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Challenges in the Early Diagnosis of AAV

Announcer:
Welcome to this episode of KDIGO Conversations in Nephrology. This episode, titled Challenges in the Early Diagnosis of AAV is provided by KDIGO and supported by Amgen. Here's your host, Dr. Vladmir Tesar.

Dr. Tesar:
We will today discuss the challenges in early diagnosis of ANCA-associated vasculitis, as early diagnosis may have a decisive impact on the outcome of our patients.

Hello and welcome to KDIGO Conversations in Nephrology. I am Dr. Vladimir Tesar, Head of Nephrology at General University Hospital in Prague. And joining me to discuss the challenges in the early diagnosis of ANCA-associated vasculitis is Dr. Duvuru Geetha. Geetha is a nephrologist and Professor at the Department of Medicine Johns Hopkins University School of Medicine, Baltimore, Maryland, USA. Her research interests include different aspects of diagnoses and treatment of ANCA-associated vasculitis, including renal transplantation in patients with ANCA-associated vasculitis. Geetha, welcome to the program.

Dr. Geetha:
Thank you, Dr. Tesar, for the kind introduction. It is a great honor for me to participate in this discussion about diagnostic delays in vasculitis.

Dr. Tesar:
Thank you. So let's begin our discussion with the first question. Are delays in diagnosis common in AAV? And what are the factors that may contribute to these delays?

Dr. Geetha:
This is a very important question and an area where we really need to focus on, Dr. Tesar. We need to increase our efforts on educating primary care physicians and patients. Delays in diagnosis are common and is an important contributor to patient comorbidities as well as healthcare expenditures. The median time to diagnosis is about 7 months with a wide range from a few weeks to over a year.

Now delays in diagnosis can be due to multiple causes, disease-related, patient-related, and healthcare system-related factors play a role. First of all, AAV is a rare disease with an incidence of 10 to 20 cases per million. So, gaining expertise is not easy. Secondly, AAV patients may have symptoms that are shared by other common diseases, and therefore, it is difficult especially for the physician of first contact. In addition, misdiagnosis is common as a number of other diseases can mimic vasculitis with infections, allergies, and other autoimmune diseases being common.

One of the classic examples is a GPA patient who presents with recurrent sinus symptoms. And some of these patients actually can go through multiple rounds of antibiotics before a diagnosis of AAV is considered. Furthermore, AAV is also a heterogeneous disease, and patients may be seen by many specialist physicians before a diagnosis is considered. I believe improving access to specialists is important, since this is one of the factors that is contributing to delay in diagnosis.

Finally, depending on the organ involvement, AAV can be silent. Classic examples include those with renal limited AAV and interstitial lung disease. But we have some good news, there is wider availability of ANCA testing so more cases of AAV have been diagnosed in the last two decades. Educating patients and physicians on the multi-system nature of AAV and related symptoms is key for early detection. Since kidneys are often involved in AAV affecting 80 to 90% of the patients, screening for renal vasculitis with urine analysis and serum creatinine should be done in all patients with suspected AAV. Delays in diagnosis can have negative health consequences, especially when a major organ like kidney is involved.

Dr. Tesar:
Many thanks for the summary of the main causes of delays in diagnosis of ANCA-associated vasculitis. And now I have the second question, how can we increase the awareness in the disease and early diagnosis?

Dr. Geetha:
Sure. Early recognition and treatment of vasculitis is critical to prevent complications. We need to recognize that patients come with different levels of education. Educational efforts should be spearheaded by vasculitis experts. Patients should be empowered through disease education and raising vasculitis awareness in the general public. Caregivers should also be educated as well. Even something simple like giving an information leaflet on diagnosis and treatment of vasculitis at the end of the clinic visit can play a huge role in raising disease awareness and improving patient engagement. The role of patient advocacy groups to increase disease awareness has been well recognized in many communities.

We should also remember that listening to patients is quite important as patients are often able to tell about disease relapse before the physician suspects that relapse. Finally, it is important to educate patients with renal vasculitis on the use of urine dipstick, which can detect hematuria and proteinuria which are early signs of renal vasculitis.

On the same page, education of trainees, physicians, and allied health professionals is equally important to raise awareness of vasculitis. We should educate them on thinking about systemic diseases when someone initially presents with sinusitis, and then with pneumonia or hearing issues, rather than treating them as different illnesses. Similarly, when someone presents with recurrent bouts of pneumonia, we should take a step back and think of non-infectious etiologies. Information should filter from the vascular experts to primary care physicians and specialists through workshops, webinars, seminars, and grand rounds.

