Fabry disease with acute cerebral infarction onset in a young patient

Ya-Nan Zhang[1], Zhen-Ni Guo[2], Hong-Wei Zhou[3], Ying-Ying Cheng[1], Jia-Chun Feng[1], Zan Wang[1]

[1]Department of Neurology, The First Norman Bethune Hospital of Jilin University, Changchun, Jilin 130021, China;
[2]Clinical Trial and Research Center for Stroke, The First Norman Bethune Hospital of Jilin University, Changchun, Jilin 130021, China;
[3]Department of Radiology, The First Norman Bethune Hospital of Jilin University, Changchun, Jilin 130021, China.

To the Editor: Fabry disease (FD) is a recessive X-linked hereditary disease. The onset age of the disease is in children and adolescents mostly. The average time from the onset of symptoms to the definite diagnosis needs 13.7 years in male patients and 16.3 years in female patients. FD happens rarely and it is easy to cause diagnosis and treatment delay. Here, we report a case of FD in a 27-year-old man who developed clinical symptoms with acute cerebral infarction onset to improve doctors' understanding of FD.

A 27-year-old man presented with 6 days of double vision. He had headache occasionally and had no nausea, no vomiting, no vertigo, no dysarthria, and no movement disorder in the course of the disease. He has a history of smoking, intermittent diarrhea, and allergic rhinitis. The patient's vital signs were temperature 36.5°C, blood pressure: 118/85 mmHg, heart rate 67 beats/min, respirations 18 breaths/min. He has a normal neurologic examination except diplaopia. His family history revealed no neurologic disorders. Magnetic resonance imaging (MRI) showed a long T2 signal in the left cerebral peduncles [Figure 1A]. Magnetic resonance angiography (MRA) showed normal anterior-posterior-circulation arteries [Figure 1B]. Three-dimensional volumetric isotropic turbo spin echo acquisition (3D-VISTA) showed the arterial wall thickening of bilateral vertebral artery, basilar artery, and bilateral posterior cerebral artery [Figure 1C and 1D]. No abnormalities of both kidneys and ureters were found in urinary ultrasound. Serum homocysteine was 44.70 μmol/L (normal: 0–20 μmol/L) and folic acid was 1.80 ng/mL (normal: 3.1–19.9 ng/mL). The high-sensitivity C-reactive protein was 11 mg/L (0–3.5 mg/L), the erythrocyte sedimentation rate was 70 mm/1 h (normal: 0–15 mm/1 h), and the nuclear antibody test was granule 1:100 positive. Lumbar puncture examination: the cranial pressure was 