

# Fabry Disease: Management in Carriers for enzyme alpha-Galactosidase A (a-GAL A)

Nithin Datla<sup>1</sup> and Dr. Rupesh Raina<sup>1,2</sup>

<sup>1</sup>Department of Nephrology, Akron Nephrology Associates/ Cleveland Clinic Akron General Medical Center, Akron, OH

<sup>2</sup>Department of Nephrology, Akron Children’s Hospital, Akron, OH



## Introduction

- Fabry disease is an X-linked recessive deficiency of the enzyme alpha-Galactosidase A (a-GAL A), resulting in the accumulation of globotriaosylceramide (Gb3) within lysosomes in a variety of cells.<sup>1-3</sup>
- It is the second most common lysosomal storage disease, with a prevalence ranging from 1:17,000 to 1:117,000. Given the rarity and nonspecific manifestations of the disease, diagnosis may be missed.<sup>2</sup>
- Fabry disease can be diagnosed in males by detecting low a-GAL A activity in leukocytes or in the plasma.
  - In women, a-GAL A activity level is unreliable for diagnosis and therefore it is necessary to perform mutation analysis of the a-GAL A gene.<sup>4</sup>
- Typical physical manifestations of include neuropathic pain, angiokeratomas or telangiectasias, thickened lips and bulbous nose, along with other nonspecific complaints such as heat or cold intolerance, abdominal pain, diarrhea, lymphadenopathy and hypo- or hyperhidrosis.<sup>5</sup>
- Carriers may be completely asymptomatic but with advancing age may develop mild to moderate left ventricular hypertrophy and valvular disease, cardiomegaly, myocardial ischemia, infarction, arrhythmias, transient ischemic attacks, stroke and end stage renal disease.<sup>5</sup>
- In the kidney, Gb3 accumulates in the glomeruli, involving podocytes, endothelial cells and mesangial cells, and also in the distal tubules resulting in early manifestations of proteinuria and polyuria.<sup>6</sup>
- We report a case of Fabry disease in a young female who was asymptomatic initially and slowly started showing renal manifestations of the disease.

## References

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## Aim

- Evaluate the diagnosis, treatment, and intervention on a patient with Fabry’s disease compared to national standards of care

## Case

- The patient is a 26 year old female referred her primary care physician for evaluation of proteinuria and hematuria with CKD stage 1 with significant history of renal diseases in the family.
- On examination she was found to have angiokeratomas in the periumbilical regions, she also had complaints of tingling/ pain in her hands and feet along with episodes of extreme heat and excessive sweating.
- Her baseline serum creatinine was 0.5 - 0.8 mg/dL
- On genetic testing she was noted to be a heterozygous carrier for the Fabry Disease.
- Enzyme Replacement Therapy (ERT) with a focus on the need for blood pressure control, metabolic derangements, lipid and diabetic control, avoidance of nephrotoxic drugs and also education about the options for renal replacement therapy in future was suggested to the patient.
- The importance of scheduled follow up visits with cardiology, renal and other subspecialties every 2-3 months to monitor the progression of disease was emphasized.

## Discussion

- Signs/symptoms suggesting major organ involvement, warranting initiation of ERT in this **symptomatic female patients** include<sup>7</sup>:
  - **neuropathic pain**, pain crises, Fabry disease neuropathy
  - **proteinuria/albuminuria NOT attributable to other causes, evidence of renal impairment (may require renal biopsy if isolated)**
- Comprehensive and timely treatment of adult patients with Fabry disease should be directed toward prevention of (further) progression to irreversible tissue damage and organ failure.
- Care should include ERT and adjunctive therapies to treat symptoms that arise due to tissue injury and prevent non-specific progression of tissue injury.
  - ERT may slow deterioration of cardiac and renal disease, while also helping in reducing pain and improving overall quality of life.
- It is recommended that ERT be initiated as early as possible in female carriers with significant disease because of risk of cardiac, cerebrovascular and neurological complications.