Journal of Inborn Errors of Metabolism & Screening
2016, Volume 4: 1–2

DOI: 10.1177/2326409816661350
iem.sagepub.com
SAGE

Editorial Letter to Special Issue Fabry Disease

Juan Politei, MD[1]

In 1998, Fabry in Germany and Anderson in the United Kingdom described for the first time and separately 2 patients with diffuse body angiokeratomas (angiokeratoma corporis diffusum).[1,2] The first author was able to follow the evolution of his patient for almost 30 years, whereas Anderson could only make 1 report on his patient. Different from Fabry, though, Anderson described some signs and symptoms not related to dermatology. In 1958, Ruiter reported that only men were hemizygously affected,[3] but on that same year, Colley et al proved involvement in women too.[4]

In 1964, Brady et al[5] reported the finding of the deficient enzyme (α-galactosidase A), generating the basis for the enzyme replacement therapy (ERT) we know today.

Since the approval of the ERT—in 2001 in Europe and in 2003 in the United States—there has been an increase in the number of scientific publications on Fabry disease. The analysis of publications available in PubMed using "Fabry disease" as search keyword showed that there had been a total of 984 reports published since 1947 to 2000. This number increased to 2375 from December 2001 to December 2015.

The possibility of a specific treatment led to a growing interest on the disease on the part of the medical community. Moreover, its particular multidisciplinary spectrum has generated a constant description of physiopathological findings that could explain the presence of the characteristic signs and symptoms.

The objective of this supplement edition is to update—in 9 papers—the practical aspects related to the Fabry disease physiopathology, diagnosis, and treatment.

One of the concepts showing a higher "evolution" has been the decision to start ERT. Several international consensuses and guidelines have tried to define the most adequate time to indicate the treatment for each patient.[6-10] Although the bibliography showed that the results were varied for the different groups of patients treated, it was easy to know that the age to start with ERT was the most significant independent variable. From that moment on the concept of "point of no return" has been repeated in several reports, since once that point in time is over, and with fibrosis in tissues previous to ERT, the possibilities of reversing an organ damage or even stabilizing it are unlikely.[11]

There are 2 agalsidase formulations in the European and Latin American markets: agalsidase alfa and agalsidase beta, enabling the physician to choose the treatment. However, the US Food and Drug Administration refused to approve the agalsidase alfa. The main difference between agalsidase alfa and agalsidase beta is the authorized dose: 0.2 mg/kg for alfa and and 1 mg/kg for beta every other week. Several recent studies suggest the existence of a dose–response effect since the 0.2 mg/kg every 2 weeks has not shown tissue substrate clearance.[12,13]

Other specific therapies, such as chemical chaperones and substrate inhibition, are being studied in prospective and controlled trials, already in phase 3. The analysis of the preliminary results opens the door to the possibility of an oral route administration treatment, at least for a group of patients with specific mutations or with the ability to diminish the substrate production.

There are still many questions unanswered. Among them, we find the need to determine whether the antibodies developed by the patients with the use of the 2 previously mentioned ERTs have a blocking effect and could reduce their effectiveness in the medium to long term, and also establishing what the most effective concomitant therapies are (antiproteinurics, statins, antiaggregants, etc) as well as the age to start ERT.

References

1. Anderson W. A case of angiokeratoma. *Br J Dermat*. 1898;1: 113-117.

[1] Fundación para el Estudio de las Enfermedades Neurometabólicas (FESEN), Quilmes, Buenos Aires, Argentina

Received February 13, 2016. Accepted for publication April 11, 2016.

Corresponding Author:
Juan Politei, Fundación para el Estudio de las Enfermedades Neurometabólicas (FESEN), Allison Bell 921, Quilmes, PC 1878, Buenos Aires, Argentina.
Email: jpolitei@hotmail.com

2. Fabry J. Ein Beitrag zur Kenntnis der Purpura haemorrhagic a nodulari s (Purpura papulosa haemorrhagic a Hebrae). *Arch Dermatol Syph*. 1898;43:187-200.
3. Ruiter M. Das Angiokeratoma corporis diffusum Syndom and Seine Hauterscheinungen. *Hautarzt*. 1958;9:15.
4. Colley JR, Miller DL, Hutt MS, Wallace HJ, De Wardener HE. The renal lesion in angiokeratoma corporis diffusum. *Br Med J*. 1958;1(5082):1226-1228.
5. Brady RO, Gal AE, Bradley RM, Martenson E, Warshaw AL, Laster L. Enzymatic defect in Fabry's disease. Ceramidetrihexosidase deficiency. *N Engl J Med*. 1967;276(21): 1163-1167.
6. Desnick RJ, Brady R, Barranger J, et al. Fabry disease, an underrecognized multisystemic disorder: expert recommendations for diagnosis, management, and enzyme replacement therapy. *Ann Intern Med*. 2003;138(4):338-346.
7. Eng CM, Germain DP, Banikazemi M, et al. Fabry disease: guidelines for the evaluation and management of multi-organ system involvement. *Genet Med*. 2006;8(9):539-548.
8. GADYTEF. Guía práctica para el diagnóstico, tratamiento y seguimiento de la enfermedad de Fabry. *Nefrología Argentina*. 2006;4:128-138.
9. GADYTEF. Primera Actualización: Guía práctica para el estudio, diagnóstico y tratamiento de la enfermedad de Fabry. *Revista de nefrología, diálisis, y trasplante*. 2007;4:159-170.
10. Biegstraaten M, Arngrímsson R, Barbey F, et al. Recommendations for initiation and cessation of enzyme replacement therapy in patients with Fabry disease: the European Fabry Working Group consensus document. *Orphanet J Rare Dis*. 2015;10:36.
11. Germain DP, Waldek S, Banikazemi M, et al. Sustained, long-term renal stabilization after 54 months of agalsidase beta therapy in patients with Fabry disease. *J Am Soc Nephrol*. 2007;18(5):1547-1557.
12. Schiffmann R, Kopp JB, Austin HA III, et al. Enzyme replacement therapy in Fabry disease: a randomized controlled trial. *JAMA*. 2001;285(21):2743-2749.
13. Tøndel C, Bostad L, Larsen KK, et al. Agalsidase benefits renal histology in young patients with Fabry disease. *J Am Soc Nephrol*. 2013;24(1):137-148.