240 mmH_2O (normal: 80–180 mmH_2O), routine examination of cerebrospinal fluid: protein 0.67 g/L (normal: 0.15–0.45 g/L), glucose 2.05 mmol/L (normal: 2.3–4.1 mmol/L), leukocytes 23×10^6/L (normal: [0–8] $\times$ 10^6/L), cerebrospinal fluid immunoglobulin IgG 68 mg/L (normal: 0–34 mg/L). Cytology: white blood cell count 27×10^6/L, 63% lymphocytes, 31% neutrophils, 6% monocytes. GQ1b antibody (blood + cerebrospinal fluid): negative, Aquaporin 4 (AQP4) (blood + cerebrospinal fluid): negative; myelin basic protein (cerebrospinal fluid): 2.88 (normal: <0.55), urine routine examination: urine protein (PRO) 3+. Twenty-four hours urine alpha1 microglobulin 29.32 mg/24 h (normal: <24 mg/24 h), 24 hours urine IgG 106.80 mg/24 h (normal: 0–17.0 mg/24 h), 24 hours urine LAM light chain 22.68 mg/24 h (normal: <7.8 mg/24 h), 24 hours urine KAP light chain 40.40 mg/24 h (normal: <14.2 mg/24 h), 24 hours urinary protein quantification 3.44 g/24 h (normal: <0.2 g/24 h), 24 hours urine microalbumin 2492 mg/24 h (normal: 0–60 mg/24 h). Re-examination of the lumbar puncture: cranial pressure 150 mmHg, routine examination of cerebrospinal fluid: protein 0.57 g/L, glucose 2.30 mmol/L, leukocytes 10×10^6/L, cerebrospinal fluid immunoglobulin IgG 55.8 mg/L. Cytology: a small amount of lymphocytes and red blood cells were observed, and no abnormal cells were observed. Renal biopsy results of light microscopy: 23 glomeruli were seen in the puncture kidney tissue, 10 of which were sclerotic, and the other glomerular mesangial cells and mesangial matrix were diffusely hyperplastic mildly, nodular hyperplasia was mildly aggravated, and diffuse podocytes were observed, swollen with marked vacuolar degeneration, and foamy appearance [Figure 2]. Renal tubular epithelial cells showed vacuolar degeneration, multifocal epithelial cells were foamy, tubular renal tubular atrophy, renal interstitial focal lymphoid, and macrophage infiltration with mild fibrosis. Vascular degeneration is occasionally seen in the walls of small arteries. Immunofluorescence: electron microscopy results of this patient found 3 glomeruli were detected. IgA(−) IgM(−) IgG(−) C3(−) C4(−) C1q(−) F(−), capillary vascular endothelial cells were significantly devitrified, and red blood cells were seen in individual lumens. The parietal cells were vacuolar degenerated and no obvious hyperplasia. Epithelial cells are swollen, vacuolar degeneration, foamy, and secondary

