Fabry disease may cause damage to the kidneys and multiple additional organ systems

- Fabry disease is a rare lysosomal disorder affecting both male and female patients. It is caused by variants (mutations) in the galactosidase alpha gene (*GLA*), leading to functional deficiency of alpha-galactosidase A (alpha-Gal A) in the lysosomes. This allows progressive accumulation of disease-causing substrates, including globotriaosylceramide (GL-3), and a cascade of tissue damage in multiple organs[1]

- Renal symptoms often begin in the 2nd and 3rd decades of life and are followed by decreasing renal function and, in some patients, renal failure. Renal manifestations are major contributors to the morbidity and mortality in Fabry disease[1]

When should you consider testing for Fabry disease? Prominent renal symptoms include:

- Proteinuria of unknown origin, microalbuminuria/albuminuria[1]
- Decreased glomerular filtration rate and progressive renal failure[1,2]
- Chronic kidney disease[1]

Additional signs and symptoms that may be present in Fabry disease include:

- **Cardiac:** Left ventricular hypertrophy; cardiomyopathy; arrhythmia and impaired heart rate variability; cardiac ischemia leading to angina and myocardial infarction[1]
- **Dermatologic:** Angiokeratoma; dyshidrosis leading to temperature and exercise intolerance[1]
- **Gastrointestinal:** Abdominal pain (often after eating); diarrhea; nausea and vomiting, which may lead to anorexia[1]
- **Nervous:** Acroparesthesia (burning pain in hands and feet); headache; neuropathic pain; pain crises; stroke; transient ischemia attack[1,3]
- **Otolaryngologic:** Cornea verticillata; dizziness/vertigo; hearing loss; tinnitus[1]

Diagnosis of Fabry disease can be challenging and often delayed[1]

Fabry disease is "often seen, rarely diagnosed"[4]

- While Fabry disease is considered "rare," many of its signs and symptoms are seen with more common disorders[1,5]
- It is estimated that patients visit an average of 10 different specialists before a Fabry disease diagnosis is confirmed, leading to a delay of ~15 years from symptom onset to diagnosis[5,6]

GLA gene sequencing confirms a diagnosis of Fabry disease[6]

- In addition, gene sequencing helps:
  - Establish the disease phenotype[7]
  - Provide additional information regarding disease prognosis and treatment[8]
  - Permit the testing of at-risk family members[7]

- It is important to note that in males with the suspected classic phenotype, an absence or low levels of alpha-Gal A activity in blood cells or dried blood spots is sufficient to make the diagnosis. However, *GLA* gene sequencing is required for women[5]

- On average, each Fabry disease diagnosis leads to the diagnosis of 5 additional family members[9]

Prompt diagnosis is important because treatment options are available.[1]

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