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Enhancing IgAN Care: The Importance of a Proactive Approach

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You're listening to *Clinician's Roundtable* on ReachMD. Here's your host, Dr. Gates Colbert.

Dr. Colbert:

Welcome to *Clinician's Roundtable* on ReachMD. I'm Dr. Gates Colbert, and joining me to share strategies for enhancing the care of patients with IgA nephropathy, otherwise known as IgA or IgAN, is Dr. Suneel Udani, who's a consulting physician with NANI, Nephrology Associates of Northern Illinois and Indiana and the Medical Director of NANI Research. Dr. Udani, it's great to have you here today.

Dr. Udani:

Dr. Colbert, thanks so much for the invitation and the opportunity to speak. This is a very dynamic and exciting topic in nephrology and science as a whole, so I'm thrilled to be here.

Dr. Colbert:

So if we start with some level setting, Dr. Udani, what do we need to know about IgA nephropathy?

Dr. Udani:

So no discussion about IgA nephropathy would be complete without stating the first fact that is, IgA nephropathy is the most common primary glomerulonephritis in the world. That being said, it's still quite rare. You know, if you talk about prevalence, it varies quite a bit, about somewhere in the range of 1 to 5 for 10,000 people. So we're still talking about a rare disease. And that's relevant in a few ways: one, it's easy to miss, especially since it initially usually presents in younger individuals that are otherwise healthy, and so it may manifest only by early onset of hypertension, elevated serum creatine that can be overlooked for other things, and microscopic hematuria that can also be overlooked.

So in terms of what to know in the first place is making sure that we recognize it and keep it top of mind, especially in young individuals that have some of these atypical presentations, like hypertension that is disproportionate to their age, elevated serum creatine, and microscopic hematuria because those may be the first clues that we have that they have underlying IgA nephropathy.

Dr. Colbert:

And when we're caring for patients with IgA nephropathy, what priority should we keep top of mind?

Dr. Udani:

The first thing, especially as we're getting better tools to treat and intervene in IgA nephropathy, is risk stratification. The kidney biopsy essentially is required to make the diagnosis of IgA nephropathy, so that is first and foremost. And within the biopsy, there are certain features that we look for: degree of interstitial fibrosis, tubular atrophy, glomerular sclerosis, and the Oxford classification, which looks at different compartments of the glomeruli and the tubulointerstitial compartment and gives us a better idea of kidney health as a whole. It may also give us an idea of how acute the presentation really is or how chronic.

Those clinical characteristics are important, but what is reliably the most relevant prognostic factor is degree of proteinuria. And whatever way you choose to estimate it, whether it's 24-hour urine collection, urine PCR, urine albumin to creatinine ratio, quantifying proteinuria at the initial evaluation in someone with IgA nephropathy, and ongoing, it really is key to appropriately risk stratify individuals.

There was a study published most recently in the last year out of the RaDaR Registry, which is a registry out of the United Kingdom, and it really takes all comers with rare diseases, in this case, IgA nephropathy, and it followed a much broader population than other

previous IgA nephropathy studies have. And it was very simplistic in its design. It's a registry study that people were followed yearly, and baseline levels of proteinuria were assessed, and then ongoing follow-up with GFR trends, interventions, etcetera.

And what we saw is that even individuals with urine protein creatinine ratios down to 0.5 g/g a threshold that we used to think was "safe," they still have very high risk for progression to end-stage kidney disease. And given that many of these patients are young—most of the diagnoses occur early in the third decade of life—we really have to think not necessarily how is my patient doing now, but what to expect for their future? Because this is really going to be a lifelong disease. It is not something that unfortunately goes away in most people. It is a chronic disease, and it will be progressive if we don't intervene appropriately.

Dr. Colbert:

So guidelines and recent studies have come out regarding IgA nephropathy and new tools, but what happens if we are not acting proactively and identifying and trying to treat these patients?

Dr. Udani:

Yeah, it's a great question, Dr. Colbert. Unfortunately, what we see is a slow, steady progression. And the thing is, it's not RPG yet, right? It doesn't manifest in the way that full-blown nephrotic syndromes do. In the most cases, people are relatively asymptomatic. Maybe their blood pressure's elevated, maybe they have a little bit of edema, but really, they're asymptomatic. And so if you're not paying attention, you could very easily miss the progression.

And unfortunately, what we know is that based on RaDaR and other studies, over a 10-year period when people have even modest degrees of proteinuria, many of those patients, 1/3, even 1/2 to any degree of proteinuria, may end up on dialysis. And you have think about, again, the total lifespan of an individual. So say they're in their 30s or 40s and they're diagnosed, they go 10 years and end up getting end-stage kidney disease and end up getting transplanted; is that transplant going to last the rest of their life? It's unlikely, unfortunately, and so they're going to end up either on dialysis at some point later on or requiring a second transplant at an older age where their condition is, unfortunately, more complicated overall.

