Fabry disease

Fabry disease is a X linked recessive inheritance, caused by a deficiency of the lysosomal enzyme alpha-galactosidase A which results in the accumulation of the glycosphingolipid, ceramide trihexose in the vascular endothelium and can lead to cerebral infarction. Male hemizygotes are generally more severely affected than heterozygote females. Clinical disease in females is thought to be due to unequal X chromosome inactivation.

Inherited causes of stroke such as Fabry's disease should be considered in young patients with stroke if an etiologic diagnosis is not reached after complete investigations. Muscle biopsy can assist with the diagnosis and guide further investigations [1].

Cardiac involvement determines outcomes; therefore, detecting early changes is important. Native T1 by cardiovascular magnetic resonance is low, reflecting sphingolipid storage.

There is a detectable prehypertrophic phenotype in FD consisting of storage (low native T1), structural, functional, and ECG changes [2].

Data suggest that myocyte storage starts in childhood and accumulates faster in men before triggering 2 processes: a sex-independent scar/inflammation regional response (LGE) and, in men, apparent myocyte hypertrophy diluting the T1 lowering of sphingolipid [3].

Enzyme-based screening methods are not suitable for female patients.

Totally, 1,000 young stroke patients (18-55 y/o, 661 with ischemic stroke and 339 with hypertensive intracerebral hemorrhage) were recruited. Sequenom iPLEX assay was used to detect 26 Fabry related mutation genes. The frequency of Fabry disease in young stroke was reviewed and compared between Asian and non-Asian countries.

Two male patients with ischemic stroke were found to have genetic mutation of IVS4+919G>A. There was no α-galactosidase A (GLA) gene mutation in female patients. The frequency in Asian stroke patients was 0.62% (male vs. female= 0.63% vs. 0.58%) with 0.72% for ischemic stroke and none for hemorrhagic stroke, compared to 0.88% (0.77% vs. 1.08%) with 0.83% for ischemic stroke and 1.40% for hemorrhagic stroke reported in Western countries.

IVS4+919G>A is the GLA mutation in Taiwanese young ischemic stroke patients. Fabry disease is more frequent among non-Asian patients compared to Asian patients.Fabry disease is a X-linked disease, and enzyme-based screening methods are not suitable for female patients.

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Giacomini PS, Shannon PT, Clarke JT, Jaigobin C. Fabry's disease presenting as stroke in a young female. Can J Neurol Sci. 2004 Feb;31(1):112-4. PubMed PMID: 15038481.
2)
Nordin S, Kozor R, Baig S, Abdel-Gadir A, Medina-Menacho K, Rosmini S, Captur G, Tchan M, Geberhiwot T, Murphy E, Lachmann R, Ramaswami U, Edwards NC, Hughes D, Steeds RP, Moon JC. Cardiac Phenotype of Prehypertrophic Fabry Disease. Circ Cardiovasc Imaging. 2018 Jun;11(6):e007168. doi: 10.1161/CIRCIMAGING.117.007168. PubMed PMID: 29853467; PubMed Central PMCID: PMC6023585.
3)
Nordin S, Kozor R, Medina-Menacho K, Abdel-Gadir A, Baig S, Sado DM, Lobascio I, Murphy E, Lachmann RH, Mehta A, Edwards NC, Ramaswami U, Steeds RP, Hughes D, Moon JC. Proposed Stages of Myocardial Phenotype Development in Fabry Disease. JACC Cardiovasc Imaging. 2018 May 11. pii: S1936-878X(18)30307-3. doi: 10.1016/j.jcmg.2018.03.020. [Epub ahead of print] PubMed PMID: 29778854.
4)
Lee TH, Yang JT, Lee JD, Chang KC, Peng TI, Chang TY, Huang KL, Liu CH, Ryu SJ, Burlina AP. Genomic Screening of Fabry Disease in Young Stroke Patients: the Taiwan Experience and a Review of the Literature. Eur J Neurol. 2018 Aug 13. doi: 10.1111/ene.13775. [Epub ahead of print] PubMed PMID: 30103270.