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Unmasking IgAN: Achieving Earlier Diagnosis

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Dr. Barratt:
This is CE with GLC, and I'm Dr. Jonathan Barratt. Here with me today is Dr. An De Vriese.

An, what should providers be thinking about when they see a patient with suspected IgA nephropathy?

Dr. De Vriese:
Well, Jonathan, the insight has grown over the past 4 years that we often recognize the disease too late, and early diagnosis is very important because timing fundamentally determines what we can achieve for our patients.

And as you know, IgAN is by nature a very heterogeneous disease. Some patients will do remarkably well for many years, even decades, with only minimal intervention, but others will silently progress and accumulate damage long before we as clinicians fully realize what's going on.

And the difficulty is that early on the disease is often asymptomatic. There's microscopic hematuria, maybe some modest proteinuria, and that can easily be overlooked or underestimated.

So why is early diagnosis important? The thing is that the pathogenesis of IgAN is dynamic. In the early phases, there's active inflammation, immune complex deposition, complement activation, ongoing injury, which is potentially modifiable. But as time goes on, chronic structural damage develops with glomerulosclerosis, interstitial fibrosis, tubular atrophy, and so on. And once that chronic damage dominates, our therapeutic window becomes much more narrow.

So, in other words, the earlier we identify the disease, the greater the chances are that we are still dealing with a modifiable process rather than with an irreversible one.

Now, the challenge is to achieve early diagnosis in a disease that's often silent, and I think it starts with awareness, both in primary care and in nephrology. Persistent microscopic hematuria should not be dismissed, especially when it's accompanied by even low-grade proteinuria. And too often in the past, these findings were followed conservatively, sometimes for years. So creating a lower threshold for referral to nephrology when there's microscopic hematuria, low-grade proteinuria, that could already make a significant difference.

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And for us nephrologists, the kidney biopsy is central for diagnosis, and perhaps it has been underused in the past. There's sometimes a reluctance to biopsy patients with preserved kidney function and just modest urinary abnormalities. But paradoxically, that's often exactly where the diagnostic yield and the clinical impact might be highest.

And in the future, biomarkers may play an increasingly important role. We are seeing some promising developments with serological markers, urinary markers, that could help us identify IgAN earlier and better define a window of opportunity. But for now, these tools are not yet fully ready for routine clinical use.

So I guess early diagnosis is important, but it's not a single intervention. It's a mindset. We have to take subtle urinary abnormalities seriously. We have to follow patients longitudinally. We have to lower our threshold for referral, for performing a kidney biopsy, and we have to recognize that what may appear mild today could represent the early phase of a progressive disease. And ultimately, the goal is clear. If we can shift the diagnosis to earlier in the disease course, we improve our chances of intervening at a stage where the disease is still modifiable, long before chronic damage locks in the long-term prognosis.

Dr. Barratt:
Thanks, An. I mean, I couldn't agree more with you. I think the real challenge for us now, with all these wonderful new therapies coming, is getting our hands on these patients as quickly as possible so that we really give them the best chance of never having to see what a dialysis machine looks like.

And I think we're going to have to be innovative in how we work with our primary and secondary care colleagues. Two secondary care colleagues come immediately to mind. One are the urologists. They see a lot of patients with hematuria, and the hope is that when they've excluded urological causes, that they make sure they think nephrology rather than discharging that to primary care and thinking the job is done. And certainly in the UK, we're trying to work hard with our urologists.

And the other are the obstetricians and midwives because certainly in the UK, and I think across Europe, when a lady is pregnant, they have their urine dipsticked regularly to look for asymptomatic hematuria. But actually, that's the first time a lady may ever have had a urine dipstick screen, and this is a great time to pick up occult glomerular disease.

So we need to think carefully, based around our healthcare systems, where are opportunities to start identifying these patients earlier?

And, I mean, I completely agree with you. We need to work within our colleagues as well to think about that threshold for kidney biopsy because I certainly work with colleagues who have a very high threshold to do a kidney biopsy, and therefore they make diagnoses very late. And it is really difficult, if not impossible, I would suggest, to resurrect a scarred glomerulus once it has gone through that process.

So I couldn't agree with what you've said more, An. I think we need to prioritize working with our colleagues to promote early referral and, within our specialty, early diagnosis, low threshold to biopsy, and once we have the diagnosis, a low threshold to intervene with disease-modifying therapies.

But I'm afraid that's all we've got time for. Thank you for joining us today.

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