UNIDENTIFIED RENAL SYMPTOMS COULD HELP IDENTIFY A FABRY FAMILY

Fabry Disease:
A Quick Reference for Nephrologists

CLINICAL DIAGNOSIS

About Fabry Disease

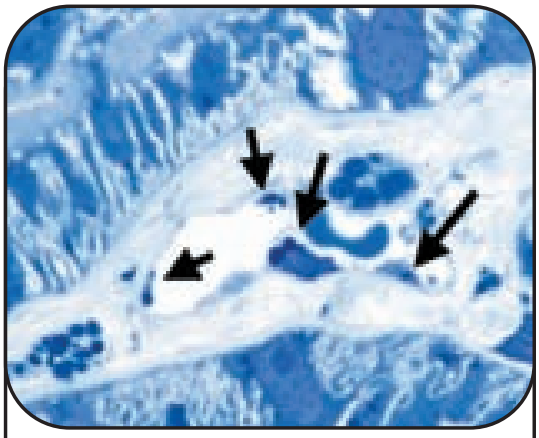
Fabry disease is a genetic disorder caused by deficiency of α-galactosidase A enzyme activity, resulting in an inability to catabolize certain lipids, particularly globotriaosylceramide (GL-3). GL-3 progressively accumulates in many body tissues, including visceral, as well as the vascular endothelium throughout the body.

Renal Manifestations

- Unexplained proteinuria
- Tubular dysfunction (polyuria, polydipsia)
- Elevated serum creatinine
- Progressive and/or unexplained chronic kidney disease, especially accompanied by near normal blood pressure[1]

Other Manifestations

- Pain in the extremities
- Impaired sweating
- Heat/cold and exercise intolerance
- Angiokeratomas (skin rash)
- Gastrointestinal complications
- In some patients, renal disease may be the only prominent manifestation[2]



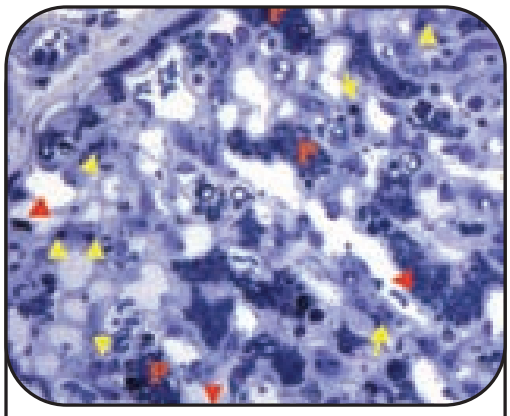
In Fabry disease, an enzyme deficiency leads to progressive cellular accumulation of globotriaosylceramide (GL-3), a lipid substrate, in the vascular endothelium and tissues throughout the body as seen in this light micrograph of the renal capillary endothelium.

CONFIRMING DIAGNOSIS

Nephrologists may be the first to identify Fabry disease. In patients with unexplained renal symptoms and a family history of renal disease, diagnostic testing can determine whether Fabry disease is the underlying cause.

Diagnostic Tests

- A renal biopsy can demonstrate deposits of the lipid substrate globotriaosylceramide (GL-3), which is characteristic of Fabry disease.
- Diagnosis in males can be made by testing for deficiency of α-galactosidase (α-GAL) enzyme activity in plasma, leukocytes, tears, biopsied tissue, or dried blood spots. In females, normal α-GAL enzyme activity does not rule out Fabry disease, and genetic analysis must be conducted.
- For assistance in locating a facility that performs genetic analysis, please contact Genzyme Medical Information at **800-745-4447** or **617-768-9000** (option 2).



