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The Complement System in the Pathogenesis of IgA Nephropathy

Announcer:
Welcome to ReachMD. This medical industry feature, titled "The Complement System in the Pathogenesis of IgA Nephropathy," is sponsored by Novartis Pharmaceuticals Corporation. Here's Dr Richard Lafayette.

Dr Lafayette:
Hello, my name is Dr Richard Lafayette and I am a nephrologist at Stanford University Medical Center in California. In this video, we will discuss the role of the complement system in immunoglobulin A (or IgA) nephropathy.

IgA nephropathy is an autoimmune disease. Its pathogenesis involves dysregulation of the complement system.[1,6,7] The complement system is an important component of innate immunity; it is crucial for defense against pathogens and clearance of immune complexes and injured cells.[6,7]

The complement system comprises three pathways:[1,6]

- The classical pathway
- The lectin pathway, and
- The alternative pathway.

The **classical pathway** is activated by the binding of the pattern-recognition molecule C1q to IgG or IgM antibodies or immune complexes.[1] The **lectin pathway** is activated by the binding of pattern recognition molecules (like mannose-binding lectins) to carbohydrates expressed on the surface of cells or pathogens.[2,7] The **alternative pathway** is continuously activated at a low level due to spontaneous hydrolysis of the C3 molecule.[1,5] The alternative pathway also amplifies the activation of the other two pathways (as this is referred to as the amplification loop).[1] Activation of these three pathways results in opsonization of pathogens, inflammation, and cell lysis.[1] Both the lectin and alternative pathways may be activated in a subset of patients with IgA nephropathy.[5]

Such activation leads to the generation of the anaphylatoxins C3a and C5a, as well as the membrane attack complex C5b9, with subsequent promotion of inflammatory mediator and matrix protein production by mesangial cells.[1,6] In 17% to 25% of patients with IgA nephropathy, evidence of lectin pathway activation was confirmed based on mannose-binding lectin co-deposition with IgA.[4,5] In more than 90% of patients with IgA nephropathy, evidence of alternative pathway activation was confirmed based on C3 mesangial co-deposition.[6] In more than 75% of patients with IgA nephropathy, evidence of alternative pathway activation was also confirmed based on properdin co-deposition with IgA and C3.[6] C1q is rarely detectable in patients with IgA nephropathy, suggesting that classical pathway activation does not contribute significantly to disease pathogenesis.[5]

Immunofluorescence data indicate that C3 glomerular deposition may be a potential independent prognostic marker in IgA nephropathy.[4,8] In a Chinese cohort of 821 patients with IgA nephropathy, those with positive glomerular C3 deposition had more severe clinical and histopathological characteristics and a higher MEST-C score.[8] In addition, patients with an increasing intensity of C3 deposition were more likely to have microscopic hematuria, fibrous crescents, interstitial inflammatory cell infiltration, and higher segmental sclerosis lesion scores.[8]

In summary, insights into the complement system are critical to our understanding of the pathogenesis of IgA nephropathy.[6] Additional

research on the complement system is needed to further understand its role in IgA nephropathy. Thank you for your time and interest in watching this video.

Announcer:
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