Fabry Disease Diagnosis in a Young Stroke Patient: A Case Report

Aslı AKSOY GÜNDOĞDU^{ID}, Dilcan KOTAN^{ID}, Murat ALEMDAR^{ID}, Zeynep ÖZÖZEN AYAS^{ID}

Neurology Department, Sakarya Training and Research Hospital, Sakarya, Turkey

We have observed a male patient with ischemic stroke, and diagnosed with Fabry disease. Here we would like to present a rare disease.

Fabry disease (FD) is a rare hereditary X-linked recessive inherited lysosomal storage disorder, caused by the mutations of α -galactosidase A (GLA) gene resulting in the deficient activity of the enzyme α -galactosidase A (α -Gal A). This pathology is responsible for the progressive neutral glycosphingolipid depositions in the lysosomes of the blood vessel walls throughout the body leading a multi-systemic disease (1). The incidence of FD is estimated at 1:40,000 in general population (2, 3). FD may cause various clinical manifestations. It is recognized that central and peripheral neurological complications are frequently seen in the course of FD, and stroke is often the first cause of hospitalization. The patients usually diagnosed late after the development of renal, cardiovascular and cerebrovascular complications that increase morbidity and mortality (1, 4). In this paper a young male FD patient who was admitted to our clinic with acute ischemic stroke attack was presented.

A 39-year-old man who presented with dysarthria and left hemihypoesthesia was evaluated. Brain magnetic resonance images (MRI) showed a left pontine infarct (Figure 1). Findings on carotid ultrasonography were normal. Electrocardiography showed sinus rhythm and echocardiography revealed left ventricular hypertrophic concentric cardiomyopathy (HCM) with an ejection fraction of 72%. Therefore, a cardioembolic origin was considered at first. A detailed family history revealed that his nephew (his sister's son) got diagnosed with FD. We learned that our patient has been experiencing typical clinical manifestations of the FD such as recurrent fever, neuropathic pain in distal extremities, painful acroparesthesias, intolerance to cold and heat, hypohidrosis, and gastrointestinal disturbances since age 7. He had no angiokeratomas or corneal symptoms. His α -Gal A activities were low (0.1 nmols/h/mL; nv >1.2), and GLA gene study revealed (c.[680G >A] (p.[R227Q])) a previously identified missense mutation with dried blood spot (DBS) method, then FD was diagnosed. He was discharged without any neurological symptoms. However, 3 months later a chronic kidney disease developed. He showed proteinuria in urine analysis, and

Figure 1a,b. Brain MRI revealed a hyperintense lesion in left side of the pons in the axial (a) and sagittal (b) T2 weighted images

Cite this article as: Aksoy Gündoğdu A, Kotan D, Alemdar M, Özözen Ayas Z. Fabry Disease Diagnosis in a Young Stroke Patient: A Case Report. Arch Neuropsychiatry 2018;55:291-292. https://doi.org/10.5152/npa.2017.19189

serum urea was elevated (270 mg/dL). Hence the patient was referred to the department of nephrology, and administered enzyme replacement therapy (ERT) with agalsidase- β . Recently, by age 43, he has been receiving ERT for one year. He has not developed another stroke attack but renal status progressed to end-stage requiring hemodialysis.

Cerebrovascular diseases are one the major manifestations of FD, and the patients commonly experience a stroke attack before the diagnosis (5, 6). In young males (age 25–44) the frequency of stroke may occur up to 12 times more frequent compared to general population. FD is also associated with white matter lesions, and vertebrobasilar artery dolichoectasia (7, 8).

In classical form of FD with deficient activity of α -galactosidase A, acroparesthesias, angiokeratomas, hypohidrosis, hearing loss, and corneal dystrophy are presented in early childhood. Due to the progressive lysosomal lipid accumulation in the vascular endothelium, renal failure, cardiac or cerebrovascular disease occurs in adulthood (9). HCM is one of the cardiovascular risk factor for stroke (10, 11). FD may cause arrhythmias, valvular heart disease and HCM. Thus a FD patient may also develop a cardioembolic stroke (6). Further investigation for FD must be performed especially in cases with combination of cerebral stroke in the vertebrobasilar artery system and proteinuria (12).

