Hypertensive encephalopathy and Multiple Ischemic Strokes as Initial Presentation of Fabry Disease

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Background Fabry disease (FD) is a rare X-linked lysosomal storage disorder disease with multiple organs involvements including central and peripheral nervous systems. It was caused by various mutations of GLA gene leading to deficiency in alpha-galactosidase. Acute stroke is one of manifestations of Fabry disease, even as only event before or after diagnosis. Fabry-specific manifestations, such as early stroke, progressive renal and cardiac failure, due to systemic cellular accumulation of globotriaosylceramide, may be partly avoided or delayed by early enzyme replacement therapy (ERT). However, correct diagnosis was often delayed up to 20 years. We reported a case of young male presenting malignant hypertension following by multiple stroke as initial manifestation of Fabry disease.

Case Report A previous healthy but heavy smoking 38-year-old man came to hospital because of gross hematuria for 2 days and extremely high blood pressure was recorded as 262/174 mmHg. He was transferred to emergency department (ED) where aortic dissection, DeBakey type II was revealed and then was admitted to intensive care unit right away. During ED stay, his neurological examinations were normal until 24h after admission. His consciousness deteriorated rapidly within hours and was intubated with mechanical ventilator. On examination, his Glasgow Coma Scale was E1V2M2 with quadriplegia, fixed doll's eyes and mid-dilated pupils but absence of light reflex bilaterally. The brain magnetic resonance imaging (MRI) revealed multiple scattered infarcts in bilateral cerebrum and right cerebellum, hemorrhage in right frontal and abnormal T2 FLAIR high signals involving brainstem, bilateral middle cerebellar peduncle & bilateral thalami, suggesting atypical presentation of posterior reversible encephalopathy syndrome (PRES) (Figure 1-AB and 2-AB). The electrocardiogram showed left ventricular hypertrophy (LVH) (Figure 3) and the echocardiography revealed the same findings, especially markedly increased left ventricular posterior wall thickness to be 21 mm (normal range 9-11 mm). His kidney function (BUN/Cr:58/5.5 mg/dL) was damaged from malignant hypertension as well. Few days later, his consciousness and muscle strength were improving after aggressive blood pressure control. But there were some neurological sequelae left such as paraparesis with increased muscle tone over limbs on discharge, 67 days after symptoms onset. He has become a man who was wheelchair-bound since then. In this admission, not only nervous system but kidney and heart were involved just like the manifestations of FD during later adulthood. No physician was aware of this possibility until 3.5 years after discharge while he was admitted to hospital again due to fever and shortness of breathe. The cardiologist found he had hypertrophic cardiomyopathy and checked the activity of alpha-galactosidase (GLA) by dry blood spots which showed reduced GLA activity. The genetic test confirmed missense mutation c. 1228A>G, p.T410A (figure 4), causing classic type FD. Enzyme replacement therapy (ERT) has been administered 2 months after confirmed FD but his kidney function deteriorated to end stage renal disease, requiring regular hemodialysis.

Figure 1-A,B

Figure 2-A, B

Figure 3. ECG showed marked LVH

Figure 4

One hemizygous missense mutation [c. 1228A>G, p.T410A] was found in exon 7 of GLA gene (pathogenic for Fabry Disease) and a [c.-10C>T] in 5'-UTR was also detected which may account for 15-20 % reduced enzymatic activity

Pedigree

Conclusion Cerebral manifestations of FD, such as acute stroke cause major disability and usually occur in younger patients with no vascular risk factors. The Neurologist always regards these strokes as cryptogenic. Since there is approved enzyme replacement therapy which may help, physicians should be aware of this scenario, especially in patients with other organ involvements such as LVH and chronic kidney disease. Screening for Fabry disease is warranted.