Membranous Glomerulonephritis

Membranous glomerulonephritis, also commonly called membranous nephropathy, is the most common cause of nephrotic syndrome in Caucasian adults, and overall a common cause of nephrotic syndrome along with focal segmental glomerulosclerosis. Microscopy shows diffuse capillary and glomerular basement membrane thickening due to the accumulation of electron dense, immunoglobulin-containing deposits along the subepithelial side of the basement membrane. Primary disease is the most common form, seen in up to 75% of patients, and these patients often test positive for autoantibodies directed against the phospholipase A2 receptor (a transmembrane receptor present in podocytes). Secondary disease occurs from exposure to drugs like NSAIDs, gold or penicillamine. It can also develop secondary to underlying malignant tumors, lupus, and chronic hepatitis B and hepatitis C.



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Characteristics

Nephrotic
Nerd-frog
Nephrotic syndrome is described by a group of signs including massive proteinuria (defined as a daily loss of 3.5 gm or more of urinary protein), hyperlipidemia, generalized edema, and hypoalbuminemia, which results from renal pathology. It may present with renal vein thrombosis.

Diagnosis

LM Thickening of Capillary and Glomerular Basement Membrane (GBM)
(LM) Light-bulb over Thick Caterpillar with Basement Membrane
On light microscopy, the glomeruli typically exhibit uniform, diffuse thickening of the capillaries and glomerular basement membrane.

EM Spike and Dome Appearance with Subepithelial Deposits
Electrons at Spiky Dome with Sub-E-pick
On electron microscopy, the thickening is seen to be caused by irregular dense immune complex deposition between the basement membrane and podocytes. The basement membrane between the deposits appear as irregular spikes and over time, the spikes thicken to produce dome-like protrusions over the immune deposits. This is commonly described as having a “spike-and-dome” appearance with subepithelial deposits.

IF Granular
Fluorescent Grains
Immunofluorescence studies on biopsy samples demonstrate a granular pattern of IgG and complement staining of the glomerular basement membrane.

Primary

Phospholipase A2 Receptor Autoantibodies
Phospholipid-bilayer (A) Apple (2) Tutu Auto Ant-tie-bodies
Primary membranous nephropathy is the most common form. Patients often test positive for autoantibodies directed against the phospholipase A2 receptor, a transmembrane receptor present in podocytes.

Secondary

NSAIDS
N-sad
Membranous glomerulonephritis can result after exposure to various types of medications. NSAIDs such as ibuprofen or diclofenac are a potential cause of membranous glomerulonephritis. If this is suspected, the NSAID should be stopped.

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Gold

Pot of Gold

Nephrotic syndrome can either be primary, or secondary to a systemic disease or to medication use. For example, the use of medicines containing gold, which was used in the past for rheumatoid arthritis, may result in membranous nephropathy. Another causative medication is penicillamine.

Solid Tumors

Tumor-guy

Another secondary cause of membranous nephropathy is the presence of a solid tumor elsewhere in the body, particularly carcinomas of the lung and colon, along with melanoma. The pathophysiology may involve deposition of tumor antigens within the glomerulus.

Hepatitis B Virus (HBV)

Happy-tie Bee Liver Character

Patients with chronic hepatitis B and hepatitis C can develop membranous nephropathy. Although both have been implicated as etiologic agents, hepatitis B has a stronger association with membranous nephropathy, while hepatitis C is more strongly associated with membranoproliferative glomerulonephritis. The pathophysiology involves deposition of viral antigens within the glomerulus.

Lupus

Loopy-butterfly

Lupus is a systemic autoimmune disease which can result in different forms of renal disease. Membranous nephropathy is one such form, secondary to deposition of antibodies and complement within the glomerulus.

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