Presentation Day 2

Lessons from the European Patient Population

Francesco Emma, MD
Bambino Gesù Children's Hospital

In rare conditions, registries and large cohort studies are essential to describe the natural history of diseases and to assess improvements in prognosis over time. Since cystinosis is very rare, this has been particularly challenging.

In addition to large cohorts of patients assembled in the North America, such as the NIH cohort, and to data that are emerging from the Cure Cystinosis International Registry, large cohorts and registry studies have been performed in Europe. The results of all these studies are complementary and produce a reliable picture of the disease, show improvements over time, and highlight unmet needs.

A fist study looked at the European pediatric dialysis registry dataset and observed that unlike other kidney diseases, the age at dialysis has progressively increased in patients with cystinosis during the years in which cysteamine has been introduced. This same study showed that compared to other children with end-stage kidney disease, patients with cystinosis are on average shorter, but that their kidney survival after transplantation is considerably better, something that had already been suggested by early data from France but needed confirmation.

More recently, a large French cohort of patients with cystinosis has analyzed the outcome of adult patients and observed that those treated before or after the age of 3 years with cysteamine had significantly better outcome. However, the number of patients in this study was too small to refine the analysis and see if there is an age limit above which the prognosis declines.

To this end, we have performed a very large study spanning 5 decades and including 453 patients from 9 countries. This study has shown that in terms of kidney function, every month of age lost to begin cysteamine treatment counts and that all efforts should be made to diagnose children very early. These results are also supported by a recent sibling study showing that on average, when two siblings are affected, the second sibling has a better evolution because he or she is treated earlier. They are also in strong support of developing neonatal screening programs, such as the one that has recently been tested in Germany. In the same study we have also demonstrated that starting early cysteamine improves growth. On the other hand, we observed no clear benefits, nor adverse effects from treatments with indomethacin or ACE inhibitors, something that is much debated in the cystinosis community. However, due to the retrospective nature of the study, these latter results should be interpreted prudently and require confirmation.

References:

- Van Stralen KJ, Emma F, Jager KJ, Verrina E, Schaefer F, Laube GF, Lewis MA, Levtchenko EN. Improvement in the renal prognosis in nephropathic cystinosis. Clin J Am Soc Nephrol 6:2485-91, 2011.
- Brodin-Sartorius A, Tête MJ, Niaudet P, Antignac C, Guest G, Ottolenghi C, Charbit M, Moyse D, Legendre C, Lesavre P, Cochat P, Servais A. Cysteamine therapy delays the progression of nephropathic cystinosis in late adolescents and adults. Kidney Int 81:179-89, 2012.
- Emma F, Hoff WV, Hohenfellner K, Topaloglu R, Greco M, Ariceta G, Bettini C, Bockenhauer D, Veys K, Pape L, Hulton S, Collin S, Ozaltin F, Servais A, Deschênes G, Novo R, Bertholet-Thomas A, Oh J, Cornelissen E, Janssen M, Haffner D, Ravà L, Antignac C, Devuyst O, Niaudet P, Levtchenko E. An international cohort study spanning five decades assessed outcomes of nephropathic cystinosis. Kidney Int 100:1112-1123, 2021
-