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On the Cover

What's the diagnosis? Nodular glomerulosclerosis has classically been described in patients with long-standing diabetes mellitus. High blood glucose levels are toxic for mesangial cells, resulting in mesangial matrix overproduction and diffuse mesangial and eventually nodular glomerulosclerosis. A similar effect on mesangial cells can be seen in monoclonal immunoglobulin deposition diseases (most commonly kappa light chain deposition disease) or in heavy smokers where some unidentified components in cigarette smoke have a toxic effect on mesangial cells in predisposed patients. Nodular expansion and glomerulosclerosis can also be seen in chronic immune complex-mediated glomerulonephritides, such as a membranoproliferative glomerulonephritis and lupus nephritis; in such instances, one can still detect immune complex deposition by immunofluorescence and electron microscopy studies. Thrombotic angiopathies that have resulted in significant mesangiolysis can present with a nodular type of glomerulosclerosis as the lesions heal and sclerose. Amyloidosis does not cause nodular sclerosis, although the mesangium may show nodular expansion by amorphous and acellular material; these do not contain collagen and therefore the basement membrane silver stains will be negative, unlike in above-mentioned causes of nodular glomerulosclerosis. (Image and text provided by Dr. Vanesa Bijol, Brigham and Women's Hospital)