Lipid Deposits in Glomerulus

P = podocyte accumulation of GL-3

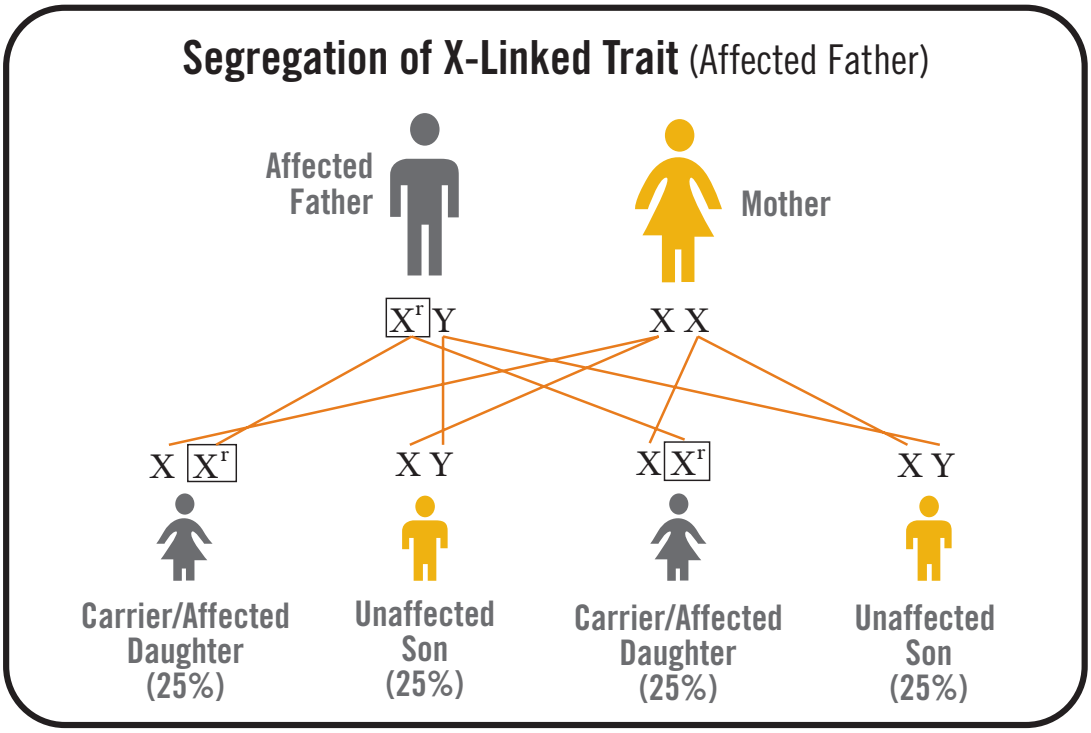
→ = endothelial accumulation of GL-3

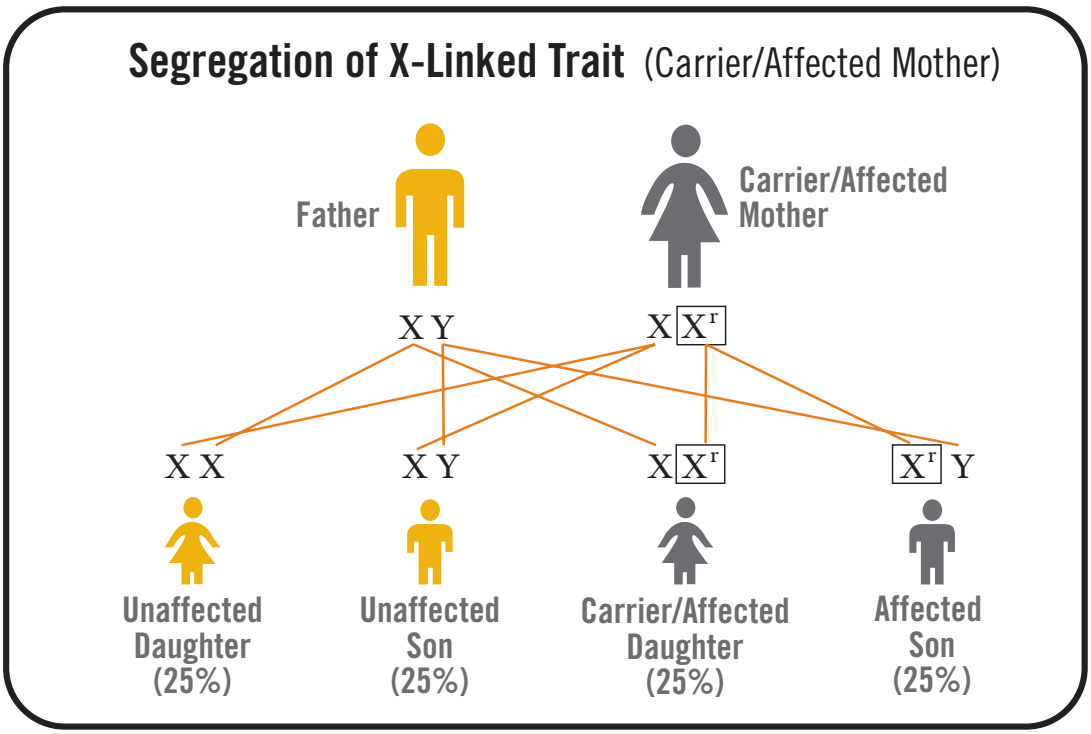
→ = mesangial cell accumulation of GL-3

GENETIC IMPACT

Males with the defective gene pass it on to all of their daughters and none of their sons. Heterozygous females have a fifty percent chance with each pregnancy of passing the defective gene to each of their offspring. Most females heterozygous for Fabry disease are clinically affected to some extent.[3,4]

Inheritance Pattern





QUESTIONS TO ASK YOUR PATIENT

If you suspect Fabry disease, consider asking your patient these questions. Affirmative answers could indicate that diagnostic testing is warranted.

Questions for Clinical Assessment

- Do you experience recurrent tingling or burning in your hands or feet?
- Have you ever experienced episodes of extreme pain of unknown cause, possibly accompanied by fever?
- Do you have trouble sweating or exercising?
- Do you find heat or cold hard to tolerate?
- Do you have gastrointestinal problems such as pain and bloating after eating, or nausea, cramps, or diarrhea?
- Do you have any small raised reddish-purple spots on your skin, especially in the "bathing trunk" area?
- Does anyone in your family have kidney failure of unknown cause?
- Do you or anyone in your family have heart disease that developed at a relatively early age of unknown cause?
- Have you or anyone in your family had a stroke at a relatively early age?

RESOURCES

Genzyme is committed to helping medical professionals get the information and resources they need to provide comprehensive care for their patients with Fabry disease.