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000000089

Correspondence to: Dr. Zan Wang, Department of Neurology, The First Norman Bethune Hospital of Jilin University, Changchun, Jilin 130021, China
E-Mail: wangzanprof@163.com

Chinese Medical Journal 2019;132(4)

Received: 06-12-2018 **Edited by:** Li-Min Chen

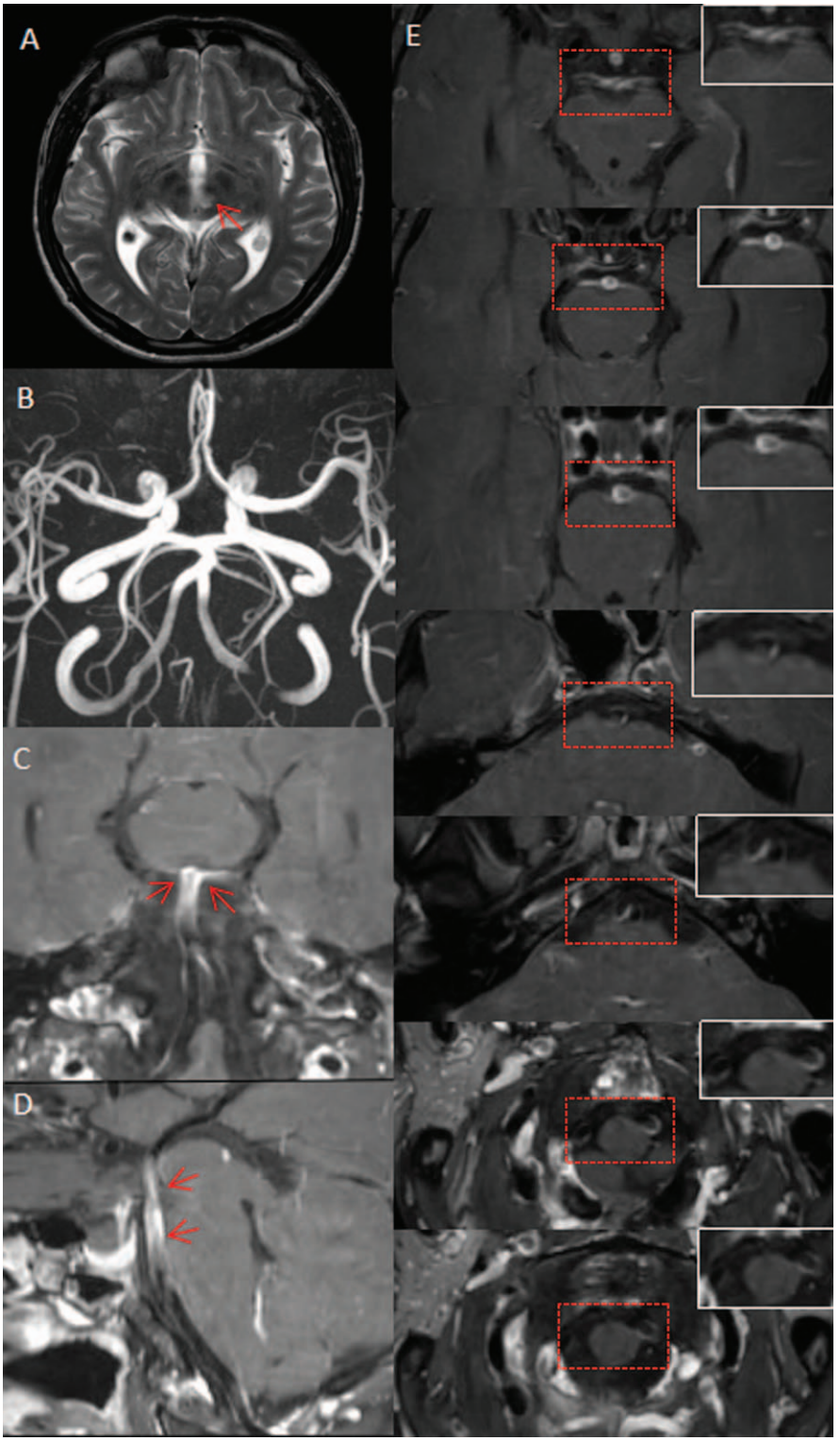

Figure 1: The magnetic resonance imaging of this Fabry disease patient. (A) MRI shows a long T2 signal in the left cerebral peduncles. (B) MRA shows normal anterior- and posteriorcirculation arteries. (C) Coronal scanning of 3D-VISTA shows the obvious arterial wall thickening of bilateral vertebral artery, basilar artery and bilateral posterior cerebral artery. (D) Sagittal scanning of 3D-VISTA. E, Axial scanning of3D-VISTA.

lysosomes are increased and a large number of myeloid bodies and zebrasomes are seen. Tubular-mesenchymal: vacuolar degeneration of tubular epithelial cells. Renal interstitial blood vessels: red blood cells seen in the lumen of individual capillaries, consistent with FD nephropathy. The genetic testing showed the c.426C>A (p.Cys142Ter) variant in the alpha-galactosidase A gene, which has been reported to be a causative mutation of FD.

