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On the Cover

What's the diagnosis?

A 24-year-old man was found to have kidney failure and hyperuricemia by a local doctor and was referred to have his kidney failure evaluated. He was neither obese nor hypertensive. The values of serum creatinine, estimated glomerular filtration rate (eGFR), and serum uric acid were 1.31 mg/dl, 58 ml/min/1.73 m², and 9.1 mg/dl, respectively. After one year of follow-up, a kidney biopsy was performed because there was no improvement in his kidney function. The kidney biopsy findings showed minor glomerular abnormalities, and 16 out of 46 glomeruli had global sclerosis accompanied by tubulointerstitial fibrosis. An electron microscopic study revealed a layered structure in the thick ascending limb cell at a low magnification. The layered structure was compatible with hyperplasia of the membranes of the smooth endoplasmic reticulum. An electron microscopic study revealed a layered structure in the thick ascending limb cell at a low magnification. The layered structure was compatible with hyperplasia of the membranes of the smooth endoplasmic reticulum. The hyperplastic lesion implied that the endoplasmic reticulum reacted to the accumulated mutated uromodulin and led to the definitive genetic diagnosis. Careful examination of electron microscopic images of the tubulointerstitial area might help to diagnose this disease.

Image Descriptions:

Left panel: A layered structure was observed in the thick ascending limb cell at a low magnification.

Right panel: At a high magnification, the layered structure was compatible with hyperplasia of the membranes of the smooth endoplasmic reticulum.

Teaching points:

A heterozygous mutation in the UMOD gene causes autosomal dominant familial juvenile hyperuricemic nephropathy. In the present case, electron microscopy revealed that the transverse section of the thick ascending limb contained a transverse section of the hyperplastic endoplasmic reticulum. The hyperplastic lesion implied that the endoplasmic reticulum reacted to the accumulated mutated uromodulin and led to the definitive genetic diagnosis. Careful examination of electron microscopic images of the tubulointerstitial area might help to diagnose this disease.

(Images and text provided by Keiko Oda, MD (Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Japan), Kan Katayama, MD (Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Japan), Kensuke Joh, MD (Department of Pathology, Tohoku University Graduate School of Medicine, Sendai, Japan), Eiji Ishikawa, MD (Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Japan), Ryuji Okamoto, MD (Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Japan), and Masaaki Ito, MD (Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Tsu, Japan)