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Expert Opinions on Characteristics of Patients With C3G at High Risk of Progression

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How do you identify patients with C3G who may be at high risk of progression?

Dr. Rizk:
Proteinuria the higher the proteinuria, the worse the outcome. But there are also you know genetic so we recommend that you do a functional assay to look for the complement dysregulation and document it. And you it's recommended that you do a genetic panel looking for genetic mutations that lead to overactivation of the complement system. And some of these genetic mutations carry prognostic information.

Dr. Nester:
Higher urine proteins and a lower GFR at presentation generally signify a patient who is going to progress faster. I believe very uh much in the biomarkers helping us be able to determine who has a more aggressive underlying complement system. We're talking about pathogenic gene variants. We're talking about autoimmune drivers of disease or nephritic factors. Those would be the major biomarkers, if you will, that will suggest those patients that are going to progress

I'll mention also, very quickly, that the biopsy is also likely to be useful.

Dr. Sethi:
You can see patients with endocapillary hypercellularity, patients who have necrosis or crescents on the biopsy, or even a membranoproliferative pattern of injury, what's called the MPGN. This you know has progressed, or is going to progress quite rapidly. Very often, these patients will also show you a fair amount of tubular atrophy and interstitial fibrosis. So this is a group that you know has poorer prognosis.

Dr. Herlitz:
So certainly, active proliferative lesions are a big thing of concern when we see those, because those in front of your eyes are likely to result in glomerular damage. That's likely to progress to glomerulosclerosis.

But what I actually find to be more reliable markers of progression, in my experience, is the presence of sclerotic glomeruli, whether they be segmentally sclerotic or globally sclerotic, and the presence of tubulointerstitial fibrosis. Those are so important because we have no way of turning back the clock. Once the glomerulus is sclerotic, we cannot make it unsclerotic. Once you have tubulointerstitial fibrosis, we have no way of remaking that tubulointerstitium.

So I really focus on really accurately assessing how much chronic damage there is, because even mild levels of chronic damage, whether it be glomerular scarring or tubulointerstitial fibrosis, especially in young patients, suggests that these patients have significant possibilities for progressive disease.

Dr. Rizk:
Find the patient with C3G, which again is a rare disease, you have the same risk factors based on labs. So kidney dysfunction, the earlier you catch them, the better off you're going to be you.

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