Diabetic Glomerulonephropathy

Diabetic glomerulonephropathy is the kidney disease seen in patients with significantly progressed diabetes. Nonenzymatic glycosylation of the glomerular basement membrane and arterioles causes initial hyperfiltration and increased GFR. Histological findings include hyaline arteriolosclerosis, mesangial expansion, type IV collagen deposition, and Kimmelstiel Wilson lesions in the glomerulus. This disease is classified as a nephrotic syndrome due to the significant proteinuria later on in the disease course.



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Pathophysiology

Nonenzymatic Glycosylation of Glomerular Basement Membrane

Nun-enzyme pouring Glue on Basement

Nonenzymatic glycosylation of the glomerular basement membrane (GBM) refers to the attachment of glucose to the molecular amino acid structure of the basement membrane in glomeruli. This happens when blood sugar is elevated chronically. It results in the loss of the negatively charged basement membrane with subsequent inability to repel negatively charged proteins. This prevents the kidneys from filtering blood normally.

Nonenzymatic Glycosylation of Arterioles

Nun-enzyme pouring Glue on Artery-o's

The glomerulus is fed by an afferent and efferent arteriole. In diabetes, chronically elevated glucose levels lead to nonenzymatic glycosylation of arterioles, where glucose becomes attached to the cellular structure of the arterioles. This results in hyaline arteriolosclerosis of the vessels and causes changes in glomerular blood flow.

Hyperfiltration

Hiker-filter-jar

In early stage nephropathy, nonenzymatic glycosylation in nephrons results in the formation of damaging reactive oxygen species. These trigger changes in nephron blood flow (due to aldosterone and other mediators) that ultimately result in dilation of the afferent arteriole, and constriction of the efferent arteriole. This mismatch results in abnormally increased GFR, called hyperfiltration. Hyperfiltration and the high pressures associated with it lead to direct damage of the glomeruli and scarring. Over a period of years, the GFR will eventually decrease as more glomeruli become scarred.

Increased GFR

Up-arrow Gopher

Increased GFR is caused by preferential arteriolosclerosis of the efferent arterioles and results in mesangial damage from hyperfiltration pressure. Another cause of increased GFR is the effect of hyperglycemic activation of the renin-angiotensin aldosterone system, resulting in increased efferent arteriole constriction.

Histological Findings

Hyaline Arteriolosclerosis

Highlighter Arteries-O-skull-roses

Hyaline arteriolosclerosis refers to the pathological deposition of protein in the vessel walls which ultimately results in luminal occlusion. This vessel pathology occurs secondary to nonenzymatic glycosylation, as well as hyperfiltration injury from increased luminal pressure in the glomeruli.

Mesangial Expansion

Maze-angel Expanding

Mesangial expansion is the proliferation of glomerular mesangial cells. This occurs secondary to non-enzymatic glycosylation, as well as hyperfiltration. Mesangial expansion can be seen on microscopy and in the correct clinical setting is suggestive of diabetic glomerulonephropathy.

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Type IV Collagen Deposition

(4) Fork Cola-gem

Type IV collagen deposition occurs within the glomerular and tubular basement membranes due to improper protein deposition.

Kimmelstiel Wilson Lesions

Camel-steel

Kimmelstiel Wilson lesions are nodular masses within the mesangial matrix, seen on microscopic slides of the glomeruli, which are diagnostic of diabetic glomerulonephropathy. These lesions represent type 4 collagen deposition as well as significant protein trapping.

Presentation

Nephrotic

Nerd-frog

When diabetic glomerulonephropathy progresses, it can result in nephrotic syndrome. Nephrotic syndrome is a group of signs including massive proteinuria defined as a daily loss of 3.5 grams or more of protein in the urine, hyperlipidemia, generalized edema, and hypoalbuminemia. Nephrotic syndrome can also be caused by several diseases other than diabetes, including membranous glomerulonephritis, minimal change disease, and focal segmental glomerulosclerosis.

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