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IgA Nephropathy Care: Ensuring Timely Detection and Intervention

Announcer:
You're listening to *Clinician's Roundtable* on ReachMD, and this episode is sponsored by Vera Therapeutics. 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 discuss the importance of early diagnosis in IgA nephropathy, or IgAN for short, are Drs. Meghan Sise and Ellie Kelepouris. Dr. Sise is the Director of Onconephrology at Massachusetts General Hospital and Associate Professor of Medicine at Harvard Medical School. Dr. Sise, thanks for being here today.

Dr. Sise:
Thanks for having me.

Dr. Colbert:
Also joining us is Dr. Kelepouris, who's the Director of the Outpatient Dialysis Program and a Professor of Clinical Medicine at Penn Medicine. Dr. Kelepouris, it's great to have you here with us, as well.

Dr. Kelepouris:
Thank you very much.

Dr. Colbert:
So, Dr. Sise, let's start with some background. Why is IgA nephropathy so difficult to detect and what are the clinical blind spots that often delay diagnosis?

Dr. Sise:
Well, like many kidney diseases, IgA nephropathy doesn't have a lot of symptoms, especially in its early stages. So the two most common ways people present with IgA nephropathy is, first, completely asymptomatically, just with blood detected in the urine on a urinalysis. The trouble is that primary care doctors don't do urinalysis. It's not part of the regular screening for healthy patients. So, these types of patients may only get a urinalysis done through life insurance screening or some other testing that leads them to be found to have blood in the urine. And so this can go on for years where no one's checking their urine, and so that leads to delay in presentation.

Other patients can notice times when their urine is dark or when they see what they think to be blood in the urine.

But again, they don't always go to the doctor, or when they do, they're perhaps told that they have a urinary tract infection. And so it can take years of having blood in the urine before patients make it to see a nephrologist.

Dr. Colbert:
Turning to you now, Dr. Kelepouris, what are some of the red flags that should prompt an early diagnostic work-up?

Dr. Kelepouris:
As my colleague, Meghan Sise, noted, the presence of blood in the urine is really a hallmark for IgA nephropathy, but it's usually microscopic. Patients don't usually see it. If they do, it may be associated with a throat infection and upper respiratory infection. And that's something that should trigger primary care physicians to think about IgA nephropathy, particularly if the patient is young with uncontrolled hypertension or hypertension that's primary with no secondary causes. That's really important. If a young person presents with hypertension and they're of East Asian descent, that makes it easier. But just the presence of microscopic hematuria or hypertension—unexplained by infection like a urinary tract infection—should really trigger a workup, particularly for IgA nephropathy and

other glomerular diseases. But particularly IgA, because it's becoming much more common: the most common GN in the world.

Dr. Colbert:
Coming back to you, Dr. Sise. When IgA nephropathy is suspected according to those criteria, how do you then approach the decision to proceed with a kidney biopsy?

Dr. Sise:
Well, I try to explain to the patient how important it is that we know for sure what the cause of the protein and blood in the urine is, and that really, there are no blood tests that can tell us for sure. And so the kidney biopsy is really the only way to make the diagnosis. And so I review with them the risks of a kidney biopsy, the biggest including bleeding, and so we think about what risk factors the patient may have for bleeding and make sure to stop blood thinners or anticoagulants ahead of time. And those are the things that, when a patient is hesitant and saying, "Why would I want to have a kidney biopsy?" We're telling them, not only do we need diagnostic precision, but also the kidney biopsy helps us prognosticate and figure out how severe the IgA nephropathy is. Sometimes we can see a lot on the biopsy that tells us more than just a blood test could tell us.

We have to remember that, especially in young people, you can have a lot of kidney injury going on before you see a rise in the serum creatinine, and these are the things we're trying to detect when we do a kidney biopsy early on in the disease, really as soon as soon as we suspect it.

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 Drs. Meghan Sise and Ellie Kelepouris about the value of early diagnosis and intervention in IgA nephropathy.

So, Dr. Kelepouris, if we take a look at the impact of early detection, could you tell us how prompt diagnosis and treatment can improve long-term outcomes for patients?

Dr. Kelepouris:
Well, prompt diagnosis and treatment are everything in this disease. Many patients who present with microscopic hematuria and hypertension, maybe low levels of proteinuria, already have established chronic kidney disease. And I try to educate the patients about how important it is to recognize that there are two things going on. There's the IgA component that we were going to talk about, but also the fact that lifestyle modification is really important, and so is blood pressure control. Obviously, the biopsy is critically important in making that diagnosis. And we know that there are only two validated markers of prognosis with IgA: proteinuria and eGFR. So identifying early on whether patients have proteinuria and microscopic or macroscopic hematuria is critically important because we have to identify those two validated markers and intervene early. And the lower the urinary protein is post treatment, the better the prognosis. So, focusing on those two markers—and they're so interconnected—is really important in changing the natural history of this disease and decreasing progression to end-stage renal disease.

If you look at most of the data in the United States, and actually, the world, most patients with IgA nephropathy present already with the chronic kidney disease stage 2, so it really is up to us to intervene and try to delay the progression of disease very early on.

Dr. Colbert:
Before we wrap up our program, I'd like to ask each of you one more question. Starting with you, Dr. Sise, what recommendations do you have for our listeners about diagnosing IgA nephropathy early and what common missteps or missed opportunities should we be on the lookout?

Dr. Sise:
I think the most important takeaway for clinicians is that you cannot be reassured just because the serum creatinine is normal, and that what we as nephrologists look at are the urinary abnormalities. As we're making our early diagnosis, these are the things that are going to tell us best what's going on in the kidneys. So hematuria and proteinuria are everything we look for in the early stages of the disease, and so following up what may be considered minor urinary abnormalities are really the window of what's happening for the first decades of people's disease with IgA nephropathy.

So following up on urinary abnormalities and considering a nephrology referral for unexplained proteinuria is really key. If a patient has a story for urinary tract infection and you give it antibiotics, and then the urinary abnormalities persist or they keep coming back with very vague symptoms, you would want to make sure that these patients are followed up and that they can get sub-specialty referrals early. I think that this is a disease that affects young people and while they may not rapidly progress to end-stage renal disease over the span of two or three years, more than half of people with IgA nephropathy are at risk of kidney failure in their lifetime. And so what we're trying to prevent with early diagnosis is kidney failure that occurs later on in life, which is so important in young patients to have long life

expectancy.

Dr. Colbert:
And Dr. Kelepouris, I'll give you the final word. From your perspective, what systemic or educational shifts could help close the diagnostic gap for IgA nephropathy?

Dr. Kelepouris:
I think it's really important to create an educational platform for our primary care physicians, our family practitioners, that the recognition of any abnormalities in someone's urine is really important. As early as you possibly can, perform the dipsticks in the urine, as we alluded to earlier. I think that population screening is really important in this disease, and working with our primary care physicians to do urinalysis or dipsticks is really important. So is working with our societies that are patient-facing to create educational programs for both patients and referring physicians. And I do think that nephrologists need to take the lead in this. It's almost a call to action to intervene early so that we can save kidney lives, because the progression is just so steep after the initial diagnosis.

Dr. Colbert:
With those important insights in mind, I want to thank my guests, Dr. Meghan Sise and Ellie Kelepouris, for joining me to share these strategies for improving the early recognition and management of IgA nephropathy. Dr. Sise, Dr. Kelepouris, it was great having you both on the program.

Dr. Sise:
Thanks so much for having us.

Dr. Kelepouris:
Thank you very much.

Announcer:
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