Better Late than Never: Genetic Diagnosis After Major Medical Events

By Dawn Laney, MS

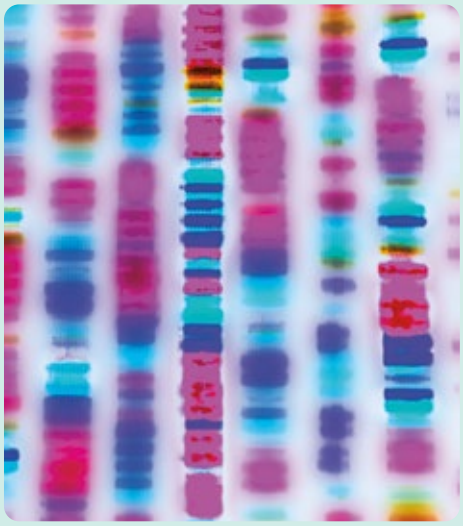
You have two doctors for your kidneys, one for your heart, one for your head, one for your eyes, and one for your overall health. You are tested, biopsied, and imaged from head to toe on a regular basis. So, when one of these doctors suggests a referral to genetics, you may wonder, "Another doctor? Is it still worth seeking a genetic diagnosis as an adult who has already had kidney failure?" The answer is a resounding "Yes!" One way to improve care in a medically complicated situation is by learning if an underlying genetic condition could be playing a role in major medical event like early kidney disease. A diagnosis provides a window into potential future medical events and allows your medical care team to most effectively address current concerns, while also developing a plan to catch and treat future symptoms early.

Let's take a specific example. Sometimes, kidney biopsies find that someone has lipid storage "consistent with Fabry disease" and suggest further evaluation. The next step would be looking for other medical history clues that an individual has Fabry disease and performing a simple blood test to confirm or rule out that condition. Why does it matter if someone has Fabry disease? There are 3 major reasons.

Reason 1. Predicting the Future: Fabry disease is a progressive X-linked genetic condition that ranges in symptoms from a childhood onset "classic" form across the spectrum to a later onset, but still life impacting, "nonclassic" form. In Classic Fabry disease, the initial symptoms begin sneakily with nonspecific complaints such as lack of sweating leading to problems

with overheating, severe belly pain and diarrhea that looks like irritable bowel syndrome, chronic fatigue, a "whorl" in the cornea that can be seen on slit-lamp exam and burning pain in the hands and feet. Over the next 20-30 years those health issues continue and are joined by chronic kidney disease, hearing loss, heart rhythm changes, enlargement of the heart, and a host of other symptoms. Patients with nonclassic disease can experience all or some of these symptoms, but usually they do not begin in childhood. Sometimes nonclassic Fabry disease will be focused on a major organ and cause onset of progressive heart disease beginning in the 30s or 40s. Other times, nonclassic Fabry disease results in kidney failure in the 50s or 60s, with heart disease not far behind. In any of these cases, the key to a good quality of life and decreasing the risk for major events in adults living with Fabry disease is having a medical team focused on treating cardiac disease and working to prevent strokes. If someone is affected with Fabry disease, but doesn't have the diagnosis, they may not be receiving the best monitoring and treatment.

