Transcript Details

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Identifying Patients at High-Risk for IgAN Progression: Key Factors to Know

Announcer:
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Dr Francis:
Welcome everyone to a podcast on IgA nephropathy and high risk for progression patients. My name is Dr Jean Francis. I'm an Associate Professor of Medicine at the Chobanian and Avedisian School of Medicine at Boston University in Boston. Over the past 15 years of my clinical practice, I have also managed many patients with IgA nephropathy in the pre- and the post-transplant setting.

In this podcast, we will discuss clinical and histopathological factors that help identify patients with IgA nephropathy at high risk for disease progression. Today I'm joined by my colleague, Dr Anthony Chang. Welcome. Please tell us a little bit about yourself, Anthony.

Dr Chang:
I'm Anthony Chang. I practice renal pathology here at the University of Chicago. I have been here for 19 years. I'm the Director of the Renal Pathology Fellowship as well as the Renal Pathology Division, and I am also involved as the Associate Program Director of the Pathology Residency Program.

We see almost 1000 kidney biopsies here at the University of Chicago every year, and so at least a handful of IgA nephropathy diagnoses are made every month in our practice. Even though we make this diagnosis very frequently and it's often known as the most common glomerulonephritis worldwide, the challenge remains how do we identify the patients who will have worse outcomes? IgA nephropathy is a heterogeneous disease, and the risk for disease progression is an important topic to discuss since up to 40% of patients with IgA nephropathy develop worsening kidney function and progress to kidney failure within 10 to 20 years of their diagnosis. So, potential indicators for disease progression vary from patient to patient and are important for nephrologists and nephropathologists to assess and take into consideration. So, Dr Francis, in your experience, how do you determine if a patient with IgA nephropathy is at high risk for disease progression?

Dr Francis:
So, in my clinical experience, predicting disease course can be challenging, especially since not all patients will experience the same rate of progression. Few metrics may be useful, like proteinuria, C3 deposition, and the MEST-C scores. High proteinuria levels may indicate high risk for disease progression. KDIGO guidelines define high-risk patients as those with proteinuria that is superior to .75 grams per day to 1 gram per day despite 3 months of optimized supportive care. Proteinuria is used also as a surrogate end point in clinical trials and is routinely monitored in the clinic while following patients with IgA nephropathy. In my practice, any persistent proteinuria of at least 1 gram per day or more despite maximized supportive therapy is high risk for disease progression. Other colleagues of mine use lower cutoffs of .75 grams per day of proteinuria, as recommended per KDIGO. Regardless of which cutoffs clinicians use, this all emphasized the importance of persistent proteinuria as a marker for IgA nephropathy progression.

Dr Chang:
So, beyond proteinuria, what other clinical factors do you take into consideration for your assessment of risk for disease progression?

Dr Francis:
That's an important question. So, proteinuria in combination with several additional risk factors can be used to determine if a patient is at high risk for progression. For example, uncontrolled hypertension is associated with poor IgA nephropathy prognosis and accelerated

disease progression. So, we need to control blood pressure very well in those patients. KDIGO guidelines recommend managing blood pressure and persistent hematuria as part of care and management for patients. Persistent hematuria has been shown to be a risk factor for kidney disease progression in patients with IgA nephropathy independent of the proteinuria. Persistent hematuria, in conjunction with proteinuria, may also be considered a high risk for disease progression. Patients with lower eGFR, or estimated GFR, at the time of diagnosis of IgA nephropathy, especially if their GFR is less than 60 mL per minute, are at high risk for progression to end-stage kidney disease. Beyond these clinical factors, histopathological characteristics of IgA nephropathy can also be used to inform patient prognosis.

Dr Chang:
I certainly agree with that last statement as a renal pathologist. Metrics from the kidney biopsy report can also be useful to predict disease progression, including the MEST-C scores and degree of C3 deposition. However, the level of C3 accumulation in the glomeruli varies between patients, and some studies have found that the intensity of C3 staining on the kidney biopsy associates with an increased risk of progression to kidney failure. And I think that adding C3 mesangial deposition to conventional risk factors may improve predictability of kidney disease progression. So, while complement staining is part of the differential diagnosis approach for the evaluation of glomerulonephritides, including IgA nephropathy, C3 staining is not required for a diagnosis of IgA nephropathy. And in my practice, I typically include this information in all of my pathology reports.

Dr Francis:
So, Dr Chang, what parameters within the MEST-C scores in your opinion are considered risk factors for disease progression?

Dr Chang:
So, the Oxford IgA nephropathy classification was first published in 2009, and initially they identified four pathologic parameters, M-E-S-T. And so, the M stands for mesangial hypercellularity. The E stands for endocapillary hypercellularity. The S stands for segmental sclerosis, and the T stands for tubular atrophy/interstitial fibrosis. And actually, in that original publication it was the Tscore that was the most significant of all of the parameters even though the other three parameters involved the glomeruli. It was later on that they added the C-score because everyone thought it doesn't quite make sense that cellular crescents is not significant, and it turns out that when you look at the original design they had excluded patients with rapid renal failure because you potentially don't know if that just represents that those patients are at the tail end of their disease progression or if there truly is a sudden change in their renal function. And so, it was later on confirmed that crescent formation is also significant and so that's why we now have MEST-C score, or MEST-C. So, patients with higher MEST-C scores also present with higher C3 deposition, and I think it is most beneficial when pathologists provide as much information as possible in their kidney biopsy reports so that nephrologists have a comprehensive picture when assessing a patient's risk for progression.

So with all this information, how do nephrologists synthesize biopsy and clinical information to determine a patient's prognosis or level of risk?

Dr Francis:
As a nephrologist, you know we rely heavily on you guys with your reporting to us to help guide us in the management of those patients. So, according to KDIGO guidelines, clinical and histological data at the time of the biopsy can be used to risk stratify patients. The International IgA Nephropathy Prediction Tool predicts long-term risks for worsening kidney function measured as a 50% reduction in the estimated GFR or the development of kidney failure. Although it calculates the risk for progression based on many of the factors we discussed today, it doesn't currently use complement staining in its assessment. I believe that together, proteinuria, C3 deposition, and the MEST-C scores, along with the consideration of a combination of other risk factors that we discussed already like hypertension, hematuria, proteinuria should provide the clinicians with the appropriate tools for identifying patients at high risk for IgA nephropathy progression.

Dr Chang:
It is certainly important to quickly identify those patients at high risk for progression so that they can be closely monitored and managed appropriately over time.

Dr Francis:
With that, thank you so much for joining us today. Thank you, Dr Chang, for being with us also, and thank you to our listeners. I hope that this podcast has provided insights into how both clinical and histopathological factors can help identify patients with IgA nephropathy at high risk for disease progression. Thank you.

Dr Chang:
It was a pleasure to be a part of this.