A case of advanced chronic kidney disease with giant mitochondria in renal tubular cells

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The kidney needle biopsy was obtained from a 67-year-old man with Chronic Kidney Disease (CDK) Stage 3 to 4 with a partial Fanconi syndrome. The light microscopic finding was non-specific mild to moderate cortical scarring of the kidney with moderate vascular disease. Light microscopy showed non-specific abnormalities including global glomerulosclerosis, moderate tubulointerstitial scarring, and moderate vascular disease. These findings are non-specific, but are common in the setting of hypertension. Electron microscopy focally detected giant mitochondria in tubular epithelial cells. We report the case here to examine the morphological features to understand the relationship between mitochondrial abnormality and CKD.

For the ultrastructure study, the biopsy was fixed in 2% glutaraldehyde and 2.5% paraformaldehyde. After post-fixation in 1% osmium tetroxide, the specimen was dehydrated through a graded ethanol series, and embedded in Eponate 12. The block was sectioned with a LEICA EM UC6 ultramicrotome and stained with uranyl acetate and lead citrate. The sections were analyzed with an FEI Tecnai G2 Spirit BioTWIN transmission electron microscope.

Electron microscopy revealed abnormal mitochondria and many of them are enlarged in size with various shapes (Figure 1). Footprints of mitochondria of this case were measured and compared with those from a kidney biopsy specimen with focal glomerulosclerosis and slight chronic tubulointerstitial inflammation (Figure 2). Dot plots of the measurement show significant difference in size between the two specimens. Some of the neighboring mitochondria had ambiguous borders suggesting that mitochondrial fusion might be a potential cause of giant mitochondria formation (Figure3). Giant mitochondria occasionally showed strange cristae.

In this case, a kidney biopsy was ordered to examine suspected proximal tubule injury because the patient suffered from partial Fanconi syndrome with high levels of monoclonal light chain [3]. Electron microscopy (or immunostaining) ruled out the possibility of light chain induced tubulopathy. The cause of the mitochondrial change is not known, but the observed morphological change in mitochondria is very similar to those reported for mitochondrial enlargement in renal tubular cells after some chemical treatment [1,2]. It is important to rule out that the patient was not treated with similar drugs causing tubulopathy. Another possibility is chronic kidney disease itself may cause such changes in mitochondria. Extensive electron microscopic study on stratified cohorts of chronic kidney disease patient is required to test this possibility.

References:

Figure 1. Mixture of cells with mitochondria of normal size (left side) and enlarged mitochondria (right side)

Figure 2. Enlarged mitochondria were detected in renal tubular cells from Fanconi Syndrome patient
Kidney biopsies from Fanconi Syndrome patient and glomerulosclerosis patient were examined by transmission electron microscopy. The sizes of the mitochondria of both specimens were determined by morphometry using ImageJ. The size of mitochondria of two specimens was significantly different as shown in the dot plot.

Figure 3. Mitochondrial Fusion?
Multiple mitochondria in Fanconi Syndrome kidney cells are packed at high density and some of them have ambiguous borders among them. This finding may suggest that mitochondrial fusion might be a potential mechanism of generation of enlarged mitochondria.