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On the Cover

What's the diagnosis? This electronmicrograph (original magnification $\times 20,000$) is from the renal biopsy of a 53 year-old woman with nephrotic syndrome. It shows fibrillar material in the glomerular basement membrane, and also in parallel "spicules" which are surrounded by podocyte cytoplasm. These fibrils measured 12 nm in average thickness. A Congo red stain showed red-green birefringent staining under polarized light microscopy and the deposits stained for lambda light chain, consistent with amyloidosis, AL lambda type. The differential diagnosis of fibrillar deposits in the kidney includes amyloidosis, fibrillary glomerulonephritis, diabetic fibrillosis, collagenofibrotic glomerulopathy, and fibronectin glomerulopathy. A combination of Congo red stain (and other amyloid stains), immunohistochemical stains, and electron microscopy permits distinction of these entities. Specifically, the thickness and distribution of the fibrils is important, with amyloid fibrils usually having a random orientation. However, amyloid deposits in the glomerular basement membrane may occasionally form distinctive spicules arranged perpendicular to the surface, mimicking the basement membrane spikes of membranous nephropathy. In this case, the spicules appear to be engulfed by the podocyte but this is likely an artifact. The pathogenesis of this peculiar arrangement of amyloid fibrils at the interface of the of the glomerular basement membrane and overlying podocyte is unknown. 63×39 mm (600×600 DPI)