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ReachMD

www.reachmd.com

info@reachmd.com

(866) 423-7849

Practical Perspectives in Myasthenia Gravis #2: Patient Stratification and Antibody Profiling—Personalizing the Disease Lens

Announcer:

Welcome to CE on ReachMD. This activity, titled “Practical Perspectives in MG #2: Patient Stratification and Antibody Profiling: Personalizing the Disease Lens” is provided by Prova Education.

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Dr. Castro:

Hello. I'm Dr. Diana Castro, and this is CE on ReachMD.

Dr. Jonathan Strober and I are diving a little deeper into generalized myasthenia gravis. So we were talking before how to make the diagnosis, right?

Dr. Strober:

Yeah, so let's start with the big picture. We talk about stratifying myasthenia. Can you just explain a little bit about what that really means in a day-to-day clinical practice?

Dr. Castro:

Yeah, I think, you can stratify it in so many ways, right? You can do it with the antibody profile. Age has a lot to do on patients—on older patients, or pediatric versus adult patients. I do see adults. And over the last 3 years, I've been seeing adults. I've learned a lot—it's a completely different disease in that group of patients. The age of onset, the symptoms, if the patients have had thymectomy or not. And I mentioned something before about adults having a lot of comorbidities, because unfortunately, we get older and we can get everything else, right? So it's very important to remember that.

So let's turn to antibody profiles. We always think of acetylcholine receptor, MuSK, and LRP4. How do you approach testing in a new pediatric case?

Dr. Strober:

Well, I mean, I think we do the same things that we do for the adult patients, right?

Like, as we keep learning about new antibodies, in the old days, it was just acetylcholine, and then MuSK came along, and then LRP4. And there are newer antibodies that are being found out all the time. So I think that's really a good place to start.

So if I see a patient who I'm really suspecting myasthenia, I will get the antibody test. In the younger kids, those that are purely ocular, especially in that really early-onset ocular myasthenia, a lot of times those antibodies will be negative, which is always difficult, versus, say, the adolescents, which is getting a little bit closer to the adult findings, where it's a little bit more common to get the antibodies and

so much more satisfying to have some tests that could be positive.

And I think also we have these new cell-based assays that are much more sensitive, that are picking up some of those patients that we consider seronegative but really are not seronegative.

Sometimes we need to repeat testing. We've had plenty of patients that have been seronegative, and over time, we're treating—maybe they're a little bit more difficult to treat. They're not responding in the way we want them to respond to treatments. We want to push our treatment further. So instead of just giving them lots of medications that may or may not be the right way for them, we may repeat the testing, and sometimes they will convert and become antibody positive after being antibody negative for a while. So I think it's important to kind of keep that in your head. It's not necessarily doing it for severity reasons. And I think just going back to the stratification issue, I think the severity of where they're coming in and how bad they are is also some way—especially when I'm looking at treatment, which we'll talk about later, like, how quickly do I need to get this patient under control? If it's just ptosis that's causing a little bit of problems, you have a little bit more time than, say, a patient who's really having problems breathing, you're talking about their swallowing, you need to kind of help them before something bad happens.

Dr. Castro:

They don't get all the way to the no breathing, no drinking, or anything like that. There are some patients that we have managed already for a little while, and you need to keep going fast, right? Like you need options that you can use, and you can continue treating the patient. You don't have huge gaps for treatment. I think that's something with new medication that I'm happy that we can start patients a little faster. And thankfully I think the insurance are doing okay with those, so hopefully we'll keep getting that.

I was going to make a comment about the acetylcholine receptor and the MuSK and LRP4. I have had several cases of patients that were seen by ophthalmologists, they did the panel, that they send it to some labs, and then I repeat it, and they are positive on the other labs. So we cannot tell exactly, but I think it's very important the physicians know or ask a neuromuscular specialist, right? If you're a general neurologist, you can ask a colleague in which place I should be sending testing, because we do get a lot of false negative in some labs.

Dr. Strober:

And the antibody status is really actually important when we talk about treatment in the future, because a lot of the newer treatments are being tested in kids who are antibody positive, and so they're approved for patients who are antibody positive. We can't necessarily use them right now in our antibody or seronegative patients. So I think trying to find those is not just helpful in confirming a diagnosis but also in getting the treatment that these patients need.

Dr. Castro:

So once we know the antibody profile, how does that shape our approach to management—like management, monitoring, counseling families? How do you do that?

