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Patient Voice

Editorials

Original Articles

Acute Kidney Injury and ICU Nephrology

Chronic Kidney Disease

Reviews

On the Cover

Case Description:

What is the Diagnosis?

A 56-year-old male with history of controlled hypertension presented with subnephrotic range proteinuria. He immigrated to the United States from West Africa in 1999, travels frequently, and was treated with prophylactic antimalarial therapy in 2012. Cardiac, ophthalmology, and neurological evaluation were unrevealing. Laboratory results revealed bland urine sediment, urine protein creatinine ratio of 0.990 g/g, serum creatinine of 1.09 mg/dl, negative HCV antibody, HIV, normal protein electrophoresis, immunofixation, and positive HBV core antibody but quantitative HBV PCR of <10 IU/ml.

Image Description:

Light microscopy (left image, periodic acid-Schiff stain) shows glomerulus with enlarged foamy podocytes (arrow); middle image (methylene blue basic fuchsin stain) shows glomerulus with magenta colored lipid inclusions in podocytes (arrow); electron microscopy (right image) shows ultrastructure of whorled myelin bodies inside podocyte.

Teaching Points:

Fabry disease (FD) is a rare, progressive X-linked inborn error of metabolism that causes a functional deficiency of lysosomal α-galactosidase (GLA) (1). Glycosphingolipids, predominantly globotriaosylceramide, accumulate within kidney (podocytes, mesangial, endothelial, tubular cells), cardiac, nerve, and capillary endothelial cell lysosomes (2), leading to multisystem disease and early death (3). Incidence ranges from 1 in 476,000 to 1 in 117,000 in the general population (4). Clinical presentation includes angiokeratomas, acroparesthesia, corneal opacities, subnephrotic proteinuria, impaired urinary concentration, arrythmias, and deafness (3). Kidney biopsy findings with characteristic myelin figures may aid in diagnosis, but measurement of GLA levels and genetic testing is required to establish the diagnosis. This patient's GLA levels were severely reduced (<0.005 U/L, normal range 0.074–0.457 U/L) on repeated measurements. Enzyme replacement therapy is the standard treatment of FD. Recently, migalastat, an oral pharmacologic chaperone of GLA, has been used to effectively treat FD with amenable genetic variants.

References

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