



EDITORIAL COMMENT

Fabry disease: Something cardiologists must always bear in mind



Doença de Fabry – um lembrete obrigatório para os cardiologistas!

Nuno Bettencourt

Unidade de Investigação Cardiovascular, Faculdade de Medicina da Universidade do Porto, Porto, Portugal

Available online 28 May 2018

In this issue of the *Journal*, Brito et al. present a very interesting work¹ based on data extracted from the Portuguese Registry of Hypertrophic Cardiomyopathy.²

Focusing on a non-mandatory question from this registry, concerning the exclusion of Anderson-Fabry disease in the differential diagnosis, the authors concluded that this entity is seldom studied in the workup of patients with unexplained left ventricular hypertrophy. According to their data, Fabry disease was recorded as excluded in only 27% of the patients included in the registry. Alpha-galactosidase A (α -Gal A) activity was assessed in 18% and *GLA* gene testing was only performed in 23% of cases. Among patients with potential red flags for Fabry disease (including concentric left ventricular hypertrophy, short or prolonged PR interval, intraventricular conduction disturbances or bradyarrhythmias requiring pacemaker implantation), fewer than half (47%) underwent specific tests (*GLA* gene testing and/or α -Gal A activity).

These results are even more striking if we note that only cardiology departments were included in the registry, which is totally voluntary, and that inclusion was not sequential.

Bearing this in mind, there is a high probability of bias toward the inclusion of better-studied patients and a higher participation of centers with better overall performance in cardiomyopathies. This means that in real-world practice the rates of Fabry disease exclusion in these patients are probably even lower than reported here.

Portugal has some of the largest series of Fabry disease patients in Europe, and these numbers are mainly due to the systematic diagnostic workup performed in reference centers for lysosomal storage diseases.^{3–6} Although some geographic distribution patterns are clearly discernible, as can be expected from an X-linked genetic disease, it is essential to maintain general awareness of this disease, for which specific therapies are available that can modify prognosis. Since cardiac involvement is frequent and is sometimes the primary or sole manifestation of Fabry disease, all cardiologists should be constantly on the alert for the possibility of Fabry disease in the study of unexplained left ventricular hypertrophy. Early diagnosis and, if appropriate, initiation of enzyme replacement therapy can change the course of this disease and may improve both symptoms and prognosis. Furthermore, identification of an index case can help identify relatives affected by disease, who may also benefit from diagnostic workup, structured follow-up and early initiation of therapy, if indicated.

DOI of original article: <https://doi.org/10.1016/j.repc.2018.03.010>

E-mail address: bettencourt.n@gmail.com

<https://doi.org/10.1016/j.repc.2018.05.002>

0870-2551/© 2018 Published by Elsevier España, S.L.U. on behalf of Sociedade Portuguesa de Cardiologia.

In an era of advanced imaging and readily available genetic testing, efforts should be made to ensure that red flags for Fabry disease in patients with left ventricular hypertrophy are identified and to encourage the use of dedicated tools for its exclusion. This paper has a clear message for all cardiologists: Fabry disease is something that must always be borne in mind in the study of patients with unexplained left ventricular hypertrophy.

Conflicts of interest

The author has no conflicts of interest to declare.

References

1. Brito D, Cardim N, Lopes LR, et al. Awareness of Fabry disease in cardiology: a gap to be filled. *Rev Port Cardiol.* 2018;37:457–66.
2. Cardim N, Brito D, Lopes LR, et al. The Portuguese Registry of Hypertrophic Cardiomyopathy: overall results. *Rev Port Cardiol.* 2018;37:1–10.
3. Aguiar P, Azevedo O, Pinto R, et al. Biomarkers of myocardial fibrosis: revealing the natural history of fibrogenesis in Fabry disease cardiomyopathy. *J Am Heart Assoc.* 2018, March;7, <http://dx.doi.org/10.1161/JAHA.117.007124>.
4. Rodrigues J, Azevedo O, Sousa N, et al. Inner ear involvement in fabry disease: clinical and audiometric evaluation of a large cohort of patients followed in a reference centre. *Eur J Med Genet.* 2018, January, pii: S1769-7212(17)30574-8.
5. Brito D, Miltenberger-Miltenyi G, Moldovan O, et al. Cardiac Anderson-Fabry disease: lessons from a 25-year-follow up. *Rev Port Cardiol.* 2014, April;33:247, e1–7.
6. Beirão I, Cabrita A, Torres M, et al. Is it Fabry disease? Diagnostic and follow-up approach. *Acta Med Port.* 2016;29:85–7.