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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

A Review of Kidney Biopsy in Complement-Mediated Kidney Diseases

Announcer:
Welcome to ReachMD. This medical industry feature, titled “A Review of Kidney Biopsy in Complement-Mediated Kidney Diseases,” is sponsored by Novartis Pharmaceuticals Corporation. Here’s Dr Mark Haas.

Dr Haas:
Hello, my name is Dr Mark Haas and I am a renal pathologist at Cedars-Sinai Medical Center in Los Angeles, CA. In this video, we will discuss kidney biopsy findings in the diagnosis of two forms of glomerular disease one more common (immunoglobulin A nephropathy and the other much rarer (complement 3 glomerulopathy).

IgA nephropathy is an immune complex-mediated lesion initiated by an autoantibody binding to an autoantigen (galactose-deficient IgA1) and, in some cases, involves activation of the lectin pathway of the complement system in addition to the alternative pathway.[1] By contrast, the pathogenesis of C3 glomerulopathy involves abnormal regulation of the alternative pathway related to mutations in and/or autoantibodies against one or more components of the alternative pathway.[7,8] Kidney biopsy is the gold standard for diagnosis of IgA nephropathy and C3 glomerulopathy in native or transplanted kidneys.[1,2] Beyond diagnosis, kidney biopsy findings are also useful for predicting prognosis and guiding treatment decisions.[1]A pathological diagnosis of IgA nephropathy or C3 glomerulopathy requires collection of an adequate tissue sample.[9] This process typically involves a needle biopsy of the kidney collected under ultrasound or computed tomography guidance.[9]

Optimally, a trained technician, pathologist, or pathologist assistant is present at the kidney biopsy with a dissecting microscope to determine tissue adequacy,[3] which generally requires a minimum of eight glomeruli.[4] The glomeruli are visualized as red circles under the dissecting microscope.[3] The tissue sample is then divided, and samples are placed into separate containers to be processed for:[3] light microscopy (with buffered formalin for paraffin embedding) for hematoxylin and eosin, periodic acid-Schiff, and Masson’s trichome and silver stains.[3] Immunofluorescence (Zeus or Michel’s tissue preservative) on frozen sections for immunoglobulins (IgG, IgA, and IgM), complement (C1q, C3, and sometimes C4 or C4d), and kappa and lambda light chains.[3,10] Some laboratories perform immunohistochemistry on formalin-fixed tissue rather than immunofluorescence.[10] Tissue for electron microscopy is fixed in 2% to 3% glutaraldehyde or 1% to 4 & paraformaldehyde.[3]

A diagnosis of IgA nephropathy requires glomerular IgA staining.[11] This staining is mainly in the mesangium, with or without concomitant capillary loop staining.[5,11] IgG and/or IgM may or may not be present but when present, staining is less intense than for IgA.[1,5] C3 is present in more than 90% of cases.[11] C1q (indicative of classical pathway complement activation) is typically absent.[12]

Electron microscopy is usually not required to diagnose IgA nephropathy but may be helpful in ruling out some other lesions.[3] Electron microscopy shows mesangial electron-dense deposits, sometimes accompanied by subendothelial and, more rarely, sub-epithelial deposits.[11] Biopsies showing IgA nephropathy are graded according to the Oxford MEST-C scores that identify five histopathological features[1]:

- M: mesangial hypercellularity[1]
- E: endocapillary hypercellularity[1]
- S: segmental glomerulosclerosis[1]

- T: tubular atrophy and interstitial fibrosis[1]
- C: cellular or fibrocellular crescents[1]

C3 glomerulopathy has two morphological forms: C3 glomerulonephritis and dense deposit disease.[2] Both can have a variable appearance by light microscopy, although the most common histological appearance is a diffuse membranoproliferative pattern,[7,8] characterized by:

- Mesangial and endocapillary hypercellularity,[8]
- A lobular appearance of the glomeruli,[8]
- And glomerular basement membrane double contours on the PAS and silver stains[7]

By immunofluorescence, C3 glomerulonephritis and dense deposit disease both show dominant glomerular staining for C3, with only weak or absent staining for immunoglobulins or C1q.[7,8] C3 glomerulonephritis and dense deposit disease are best distinguished from each other by electron microscopy.[13] With C3 glomerulonephritis characterized by mesangial, subendothelial, subepithelial, and intramembranous or transmembranous deposits of varying electron-density.[7,13] And dense deposit disease by highly electron-dense, ribbon-like deposits within the glomerular basement membrane.[7] However, some cases of C3 glomerulopathy may have electron microscopic features of both C3 glomerulonephritis and dense deposit disease.[13]

In summary, kidney biopsy is the gold standard for diagnosis of IgA nephropathy and C3 glomerulopathy.[1,2] The accurate interpretation of kidney biopsy findings is important not only for diagnosis but also guiding clinical management of these conditions. Thank you for your time and your interest in this video.

Announcer:

Updated ICD-10 codes were recently approved for complement-mediated kidney disease.[14]

Learn more about how these ICD-10 codes aim to address gaps in diagnosis, surveillance, and research of complement-mediated kidney disease[15-17] on the Renal Halls of Science.

This program was sponsored by Novartis Pharmaceuticals Corporation. If you missed any part of this discussion, visit ReachMD.com/IndustryFeature. This is ReachMD. Be Part of the Knowledge.

References:

1. Mehdi A, Taliercio JJ. *Cleve Clin J Med*. 2003;90(6)(suppl1);e1-e4, doi:10.3949/ccjm.90.e-s1.02
2. Caravaca-Fontá F et al. *Nephron*. 2020;144(6);272-280. doi:10.1159/000507254
3. Walker PD et al. *Mod Pathol*. 2004;17(12):1555-1563. doi:10.1038/modpathol.3800239
4. Cattran DC et al. *Kidney Int*. 2009;76(5):534-545. doi: 10.1038/ki.2009.243
5. Robert IS et al. *Kidney Int*. 2009;76(5):546-556. doi: 10.1038/ki.2009.168
6. Trimarchi H et al. *Kidney Int*. 2017 May;91(5):1014-1021. doi:10.1016/j.kint.2017.02.003
7. Barbour TD et al. *Semin Nephrol*. 2013;33(6):493-507.
8. Hou J et al. *Glomerular Dis*. 2022;2(3):107-120. doi:10.1159/000524552
9. Mukhtar KN et al. *J Pak Med Assoc*. 2012 Sep;62(9):880-882.
10. Smith RJ et al. *Nat Rev Nephrol*. 2019;15(3):129-143. doi:10.1038/s41581-018-0107-2
11. Pattrapornpiut P et al. *Am J Kidney Dis*. 2021 Sep;78(3):429-441. doi:10.1053/j.ajkd.2021.01.024
12. Maillard N et al. *J Am Soc Nephrol*. 2015;26(7):1503-1512. doi:10.1681/ASN.2014101000
13. Medjeral-Thomas NR et al. *Clin J Am Soc Nephrol*. 2014;9(1):46-53. doi:10.2215/CJN.04700513
14. Centers for Medicare & Medicaid Services. Accessed September 26, 2023. https://www.cms.gov/medicare/coding/icd10
15. Sun AZ et al. *Perm J*. 2020;24(2):19.126. doi:10.7812/TPP/19.126
16. Dendooven A et al. *BMC Nephrol*. 2021;22(1):193. doi:10.1186/s12882-021-02365-3
17. Kwon CS et al. *J Health Econ Outcomes Res*. 2021;8(2):36-45. doi:10.36469/001c.26129

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