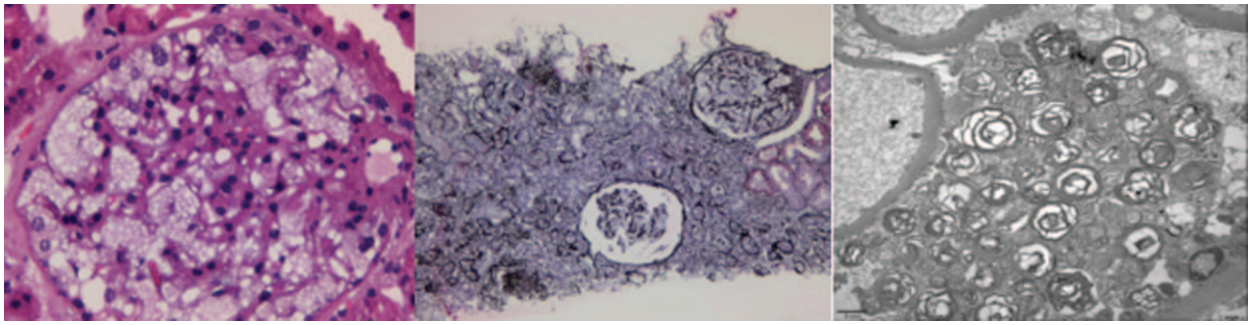

Figure 2: Kidney pathological manifestations of FD patient under light and electronic microscopes: Kidney light microscopy: glomerular diffuse podocyte swelling with vacuolar degeneration and foamy appearance markedly (HE×400). Focal tubular atrophy, renal interstitial focal lymphoid, macrophage infiltration with mild fibrosis (PASM ×200). Kidney electron microscope: swelling, vacuolar degeneration, foamy, secondary lysosomes increased and see a large number of myeloid bodies and zebrasomes.

The FD, also known as Anderson FD, was named after Johann Fabry and William Anderson, which belongs to the recessive X-linked genetic disease. The pathologic accumulation of the metabolic substrate of α-GalA-globotriaosylceramide (Gb3) in kidney cells, blood vessel walls and nervous system cells, which in turn causes multiple organs and systems damage,[1] such as stroke, renal insufficiency, cardiovascular injury, cutaneous keratoderma, and other multisystem clinical symptoms, is a lysosomal storage disease.[2]

Over 50% of male patients with FD and about 20% of female patients develop renal disease.[3] Proteinuria is an important indicator of renal damage in FD. The most common central nervous system damage was transient ischemic attack and ischemic stroke.[4] The incidence of stroke in patients with FD from 25 to 44 years old is 12 times higher than that of the general population.[5-7] The average onset age of is about 40 years old.[8]

This case is a young male patient, mainly characterized by cerebral infarction and proteinuria without obvious family history. The possibility of vasculitis should be considered when a stroke occurs in a young patient. High-resolution MRI vascular wall imaging achieved imaging of the arterial wall, and provided an important basis for the diagnosis of the disease. Pathologic examination and genetic testing should be performed in time for the patients suspected of FD to avoid delaying FD diagnosis. The therapy involves the substitution of recombinant α-galactosidase A as well as individual treatment of the symptoms. This patient was treated symptomatically, the symptoms of diplopia were slightly improved and discharged.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Conflicts of interest

None.

References

1. Blaydon D, Hill J, Winchester B. Fabry disease: 20 novel GLA mutations in 35 families. Hum Mutat 2001;18:459. doi:10.1002/humu.1219.
2. Brady RO, Schifftnann R. Clinical features of and recent advances in therapy for Fabry disease. JAMA 2000;284:2771–2775. doi:10.1001/jama.284.21.2771.
3. Germain DP. Fabry disease. Orphanet J Rare Dis 2010;5:30. doi: 10.1186/1750-1172-5-30.
4. Sims K, Politei J, Banikazemi M, *et al*. 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. doi: 10.1161/STROKEAHA.108.526293.
5. Lidove O, Chauveheid MP, Caillaud C, *et al*. Aseptic meningitis and ischaemic stroke in Fabry disease. Int J Clin Pract 2009;63:1663–1667. doi: 10.1111/j.1742-1241.2009.02115.x.
6. Dubuc V, Moore DF, Cioia LC, *et al*. Prevalence of Fabry disease in young patients with cryptogenic ischemic stroke. J Stroke Cerebrovasc Dis 2013;22:1288–1292. doi:10.1016/j.jstrokecerebrovasdis.2012.10.005.
7. Mitsias P, Levine SR. Cerebrovascular complications of Fabry's disease. Ann Neurol 1996;40:8–17. doi: 10.1002/ana.410400105.
8. Saposnik G, Lanthier S, Mamdani M, *et al*. Fabry's disease: a prospective multicenter cohort study in young adults with cryptogenic stroke. Int J Stroke 2012;7:265X73. doi: 10.1111/j.1747-4949.2011.00734.x.

How to cite this article: Zhang YN, Guo ZN, Z HW, C YY, Feng JC, Wang Z. Fabry disease with acute cerebral infarction onset in a young patient. Chin Med J 2019;132:477–479. doi: 10.1097/CM9.0000000000000089