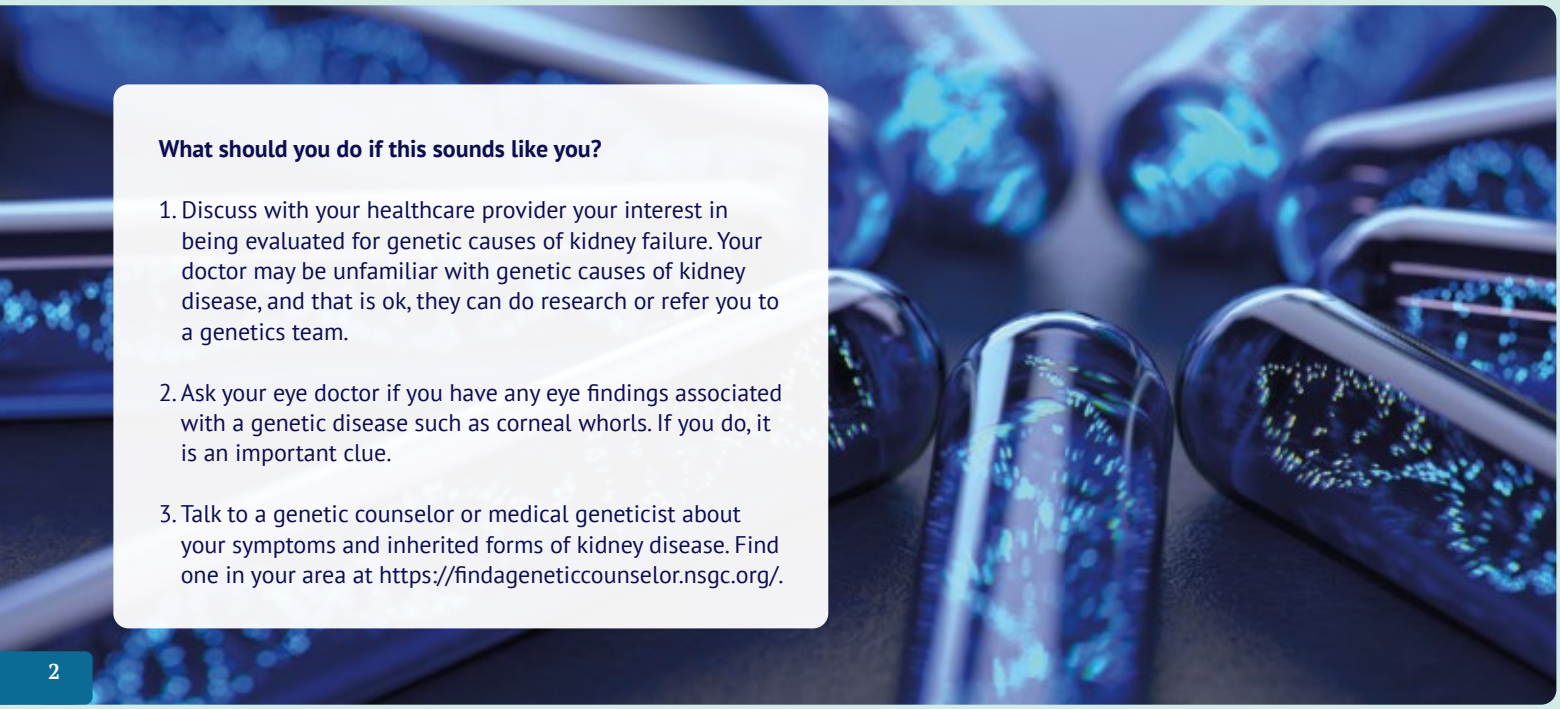
Reason Number 2: Targeted therapy: There are two United States Food and Drug Association (FDA) approved medications that address the root cause of Fabry disease: agalsidase beta (Fabrazyme ®, Sanofi-Genzyme) and migalastat (Galafold ®, Amicus Therapeutics). In all cases, treatment is most effective when



begun as early as possible. This means that diagnosing a genetic disease reduces the time to beginning the best, most effective treatment and leading to the best outcomes.

Reason Number 3: Your Family. When someone is diagnosed with a genetic condition, it has implications for their family members. After a diagnosis, doctors should take a detailed family history to find out if other family members might have or will be affected by some or all of these health issues. If these clues suggest the condition, testing of blood or saliva is the next key step. Treatment can begin earlier which leads to better outcomes. Medical geneticists and genetic counselors are health care providers who are specially trained to take family histories, identify at-risk family members, seek out clues to underlying genetic conditions, organize genetic testing, interpret genetic testing results, and discuss therapeutic options, including clinical trials. Could any doctor order the testing? Sure! But in genetics the "what next" is often just as important as the testing.

Fabry disease is just one example, but it embodies the importance of investigating the underlying causes of early renal failure, particularly if many people in a family have had earlier onset proteinuria or kidney disease. If kidney disease runs in a family, begins in 40s or 50s (without diabetes), or happens in combination with symptoms such as early hearing loss or burning pain it may be worth talking with a healthcare provider about possible genetic causes of renal disease. A genetic consult and testing can help determine if there is an underlying genetic cause for kidney problems and who else in the family might be at risk. Identifying a genetic cause can then open the door for targeted treatment that is most effective and help other family members receive early treatment. All of these can improve the quality and quantity of life for patients, and that's the whole point. You can learn more about genetic causes of kidney disease at: https://www.uclahealth.org/core-kidney/genetics-and-ckd or by viewing Genetic causes of Renal Failure video at https://www.dpcedcenter.org/what-is-kidney-disease/what-causes-kidney-disease/.



What should you do if this sounds like you?

1. Discuss with your healthcare provider your interest in being evaluated for genetic causes of kidney failure. Your doctor may be unfamiliar with genetic causes of kidney disease, and that is ok, they can do research or refer you to a genetics team.

2. Ask your eye doctor if you have any eye findings associated with a genetic disease such as corneal whorls. If you do, it is an important clue.

3. Talk to a genetic counselor or medical geneticist about your symptoms and inherited forms of kidney disease. Find one in your area at https://findageneticcounselor.nsgc.org/.