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Building a Multidisciplinary Approach to IgA Nephropathy Care

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:
This is *Clinician's Roundtable* on ReachMD, and I'm Dr. Gates Colbert. Joining me to discuss individualized, multidisciplinary care for IgA nephropathy patients is Dr. Abdallah Geara and Dr. Ellie Kelepouris. Dr. Geara is an Associate Professor of Clinical Medicine, the Clinical Director of the Glomerular Diseases Program, and Director of Onconephrology at Penn Medicine in Philadelphia. Dr. Geara, thanks for being here today.

Dr. Geara:
Thank you, and looking forward to our discussion.

Dr. Colbert:
Also joining us from Penn Medicine is Dr. Kelepouris. She's a Professor of Clinical Medicine, the Vice Chief of Clinical Affairs, and the Medical Director of Outpatient Dialysis Programs. Dr. Kelepouris, it's great to have you here as well.

Dr. Kelepouris:
Thanks for having me, Gates.

Dr. Colbert:
So Dr. Kelepouris, I'll start with you for some context. What are some of the most telling signs, both in lab work and clinical presentation, that prompt you to consider IgA nephropathy in your differential diagnosis?

Dr. Kelepouris:
IgA nephropathy can present at any age, and it has a range of presentations. It could start with asymptomatic microscopic hematuria to rapidly progressive glomerulonephritis. So it's a dilemma. Gross hematuria, called synpharyngitic hematuria, or the old Berger's disease, is a much more common presentation in children, whereas subclinical disease or intermittent microscopic hematuria is more commonly seen in adults.

Additionally, proteinuria is really important, but it may or may not accompany the presence of microscopic hematuria. And although proteinuria is an important surrogate marker of disease, an elevated serum creatinine may also emerge later. But they're critical to assess disease severity and not just disease presentation. To really define IgA nephropathy, you have to perform a kidney biopsy. So a kidney biopsy remains the gold standard, but knowing when to pursue it can vary based on context and on clinical presentation.

I think it's important to know that lack of symptoms leads to delays in workup or missed referrals, so you have to be—it's really important—very, very carefully analyzing your patient's presentation and have a really good multidisciplinary team, as we'll talk about later, to really address patient concerns.

Dr. Colbert:
Turning to you now, Dr. Geara, let's say IgA nephropathy is the leading diagnosis. What comprehensive strategies do you use to confirm it?

Dr. Geara:
Well, in order to confirm a diagnosis of IgA nephropathy, you need a kidney biopsy. There are a few steps that we should undertake

before and after the kidney biopsy to evaluate for other differential diagnosis. As Dr. Kelepouris mentioned, the presentation can be asymptomatic, but also the lab findings are compared with nephritic syndrome, and some other differential diagnoses that are well known for nephritic syndrome can be ANCA-associated vasculitis, lupus nephritis, and some other differential diagnosis that require some serologic workup, in addition to viral workup and autoimmune workup.

But most of these workups will be negative, and that will push us toward doing a kidney biopsy that will confirm diagnosis of IgA nephropathy. The kidney biopsy has both diagnostic and prognostication values. We know that on the kidney biopsy, the Oxford classification did specify the MEST-C scoring, and the high MEST-C score is associated with worse prognosis for these patients.

After doing a kidney biopsy, another step is required before moving ahead with the therapies: evaluating for secondary causes of IgA nephropathy. And the secondary causes of IgA nephropathy can be liver disease, HIV, other viral etiology, infection-related IgA deposition in the kidney, IgA glomerulonephritis, and some other differential diagnoses that could be compatible with secondary IgA nephropathy. I forgot to mention inflammatory bowel disease is also a common concomitant disease with IgA nephropathy.

Dr. Kelepouris:
Abdallah, what biomarkers are really being studied to go along with the diagnosis? And is there any information you can give us about that?

Dr. Geara:
Yeah, I think there are several biomarkers. Again, in terms of biomarkers for IgA nephropathy, the most common one that we talk about is galactose-deficient IgA1. I think as far as diagnostic value of all the biomarkers, including galactose-deficient IgA1 for diagnostic purposes, the hope is quite low that it will be like a diagnostic biomarker, mainly because there is a lot of overlap between the healthy population and patients who have the disease manifestation.

I think that we have better hope for galactose-deficient IgA1 and some other biomarkers as markers of disease severity, disease relapse, or maybe tapering or adjusting therapy based on these biomarkers. I think that's where the hope is in the future—hopefully that these biomarkers will be utilized the most.

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. Abdallah Geara and Ellie Kelepouris about how we can comprehensively diagnose and treat patients with IgA nephropathy.

Now, Dr. Geara, let's shift gears and talk about management. Once IgA nephropathy is confirmed, how do you individualize your treatment strategy, particularly when managing complications like hypertension or proteinuria?

Dr. Geara:
Yeah, we know that for IgA nephropathy, the guidelines and the management right now are changing quite a bit, and this is driven by the available tools. We have four medications that were approved recently over the last couple of years, including targeted-release formulation of budesonide, Nefecon. We have iptacopan, we have sparsentan and atrasentan, and we are expecting a few other medications to be approved.

