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Achieving Success in IgAN & FSGS

Announcer:
Welcome to CME on ReachMD. This episode is part of the Global Kidney Academy and is brought to you by Medtelligence.

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Dr. Griffin:
The management of patients with chronic kidney disease and IgA nephropathy or focal segmental glomerulosclerosis poses challenges, and these patients face increased long-term risks of morbidity and mortality. How can we diagnose these patients early in the course of their disease progression and what is the current standard of care? Are there any insights to be gained from recent clinical trials that can aid us in achieving sustained proteinuria remission and improving patient outcomes?

Join us as we discuss how early diagnosis and emerging treatments will help us achieve successful outcomes in patients with IgA nephropathy and FSGS.

This is CME on ReachMD and I'm Dr. Sian Griffin.

Dr. Floege:
And I'm Jurgen Floege.

Dr. Gesualdo:
And I am Dr. Loreto Gesualdo.

Dr. Griffin:
We have a lot to discuss today so let's begin. We'll start with a look at immunoglobulin A nephropathy, or IgAN, with a very interesting case presentation from Loreto.

Dr. Gesualdo:
Well, this is a 33-years-old Caucasian man that presented to our attention with whooping cough in child, bronchial asthma under chronic treatment with beclomethasone for multirole inhalation, atopic dermatitis, and finding of proteinuria and microhematuria on standard urine examination in October 2016. There's a – this is the classic, you know, patient. It is very frequent, you know, to see this phenotype in IgA nephropathy patient. It is what we call urinary abnormalities.

So, this was a – a patient that presented the first time to the nephrologist with a proteinuria of higher than 3g with microhematuria. We did a biopsy, and this mast is, you know, classification of mast was no presenting and mesangial proliferation so, was an M1 E0 S0 T0 C0 mast classification. So, they started to treat him with the standard of care.

Dr. Floege:
To note, the GFR was normal, was it?

Dr. Gesualdo:
That was very normal so, it was 89 mL/min if I remember very well. So, they decided to go with a correct lifestyle plus standard of care therapy RAS inhibition. We were in 2016. So, it started with the irbesartan but it moved after to ramipril 10 mg, per day. And he responded very well. His proteinuria started to reduce, and he was, you know, getting 1.5. They decided to increase the amount of ramipril. They put, you know, the patient from 10 mg up to 20 mg and it did it very well. There was not, you know, 20 mg of ramipril and

the proteinuria was going down less than 1 g. But, in the 2018 – 2019, his proteinuria was still, you know, under 1g, but the GFR started to reduce. So, it started to reduce going down and also the serum creatinine was starting, you know, to grow. So, they were following the patient and he got it, you know, until February 2023, that he got a 2 mg/dL of serum creatinine and the proteinuria 1.5. So, they decided to add on the top of the RAS inhibition a gliflozin. 10 mg of dapagliflozin was added, and actually the patient came to my attention and I decided that was at the end of March, I decided to do again the biopsy and his MEST was M1 E1 S1 T1 C0 so, as you know Jurgen, I at that point, for me, E1 is still active, you know, lesion but you have also S1 T1. Since the patient is a young patient, I decided to start with corticosteroids. So, this is the case. So, we should discuss on this, I think. What do you think?

Dr. Floege:
Well, he's a perfect illustration of the dilemma we have. I'm a strong believer in supportive care, but supportive care in many of these patients is not the miracle cure. No doubt about that. And right now we often didn't have much better than systemic steroids.

So, he has a long lifespan and clearly, he doesn't want to be on dialysis by the age of 60. We're used to thinking in terms of few years, we have to think in terms of decades here.

Dr. Gesualdo:
I agree 100%. For this reason, I decided, you know, to go with corticosteroid therapy. In Italy today we can, you know, use the – the classical Pozzi schema or the Manno schema because we don't get – have, you know, budesonide as you have, you know, in Germany. But I think that this patient deserved at the beginning immunosuppression and maybe he deserves more renal cardio protection and there are, you know, other drugs that are coming and the goal is, as you know, the KDIGO study does, you know, to get the blood pressure under – under 120 and the proteinuria level less than 1. More, you know, less is the proteinuria, better for sure will be the outcome and

Dr. Floege:
But, there's a high likelihood that we will drop this criteria in terms of proteinuria. We've just learned from RADAR, the beautiful analysis, that even what we considered safe proteinuria below 1 g per day is not safe.

Dr. Gesualdo:
No. I agree.

Dr. Floege:
Loreto, what insights from recent clinical trials may reshape our treatment strategy and improve outcomes for patients with IgA nephropathy like yours?