So if we do not think proactively and if we do not act and intervene with tools that are becoming more available, what we should expect is that there is a slow but steady progression of renal dysfunction to end-stage kidney disease.

Dr. Colbert:

For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Gates Colbert, and I'm speaking with Dr. Suneel Udani about how we can mitigate the risk of irreversible kidney damage in patients with IgA nephropathy.

So, Dr. Udani, it's become clear from our discussion that it's important to take a proactive approach to IgA care, but what are some challenges that can keep us from intervening early?

Dr. Udani:

First of all, diagnosis and risk stratification. Many of us try to practice guideline-based therapy, and because of the rapidly evolving field in IgAN and other glomerular diseases, the guidelines have not been able to keep up with the evidence that's there.

So why is that relevant to your question? I think that it becomes much too easy to act with therapeutic inertia. Now what do I mean by that? We see a patient in front of us, we say, oh, their urine protein ratio's 0.9, it's 1.1, 1.2, even 0.8. The serum creatinine hasn't changed in the last year, but if you peek back the last 5 years, it's been a slow progression. So again, it's very easy to overlook these things and the progression if we're not paying attention closely.

The next step is actually intervening. I think that nephrologists have not had a lot of tools in our toolbelt for the last three decades. And as a result, there is a certain level of discomfort or I'll say an uncomfortable feeling when we initiate newly approved because we haven't had any. And so when there are new therapies available, naturally, there's anxiety about doing that. What's the expected side effect profile? What's been that person's individual experience? And a patient may ask, 'What's been your experience with it?' And of course, you have to be honest and say if you only have limited experience, you share that with them.

And so we then have to go back to the evidence and say, "Okay, do I have enough faith in this evidence, do I have enough understanding of this evidence to pull me out of that therapeutic inertia? Is it enough for me to act?" And I think that's really the issue, are we willing to act? Because it's much easier to say yes, things are okay, and I don't want to expose someone to a new drug or a new therapy that we don't have 20-year data on. But unfortunately, that person doesn't have 20 years; their renal function will deteriorate before that.

Dr. Colbert:

And with those challenges in mind, how can we overcome them?

Dr. Udani:

It's a great question. Being vigilant is the key, and again, not being kind of timid about new therapies. I think that we have followed proteinuria with all of our patients with diabetic kidney disease and nondiabetic kidney disease for years. And so we know that that is something we can follow, something we can easily measure, and it's something that we're comfortable with.

The other thing is just familiarizing ourselves with how these new therapeutic classes work because I think that naturally, there's a lot of information, and if we're uncomfortable with them then, of course, we're much more reluctant to initiate therapy. So there is going to be a steep learning curve for nephrologists as a whole and a level of discomfort that we have not had before. And I think as long as we acknowledge this, as long as we counsel each other, and as long as we lean on each other, those experts; there are people that, of course, have had more experience, and so those are the people to go to and say, "I have this patient with this. What's been your experience? Have you used it? What do you expect? How should I counsel my patients?" so that we all grow more comfortable with these therapies and then we can advise our patients accordingly.

Dr. Colbert:

And before we close out, Dr. Udani, are there any other strategies for enhancing IgA nephropathy care that you'd like to share with our audience today?

Dr. Udani:

I think that patient education is key because ultimately, a motivated patient will be the most dynamic force for change. So helping them understand why we should be concerned. That first visit with a patient is key to help them understand how we think IgA develops and why we're going to pick the therapies we're going to pick. And then helping them understand the rationale for our action. That we are worried about, not them tomorrow, not them next week, but I'm worried about them 5 years from now, 10 years from now, etcetera.

And then what do we know is helpful? We know lowering proteinuria across disease spectrums is helpful, whether to IgA or other diseases. So if we have therapies that we can utilize that can do that, let me get comfortable with those and let me implement those.

Once you start utilizing these therapies, of course, your comfort level, it's just like we prescribe statins or ACE inhibitors or ARBs, they become much more commonplace, and our ability to uptake these therapies and then implement them will be much more easy.

Dr. Colbert:

Well, with those strategies and best practices in mind, I want to thank our guest, Dr. Suneel Udani, for joining me to discuss how we can optimize IgA nephropathy care. Dr. Udani, it was great having you on our program.

Dr. Udani:

Dr. Colbert, thanks so much for giving me the opportunity and having this discussion.

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