Fabry Disease
Nephrologists Can Identify Families at Risk
PREVALENCE AND CONSEQUENCES OF FABRY DISEASE

Fabry disease is a progressive, often life-threatening genetic disorder that affects men, women, and children of all ethnicities. The hallmark of the disease is the cellular accumulation of a lipid substrate called globotriaosylceramide (GL-3). GL-3 accumulation affects organs throughout the body, including the kidneys.

Nephrologists are in a unique position to identify early signs of the disease.

Prevalence of Fabry disease in the dialysis population is approximately 100x to 1000x higher than in a reference population (Australian study)\(^1\)\(^-\)\(^10\)

- Prevalence of Fabry disease in a reference population (Australian study) is 1 in 117,000\(^1\)
- Prevalence estimates in the dialysis population range from 0.1% to 1.2%\(^2\)\(^-\)\(^10\)
- Nephrologists are critical to the diagnosis and management of patients with Fabry disease

Renal Manifestations Over Time

Undiagnosed and unmanaged, Fabry disease reduces life expectancy\(^19\)\(^,\)\(^20\)

- The disease can affect the renal, cardiac, and cerebrovascular systems\(^13\)
  - Nearly 40% of females exhibit significant kidney involvement, with mean age at onset and disease progression similar to that reported in males\(^15\)
- Life expectancy is reduced by up to 20 years in males and 15 years in females, according to natural history data\(^19\)\(^,\)\(^20\)
- People with Fabry disease are at risk of developing ESRD between the third and fifth decades of life\(^11\)\(^-\)\(^14\)
  - Fabry disease may account for between 3 in 1,000 and 7 in 1,000 unexplained end-stage renal disease (ESRD) cases\(^5\)\(^,\)\(^9\)
  - The Centers for Medicare and Medicaid Services classifies Fabry disease as a primary cause of ESRD.
UNEXPLAINED RENAL MANIFESTATIONS COULD INDICATE FABRY DISEASE

The heterogeneous nature of the disease results in delayed diagnosis\textsuperscript{13,19}

- From symptom onset to a diagnosis of Fabry disease, there was a delay of approximately 15 years in both males and females (14.2 years for males and 15.7 years for females).\textsuperscript{15}
- Connecting seemingly unrelated symptoms to Fabry disease can help avoid diagnostic delays.\textsuperscript{12}
- Screening dialysis patients for Fabry disease is key to identifying patients and families. The dialysis setting offers an enriched population that enables efficient screening. For every index patient diagnosed, an average of 5 additional affected family members may be identified.\textsuperscript{22}

Misdiagnoses are Common

The symptoms of Fabry disease can be confused with rheumatoid or juvenile arthritis, rheumatic fever, erythromelalgia, Raynaud’s syndrome, neurosis, lupus, acute appendicitis, or multiple sclerosis.\textsuperscript{2,14-16} Pain, especially in children, can be dismissed as malingering.\textsuperscript{2}

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As a nephrologist, you have an opportunity to identify patients earlier and reduce the typical diagnostic delay many Fabry patients suffer.

In some patients, renal disease may be the only prominent manifestation\textsuperscript{2}

- Kidney manifestations may include:
  - Proteinuria
  - Tubular dysfunction (polyuria, polydipsia)
  - Elevated serum creatinine
  - Podocyte injury
  - Glomerular sclerosis
  - Fibrosis
  - Renal failure/ESRD\textsuperscript{1}
  - Proteinuria, decreased GFR, and/or elevated serum creatinine may be present as early as childhood\textsuperscript{21}

- Non-renal manifestations may include:
  - Neuropathic pain in the hands and feet
  - Impaired sweating
  - Heat/cold intolerance
  - Angiokeratomas
  - Early cardiac hypertrophy and arrhythmia
  - Early TIA/stroke

Pervasive accumulation of GL-3 eventually causes tissue ischemia and fibrosis and may lead to life-threatening consequences that can be irreversible, particularly in the kidneys.

GL-3 inclusions (arrows) in the renal capillary endothelium.
INCLUDE FABRY DISEASE IN THE DIFFERENTIAL DIAGNOSIS

Screening dialysis patients for Fabry disease is key to identifying patients and families.

European Renal Best Practice recommends screening males under age 50 with unexplained CKD and females of any age with unexplained CKD and other symptoms associated with Fabry disease.23

• Diagnostic testing starts with a blood draw that can be easily incorporated into standard clinical practice. The clinician only needs to draw blood and send it out.

• A number of laboratories across the United States perform diagnostic testing for Fabry disease; your practice may be affiliated with one of them.

Renal biopsy may not be sufficient to confirm diagnosis but can be used to track disease progression and guide disease management in confirmed cases; biopsy may demonstrate GL-3 storage and signs of injury, including glomerular sclerosis, which may be present as early as childhood.1

A geneticist can assist in arranging for diagnostic testing. Or contact Sanofi Genzyme Medical Information at 800-745-4447, option 2.

CASE REPORT

Fabry Disease Presenting as Unexplained Proteinuria

SHAGUN CHOPRA, MD

Patient: 32-year-old white male
Presenting symptom: Proteinuria
Other signs and symptoms: Corneal verticillata, angiokeratoma, heat intolerance
Diagnosis: Fabry disease

Patient History and Current Status

The patient, an active-duty United States Marine, presented with mild proteinuria (600 mg/24 hr) at age 29 and was referred to a nephrologist. No other symptoms were noted, no diagnosis was made, and the patient returned to military service.

Three years later, the patient visited an ophthalmologist for a routine eye exam. The ophthalmologist observed corneal verticillata and referred the patient back to his primary care physician to determine the underlying cause. The PCP performed a full physical exam and again detected proteinuria. The patient was referred to another nephrologist, who found that his protein level had increased to 3 g/24 hr although he was still otherwise asymptomatic. Biopsy revealed substrate accumulation in the renal capillary endothelium. The nephrologist suspected Fabry disease and discussed this possibility with the patient, who reported other common Fabry signs and symptoms including angiokeratoma and heat intolerance. Genetic testing confirmed the diagnosis.

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Nephrologists can identify families at risk for Fabry disease

- Prevalence of Fabry disease in the dialysis population is approximately 100x to 1000x higher than in a reference population (Australian study)
- Undiagnosed and unmanaged, Fabry disease reduces life expectancy by up to 20 years in males and 15 years in females
- Diagnosis may be delayed up to 15 years in both males and females
- Unexplained renal manifestations could indicate Fabry disease
- Screening dialysis patients for Fabry disease is key to identifying patients and families

References:

For more information on Fabry disease, including diagnostic testing, contact Sanofi Genzyme Medical Information at 1-800-745-4447, option 2.

Fabrycommunity.com
RegistryNXT.com

Patient Resources
Sanofi Genzyme Case Managers
genzymesupportservices.com
1-800-745-4447, option 3

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