCR 557.2mg/g, 24-h urine protein 815.4mg, 24-h urine albumin 591.2mg/g, and RBC 2-4/HPF. There were no autoimmune antibodies in serological tests. A renal biopsy was conducted. Light microscopy showed foamy cytoplasm of the endothelium of glomerular capillaries (Fig.1). Electronic microscopy identified diffuse foot process effacement and laminated lipid droplets in the glomerular epithelium, tubular epithelium and interstitium (Fig.2). Echocardiography presented left ventricular hypertrophy. The α -GAL decreased to 0.30 μ mol/h/L (normal range >2.35 μ mol/h/L), and lysoGb increased to 10.3ng/mL (normal range <1.74ng/mL). The genetic test identified a c656T>C mutation in GLA exon5, a likely pathogenic variant of Fabry disease. We diagnosed Fabry disease. Looking into his family together, the twin brother and younger sister had the same genetic abnormalities. The younger sister did not have any symptoms (Fig.3). After diagnosis, α -GAL 95mg was administered intravenously once every two weeks. A follow-up test after 6 months revealed lysoGb3 4.38ng/mL, α -GAL 1.36 μ mol/h/L, serum Cr 0.97mg/dL, UPCR 580.7mg/g, and no significant change in echocardiography. His Fabry disease is well controlled. Not only genetic mutations but also environmental or epigenetic factors possibly influence the clinical manifestations of Fabry disease.

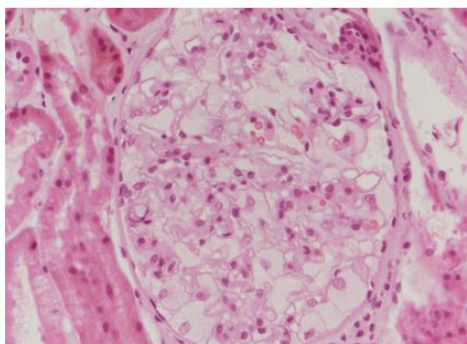


Fig. 1

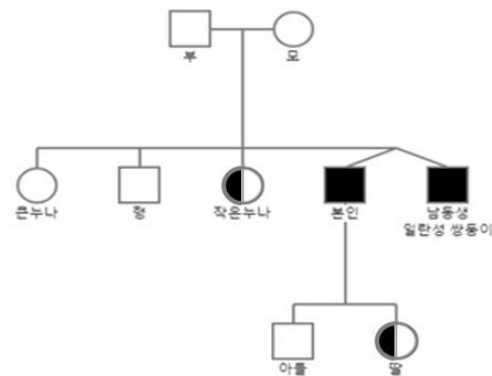


Fig. 3

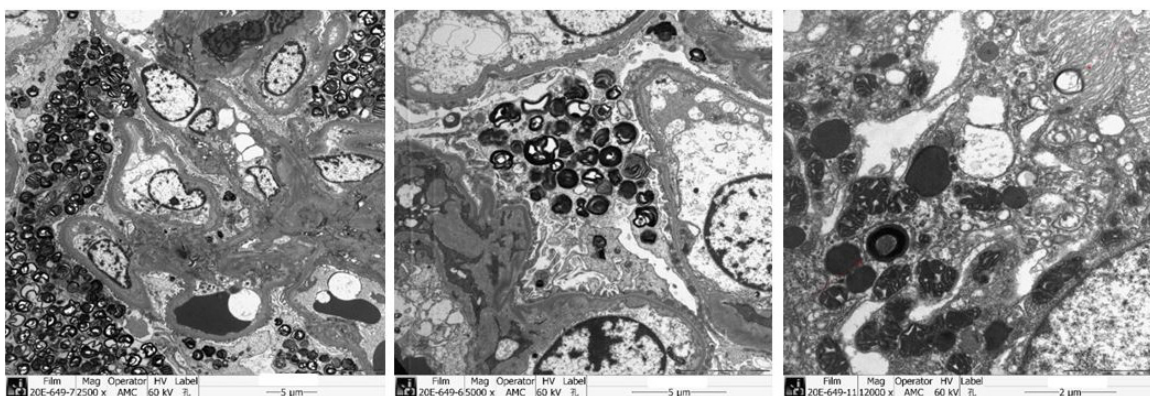


Fig. 2