Online learning, why our website dedicated to diagnosing and managing vasculitis may be helpful for physicians, we should especially educate them on the various ways vasculitis can present and the best approach to diagnosing the various vasculitis as well as the treatment options. Educating on recognizing disease and treatment-related complications and managing these complications is paramount to improving outcomes.

Dr. Tesar:
Many thanks for sharing with us these very important ideas how to improve early diagnosis of ANCA-associated vasculitis.

For those just tuning in, you are listening to KDIGO Conversations in Nephrology. Our today topic is challenges in early diagnosis of AAV. I am Dr. Vladimir Tesar, and I'm speaking with Dr. Duvuru Geetha.

And my third question is on a bit different topic. Can we rely on ANCA positivity, or is it necessary to have a histology confirmation?

Dr. Geetha:
Sure. So, ANCA can be actually negative in 10 to 30% of cases, depending on where and when the studies were conducted. For example, the incidence of ANCA-negative disease is higher in European cohorts. We have to remember the use of antigen specific immunoassay is important. And when diagnosis is in doubt, histologic confirmation is needed to guide immunosuppressive therapy. ANCA-negative patients are also more likely to have renal-limited disease or disease limited to upper respiratory tract.

Dr. Tesar:
So would you recommend renal biopsy in all patients with ANCA positivity and suspected AAV and renal involvement?

Dr. Geetha:
Yeah, so kidney biopsy, you know, is one of the organs where you have a high diagnostic value with a greater than 90% yield. But more importantly, the kidney biopsy gives prognostic information. So we should consider kidney biopsy, especially if there are no contraindications in all patients.

A diagnostic kidney biopsy is often indicated in patients who are ANCA negative to exclude vasculitic mimics like other systemic rheumatic diseases, infections, and malignancies. But what we do need to remember however, is that a kidney biopsy should not delay treatment initiation.

Dr. Tesar:
In your opinion, is there any role of repeat biopsy in ANCA-associated vasculitis?

Dr. Geetha:
This is an excellent question and a really unexplored area. So we currently use resolution of hematuria as one of the markers for renal remission. But close to 50% of the patients have persistent hematuria at 6 months post induction therapy. In a single-center study of protocol biopsies, there was evidence of disease activity after clinical remission was achieved in some of the biopsies. We all know that

treatment-related side effects, especially infections are common during induction therapy. Therefore, repeat biopsies should be considered in patients with persistent hematuria and those with poor response to therapy to guide immunosuppression, especially with the changing landscape in the treatment of AAV.

Dr. Tesar:
Many thanks. And probably the most important is my last question. How should we collaborate with our colleagues across specialties in order to diagnose as early as possible to patients with ANCA-associated vasculitis?

Dr. Geetha:
Again, an excellent question. So, diagnosing and managing AAV requires a team of experts who are familiar with vasculitis, the different treatment options, and complications related to both vasculitis and treatments. Given the multi-system involvement in vasculitis, shared decision-making and collaboration among specialists is a central pillar, both in diagnosis and follow-up.

The model in most vasculitis centers is to have a collaborative team with nephrologists, rheumatologists, pulmonologists, and ENT specialists who have special interest and training to take care of vasculitis patients. Collaboration is especially important when presentation is atypical. For example, when a patient with recurrent sinusitis is evaluated by a rheumatologist but the ANCA test is negative. However, if the patient has hematuria, a nephrologist can do a kidney biopsy to confirm a diagnosis of vasculitis. Similarly, collaboration is important to diagnose refractory disease, vasculitis mimics, and disease relapse.

Dr. Tesar:
Many thanks. Before we close, Geetha, are there any final messages or takeaways you'd like to leave with our listeners?

Dr. Geetha:
I think the three main messages I would like the audience to take away are: A, number one, education, both from a patient perspective and a healthcare professional perspective. And then number two is access to vasculitis experts because that's a common cause of delay in diagnosis. And number three is collaboration amongst specialists because that is really key both in managing disease as well as the complications related to disease and treatment.

Dr. Tesar:
I completely agree. And I hope that you all enjoyed our discussion today. I want to thank my guest, Dr. Duvuru Geetha, for joining me. Geetha, many thanks for accepting my invitation to our program.

Dr. Geetha:
Dr. Tesar, it has been a great honor to participate. I hope that today's discussion has not only reflected our current situation on the delays to diagnosis of AAV, but also has highlighted some of the steps we can take to diagnose vasculitis early.

Dr. Tesar:
Thank you. I am Dr. Vladimir Tesar. To access this and other episodes in our series, visit KDIGO on Spotify, or KDIGO.org/podcast. Thanks for listening.