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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

C3G Care Collaboration: Best Practices for a Multidisciplinary Approach

Announcer:
You're listening to *Clinician's Roundtable* on ReachMD, and this episode is sponsored by Novartis Pharmaceuticals Corporation. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome *to Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and joining me to share their viewpoints on collaborative care for patients with complement 3 glomerulopathy, or C3G for short, are Drs. Yoni Peleg and Abdallah Geara. Dr. Peleg is an Assistant Professor of Medicine in the Division of Nephrology and Hypertension at the Feinberg School of Medicine at Northwestern University. Dr. Peleg, it's great to have you with us.

Dr. Peleg:
Thank you very much for having me. I'm glad to be here.

Dr. Turck:
And Dr. Geara is an Associate Professor of Clinical Medicine and Clinical Director of the Glomerular Diseases Program at the Perlman School of Medicine at the University of Pennsylvania. Dr. Geara, thanks for being here today.

Dr. Geara:
Thank you for inviting me.

Dr. Turck:
So if we begin at the start of the care journey, Dr. Peleg, what would lead you to suspect a patient has C3G? And how would you confirm a diagnosis?

Dr. Peleg:
So C3G is a glomerular nephritis, so when a patient would first come to my clinic, and I would have a concern for a glomerular nephritis, C3G would oftentimes be on my differential diagnosis. Now C3G is not very common. The annual incidence is something like 1 out of 1,000,000 patients. So it wouldn't be very high there necessarily, but it is something I would certainly think about. So if a patient were to come in with abnormal kidney function and a urine that would have me concerned for a glomerular disease, such as having albumin in the urine or blood in the urine, it certainly would be something on my differential diagnosis. And then when I look into more of the history before the kidney biopsy, which is the only way to confirm the diagnosis, it might go up higher on my differential.

Dr. Turck:
And once that patient is diagnosed with C3G, Dr. Peleg, when would you refer them to a specialist like Dr. Geara?

Dr. Peleg:
Once the patient is first diagnosed with C3G, there are a couple of things that I would like to do first before sending out a referral to a C3G specialist. I first, especially if the patient is older, would like to do a screen for a monoclonal gammopathy. And the reason is that for patients who are newly diagnosed with C3G who are older in age, very often the trigger of their C3G is the monoclonal gammopathy, and actually treatment of the C3G in that scenario would be treatment of the monoclonal gammopathy.

Whether or not to refer someone to a specialty center will depend a lot on how the patient looks clinically. What is the patient's kidney function? What is the degree of the protein in the urine? If the patient has relatively mild amount of protein in the urine – say less than

1,000 milligrams or 1,500 milligrams per day and normal kidney function – I may actually elect to first treat conservatively with RAAS inhibition and blood pressure control. If, however, the patient seems to be at higher risk for progressive disease, such as high levels of protein in the urine and already having abnormal kidney function, I would have a lower threshold to offer that patient immunosuppression. And the initial immunosuppression I would use is mycophenolate and prednisone therapy, and if that patient is not responding to that therapy, I think it would be appropriate for that patient to be evaluated at a specialty center for further considerations of additional therapies as well as potentially clinical trials.

Dr. Turck:
For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Drs. Yoni Peleg and Abdallah Geara, about collaborative care strategies for patients with complement 3 glomerulopathy, or C3G.

Now if we switch gears here a bit, Dr. Geara, would you share a case that demonstrates how you worked with the multidisciplinary care team to provide patient-centered care?

Dr. Geara:
So I will give you a couple of cases to illustrate the importance of a multidisciplinary approach. The first patient was a 19-year-old that was diagnosed with C3G and referred for a second opinion. The first step in the second opinion evaluation was to review the biopsy to make sure that we're not missing, for example, another form of immune complex GN, to make sure it's truly C3G. And then the next step was to send for a complement mutation evaluation and also complement functional evaluation. And the third step was to refer the patient for a clinical trial.

The second patient is a 50-year-old female patient that was diagnosed with C3G. The hematologic evaluation did show that she does have monoclonal gammopathy of undetermined significance. And in this situation, after confirming the diagnosis with a pathologist, I referred this patient for a full hematology evaluation, and she did receive clone-directed therapy. And currently her C3G is in complete remission.

So this is why it's important to have all these elements of this multidisciplinary group from the hematology, pathology, and also have the capacity to send for complement evaluation to a reference lab or to local lab if possible in order to treat these patients appropriately.

Dr. Turck:
And before we close, I'd like to bring this all together and have each of you share some best practices for collaborating with the C3G care team. Dr. Peleg, let's hear from you first.

Dr. Peleg:
So when I newly diagnose a patient with C3G, there are a couple of other providers that I'd like to get onboard in terms of a care team. C3G oftentimes is a renal-limited disease. So oftentimes it's the nephrology providers who are really championing the patient's care. However, there are instances, particularly when a younger patient is diagnosed with C3G, that there might be some extra renal manifestations, such as drusen deposits in the back of the eye or lipodystrophy, and in those situations, it would make sense to get an ophthalmologist or an endocrinologist respectively onboard. I also would get the hematology/oncology onboard if I unmasked a monoclonal gammopathy in an older patient with C3G, as I alluded to earlier in the interview. The treatment for C3G for patients who have a monoclonal gammopathy is treatment of the monoclonal gammopathy under the supervision and expertise of hematology/oncology. And it's been shown that if you're able to successfully treat the gammopathy and get the patient into deep hematologic remission, that's associated with improved renal outcomes in patients with C3G associated with a monoclonal gammopathy. Lastly, unfortunately a lot of these patients may progress to end-stage kidney disease, and certain studies may actually say as high as 40 percent of patients after 7 years may actually need a new kidney or start dialysis. And we, of course, would love for all of our patients to get transplanted. We have to keep in mind that these patients have a high risk of having recurrent C3G in the new allograft, so it's important to work very closely with the transplant nephrology team before these patients are transplanted so that there is a good plan in place to help prevent recurrent disease in the transplant.

Dr. Turck:
Thank you, Dr. Peleg. And Dr. Geara, I'll give you the final word.

Dr. Geara:
So when we are managing patients with C3G, it all starts with reviewing the pathology with a pathologist. So we try to get the slides to review the slides for the histologic lesion. And also we do review using immunofluorescence. And in some situations, we do perform pronase digestion in order to evaluate for any masked immunoglobulin deposit.

As a next step, if the patient does have a paraprotein-related C3G, I do engage hematology for further clone-directed therapy. As I'm doing this, I make sure that the patient does have evaluation for complement pathway. This evaluation will be an evaluation for

complement mutation, genetic testing, and also will be an evaluation for an acquired antibody for the complement pathway and functional assessment of the complement pathway.

And after we do this, the third step will be to evaluate this patient's candidacy for a clinical trial. The current treatment that are available for C3G are suboptimal. And I prefer to send all my patients, if they are eligible, to be enrolled in a clinical trial for the newer molecule or for newer medications that are being evaluated for C3G therapy.

Dr. Turck:
Well with those best practices in mind, I want to thank my guests, Drs. Yoni Peleg and Abdallah Geara, for joining me to discuss the multidisciplinary management of C3G. Dr. Peleg, Dr. Geara, it was great having you both on the program.

Dr. Peleg:
Thanks very much for having me.

Dr. Geara:
Thank you again for inviting me.

Announcer:
This episode of *Clinician's Roundtable* was sponsored by Novartis Pharmaceuticals Corporation. To access this and other episodes in this series, visit ReachMD.com/Clinician's Roundtable, where you can Be Part of the Knowledge. Thanks for listening!