Despite the presence of a cardiovascular risk factor for stroke, our paper demonstrates the value of taking a proper medical treatment and family history while evaluating a young stroke patient. Early diagnose of the disease is important for treatment with ERT.

Peer-review: Externally peer-reviewed.

Informed Consent: Written informed consent was obtained from the patient for publication of this report and any accompanying images.

Author Contributions: Concept - AAG; Design - AAG; Supervision - DK; Resource - MA, Materials - ZÖA; Data Collection and/ or Processing - AAG; Analysis and/or Interpretation - MA; Literature Search - ZÖA; Writing - AAG; Critical Reviews - DK.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

- Desnick RJ, Ioannou YA, Eng CM. α -Galactosidase A deficiency: Fabry disease. In: Scriver CR, Beaudet AL, Sly WS, Valle D, editors. *The Metabolic and Molecular Basis of Inherited Disease*, 8th ed. New York: McGraw-Hill; 2001. pp.3733–3774.
- Spada M, Pagliardini S, Yasuda M, Tükel T, Thiagarajan G, Sakuraba H, Ponzzone A, Desnick RJ. High incidence of later-onset fabry disease revealed by newborn screening. *Am J Hum Genet* 2006;79:31–40. [\[CrossRef\]](#)
- Hwu WL, Chien YH, Lee NC, Chiang SC, Dobrovolsky R, Huang AC, Yeh HY, Chao MC, Lin SJ, Kitagawa T, Desnick RJ, Hsu LW. Newborn screening for Fabry disease in Taiwan reveals a high incidence of the later-onset GLA mutation c.936+919G>A (IVS4+919G>A). *Hum Mutat* 2009;30:1397–1405. [\[CrossRef\]](#)
- Mehta A, Ricci R, Widmer U, Dehout F, Garcia de Lorenzo A, Kampmann C, Linhart A, Sunder-Plassmann G, Ries M, Beck M. Fabry disease defined: baseline clinical manifestations of 366 patients in the Fabry Outcome Survey. *Eur J Clin Invest* 2004;34:236–242. [\[CrossRef\]](#)
- Møller AT, Jensen TS. Neurological manifestations in Fabry's disease. *Nat Clin Pract Neurol* 2007;3:95–106. [\[CrossRef\]](#)
- Sims K, Politei J, Banikazemi M, Lee P. Stroke in Fabry disease frequently occurs before diagnosis and in the absence of other clinical events: natural history data from the Fabry Registry. *Stroke* 2009;40:788–794. [\[CrossRef\]](#)
- Politei J, Schenone AB, Burlina A, Blanco M, Lescano S, Szlago M, Cabrera G. Vertebrobasilar dolichoectasia in Fabry Disease: the earliest marker of neurovascular involvement? *J Inborn Errors Metab Screening* 2014;2. [\[CrossRef\]](#)
- Fellgiebel A, Müller MJ, Ginsberg L. CNS manifestations of Fabry's disease. *Lancet Neurol* 2006;5:791–795. [\[CrossRef\]](#)
- Mehta A, Hughes DA. Fabry Disease 2002 Aug 5 [Updated 2013 Oct 17]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2018. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK1292/>
- Maron BJ, Olivetto I, Bellone P, Conte MR, Cecchi F, Flygenring BP, Casey SA, Gohman TE, Bongioanni S, Spirito P. Clinical profile of stroke in 900 patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002;39:301–7.
- Nishimura K, Uehara T, Ishibashi-Ueda H, Anzai T, Toyoda K. Cardioembolic stroke in the cardiac variant of Fabry disease. *Neurol Clin Neurosci* 2015;3:78–80. [\[CrossRef\]](#)
- Röls A, Böttcher T, Zschiesche M, Morris P, Winchester B, Bauer P, Walter U, Mix E, Löhr M, Harzer K, Strauss U, Pahnke J, Grossmann A, Benecke R. Prevalence of Fabry disease in patients with cryptogenic stroke: a prospective study. *Lancet* 2005;366:1794–1796. [\[CrossRef\]](#)