Dr. Gesualdo:
Well, that we are living a new era in nephrology. We have, you know, new drugs that are changing our standard of care. We are moving from the RAS inhibition. We are adding, you know, gliflozin and very soon we will be able also to add on the top of RAS inhibition and gliflozin, you know, new drugs. Maybe, you know, we will move from the RAS inhibition and gliflozin to sparsentan and gliflozin because PROTECT trial was showing that, compared to irbesartan to the RAS inhibition, sparsentan that is a dual blocker, that blocks the ET1 and AT1 was able to reduce more than 50% compared to irbesartan the proteinuria in patient with IgA nephropathy.

Dr. Griffin:
For those just tuning in you're listening to CME on ReachMD. I'm Dr. Sian Griffin and here with me today are doctors Jurgen Floege and Loreto Gesualdo. We're discussing strategies for success in IgA nephropathy and FSGS.

Dr. Floege:
So, Sian, how can we achieve early diagnosis in patients with focal segmental glomerulosclerosis, or FSGS, and does proteinuria play the same role as with IgA nephropathy?

Dr. Griffin:
Yes, thank you. Proteinuria is clearly highly significant in FSGS as well as with IgA nephropathy and I was very interested in your comment, Loreto, that re-biopsying your patient with IgA nephropathy to reassess.

Dr. Gesualdo:
That was a wise choice, I think.

Dr. Griffin:
Mmhm. And I think biopsies are incredibly important, not only to make a diagnosis in somebody who's presenting newly to you, but also in these patients who don't have an ideal response to their current treatment, to really guide where we're going next with things. Just coming back to – IgA nephropathy, I think with these additional treatments coming online, the biopsy is going to become absolutely key

and perhaps guide in which of the dominant pathways.

Dr. Gesualdo:
But this does apply also for cause of glomerulosclerosis because I think that, you know, what, you know, the DUPLEX study is teaching us that we need to, you know, to better phenotype the patient.

Dr. Griffin:
Absolutely.

Dr. Gesualdo:
You know, to treat better them because you are going to tends to you know, there's a huge pipeline in nephrology. We will have, you know, many drugs, so we will be able to do precision medicine. What do you think, Floege, do you agree with this?

Dr. Floege:
Sure, sure, and FSGS seems to be a particular case. Maybe you want to comment on the more recent studies.

Dr. Griffin:
Yeah, so – so with FSGS, it's very much a pathological diagnosis, it's not a clinical diagnosis, and we know that there are many initiators of podocyte injury that will eventually culminate in what we see down the microscope and call these FSGS lesions. But yes, a wide range of insults can come on perhaps to an individual with a susceptible genetic background and so the treatments are going to be very different. When we assess proteinuria in FSGS, Jonathan Troost of Michigan has recently developed a disease-specific assessment of proteinuria, using three large cohorts of well-phenotyped patients and has found a tighter definition of partial remission, which is associated with a much more favorable outcome than the traditional partial remission endpoint we use. And I think that's going to be very valuable when we're rapidly evaluating the impact of new drugs, to have these surrogate markers to assess what progress we're making with individual patients.

Dr. Griffin:
Well, this has certainly been a fascinating conversation but, before we wrap up, I'll invite you each to share a final take-home message with our audience. Jurgen, what do you hope our listeners will leave with today?

Dr. Floege:
Diagnose early, start supportive care, don't wait too long to optimize it. Hit hard and early and the goal is proteinuria as low as possible. There is no safe proteinuria.

Dr. Griffin:
And Loreto, how about you?

Dr. Gesualdo:
Well, I think that nephrology is leading a new era. We have now new drugs that can, you know, slow the progression of renal disease, it can protect the heart. So, it's important, the early diagnosis, because early diagnosis, it means to treat early and better the patient, and this means not anymore dialysis. So, please, try to identify patient with CKD. We know only 10% of them, we are missing all the other one. So, early diagnosis first.

Dr. Griffin:
Yeah. I think my reflection on that is that a lot of this comes down to primary care and the first people that see patients. So, the importance of measuring blood pressure, checking urine dipsticks and ensuring we catch these patients before they are on the slope of decline.

Dr. Griffin:
Unfortunately, that's all we have time for today. So, I want to thank our audience for listening in and also thank both Dr. Jurgen Floege and Dr. Loreto Gesualdo for sharing all of your valuable expertise and insights. It was great speaking with you today.

Dr. Gesualdo and Dr. Floege:
Thank you.

Announcer:
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