Medical Information

Genzyme offers access to a network of medical specialists with expertise in Fabry disease. In addition, providers can request Fabry disease-related scientific papers, educational materials, and information on diagnostic testing and genetic counseling. Call **800-745-4447** or **617-768-9000** (option 2).

Fabry Registry

The Genzyme Fabry Registry is an international, longitudinal database dedicated to improving the understanding of Fabry disease. To learn more call **617-768-9000**, ext. 17024 or visit **www.fabryregistry.com**.

Fabry Community

Genzyme offers patient and physician resources at **www.fabrycommunity.com**.

Fabry Research

Patients and practitioners can request information on current clinical trial programs for lysosomal storage disorders such as Fabry disease at **800-745-4447** or **617-768-9000** (option 2).

REFERENCES

1. Warnock DG, West ML. Diagnosis and Management of Kidney Involvement in Fabry Disease. Adv Chronic Kidney Dis 2006;13:138-147.

2. Nakao S, Kodama C, Takenaka T, et al. Fabry disease: detection of undiagnosed hemodialysis patients and identification of a “renal variant” phenotype. Kidney Int 2003;64:801-7.

3. MacDermot KD, Holmes A, Miners AH. Anderson-Fabry disease: clinical manifestations and impact of disease in a cohort of 60 obligate carrier females. J Med Genet 2001;38:769-775.

4. Gupta S, Ries M, Kotsopoulos S, Schiffmann R. The relationship of vascular glycolipid storage to clinical manifestations of Fabry disease: A cross-sectional study of a large cohort of clinically affected heterozygous women. Medicine 2005;84:261-268.

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