This increases the tools that we have in our hands to treat IgA nephropathy. And the current understanding of IgA nephropathy pathophysiology does drive us to treat the two big buckets that are driving the disease progression. One of them is inflammation due to the IgA deposition and complement activation. The other one is treating the chronic kidney disease component of the IgA nephropathy.

So first, addressing proteinuria will require an extensive counseling regarding lifestyle modification, including weight loss, smoke cessation, adjustment of the diet—more specifically, low-salt diet. In addition to this, it does require that traditional chronic kidney disease management medication that includes RAS blockade, SGLT2, possibly in the future GLP-1 inhibitor. And we do have also sparsentan and atrasentan, which show very good results as far as proteinuria control and CKD progression when it comes to IgA nephropathy. So this is the big bucket, what's related to chronic kidney disease management and proteinuria management.

As far as the other bucket, which does address the IgA formation, the tools that we have right now include systemic corticosteroids and targeted-release formulation of budesonide, Nefecon, in addition to also other immunosuppressants like mycophenolate mofetil. And we do have also a complement inhibitor, iptacopan, that was recently approved for IgA nephropathy.

So a combination of medications that address all these pathways is required in the majority of patients with IgA nephropathy.

Dr. Colbert:
And coming back to you, Dr. Kelepouris, could you walk us through what an interdisciplinary care team should look like for IgA nephropathy, and how incorporating these specialists can improve outcomes?

Dr. Kelepouris:
It's very well known that patient-centered care is the best care, and an interprofessional team to educate patients and clinicians on IgA nephropathy is really the medium that we can use to really provide patient-centered care for greater outcomes.

Although nephrologists may lead the team, it's really the other members of the team that really make tremendous contributions, both to lifestyle modification, as Dr. Geara talked about, as well as supportive care. The dietitians as members of the team are highly valued because they can guide patients to sodium, protein intake, weight loss, as well as smoking cessation, and all those can significantly impact outcomes.

Crucial to the success of interdisciplinary care is the presence within a team of a pharmacist. Pharmacists can assist with optimizing regimens and providing an analysis of out-of-pocket costs for medications that can be very, very expensive and hard to get for patients who have social determinants of health that are not favorable for very expensive medications. Managing polypharmacy is really important. I have patients who say to me, "Dr. Kelepouris, I can only take four medications. Which are the most important ones?" And so educating patients as to the importance of their medications and addressing polypharmacy concerns is really very important. And finally, I think what pharmacists contribute, which is really, really crucial, is monitoring nephrotoxic agents and medications that have interactions with other medications. So defining a really safe, effective treatment plan is really very, very important.

To round out the team, very important members of the team are our allied professional health providers, physician's assistants, and also primary care physicians. So we need to have better screening of our patients in the community in order to diagnose this disease which, as we said, can present with a mosaic of findings, including simply microscopic hematuria. So education can be provided to primary care physicians, and they become a really integral part of this team.

And finally, I think the pediatricians are really very important. Pediatricians are really important in East Asia, where this disease really is generally endemic/pandemic. And just screening of children within at-risk populations and using pediatricians' skill I think is really very important.

So I would say that we really need multidisciplinary care to provide the highest level of care for these patients, and integrating a care team is crucial to providing this optimal management of IgA nephropathy. And finally, I think an interdisciplinary team leads patients to make very good decisions, including what medications to choose and also clinical trial selection, which I think is very important in this disease and can define better outcomes.

Dr. Colbert:
Before we come to the end of our program, I'd like to ask each of you to share one critical takeaway about comprehensive care for IgA nephropathy. Dr. Geara, let's start with you.

Dr. Geara:
It is well known that IgA nephropathy is diagnosed late in the United States. I think three fourths of the patients are diagnosed with stage three and beyond. This highlights the need for early diagnosis and early recognition across all specialties, specifically, like Ellie mentioned, primary care providers, urologists, nurse practitioners, PAs that are seeing these patients and identifying these subtle findings being hematuria and proteinuria. And this will hopefully lead to early referral and early management of these patients and change their prognosis significantly for this very severe progressive disease.

Dr. Colbert:
And Dr. Kelepouris, I'll give you the final word.

Dr. Kelepouris:
Thank you, Gates. I agree with Dr. Geara, and the points that he made are very important. I would also stress the patient voice and interdisciplinary care and communication with patients and their providers—both the family providers as well as their pediatricians.

I think population screening in the United States is not as robust as it can be, particularly for this disease. So it really does take a village to make the diagnosis. As Dr. Geara said, patients are diagnosed late in the disease, and we need more early diagnosis and a very successful integrated team in order to early diagnose and provide supportive care as well as advanced care and alter the natural history of this disease.

Dr. Colbert:
With those key insights in mind, I want to thank my guests, Dr. Abdallah Geara and Dr. Ellie Kelepouris, for joining me to share their insights on how we can provide personalized care for patients with IgA nephropathy. Dr. Geara, Dr. Kelepouris, it was great having you both on our program.

Dr. Kelepouris:
Thank you very much.

Dr. Geara:
Thank you.

Announcer:
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