Dr. Strober:

I mean, I think having antibody positive also helps talking to the parents about what this is all about, right? Like, we can have this nebulous idea of what is myasthenia, and we talk about what myasthenia is with the acetylcholine receptors and the problems with fatigue and weakness developing and why sometimes they look great and sometimes they don't look great. So I think having the antibody positive gives that family kind of something that they can be like, okay, I understand what this is all about a little bit easier than this kind of just idea is we think this is what's going on.

And then when we talk about treatment, we're also talking about, well, now we're going to attack not just the acetylcholine receptor problem with Mestinon, but we're going to try and help get rid of these antibodies that are there that are causing the problem. So, initially, when we started treating myasthenia, all we had were the same treatments that we had for adults, and we were using, right? So we use steroids, which, as pediatric practitioners, we use all the time but hate all the time because they're just so bad for especially growing kids. So there's so many more components to a pediatric patient than the adult patient. But like you said, the adult patient may have diabetes, and steroids may not be a great option for that patient or a pediatric patient with diabetes, so the comorbidities are important as well.

And then the Imuran, mycophenolate, methotrexate—some of the older medications we used because it's all we had, but they still kind

of were scary in the pediatric population, and we didn't have the data. There was some data coming out in adults, and we kind of used that, and we had our rheumatology friends who can help us with figuring out doses and stuff like that.

But now we have newer medications that are coming out that are actually being more focused and targeted to what the problem is. And so it really helps you feel a little bit more comfortable, especially when they're going to school, there's illness around all the time, so you worry about immunosuppressing them to the point where they're going to get sick all the time. How can we focus our therapies so that we're not causing other problems systemically, versus just treating the problem that we need to treat to help these patients get better?

Dr. Castro:

Exactly. And obviously, you explained that really well, but something that we also have to think is that hard—but it is a little hard when you try to use the tools that are already existing for adult patients, and then you're trying to apply that in the little ones, right? So I start using these tools 10 and above. Like, if it's a patient that is cognitively very well there, that knows what kind of questions that the MG-ADL or QMG will apply, I will use it, and I use it every single visit.

But again, the problem is they are not 100% for pediatric patients. So I always laugh, because it's can you do your work? Well they don't have a job. They have school. So how do you adapt the assessment tools to the pediatric population?

For those just tuning in, you're listening to CE on ReachMD. I'm Dr. Diana Castro, and here with me today, a good friend and colleague, Dr. Jonathan Strober. We're discussing practical perspectives in myasthenia gravis.

Dr. Strober:

Yeah, I mean, I think, as you said, you want to have something that you can monitor in the patients, because I think that patients with myasthenia are really hard when they come into the clinic, right? You're just seeing them at one point in time, and it could be a good day. Maybe they got a good night's sleep and they just took their Mestinon that morning, and it's just been an hour since they took it, so they're looking all great. Or they've been up all night because they've been worried about something that's going on. And maybe they didn't get their Mestinon that morning because they were running late. So many issues. So when you see them in clinic, it's just a one-time thing.

So I think while they don't have a job, like you said, like seeing how are they doing with the other kids? How are they doing in school? Are they having trouble in school? Are they able to get around? Are they too tired when they get from one class to another that they're having a hard time focusing on what the teacher is saying and getting their work done in the classroom? So I do try to use a lot of history from what the parents and the kids tell me.

But the QMG, I think, is a really hard tool to use in the pediatric population because there's so much involved and so many functional tests, and there's timed, like, you can't have a 5-year-old keep his arms out for too long, because they're just going to get bored.

Dr. Castro:

So what age do you use from the QMG?

Dr. Strober:

I do a modified QMG. In the adolescents, so maybe 10-12, depending on the kid, depending on their maturity level, I'll try to do something more. I like the MG-ADL, just because you're getting a better sense of what they're experiencing on a daily basis, although I don't think it necessarily is great for the younger kids. And I find sometimes that the kid will tell me one story and the parents will tell me another story, so there's always the perspective between the two. So I think the scales are there, and I think we can work on developing new tools that are based on those. And I think that we're trying to do that and say can you do 10 squats? Can you sip out of a straw? Certain things like that that a kid can do that are a little faster than what we get in the QMG, but it's really nice to have those tools so that you can have something to go, okay, what I'm doing is going in the right direction, or we're not going in the right direction, but it is that kind of balance between the history, like what's happening on the outside and what you're seeing in clinic at the same time.

Dr. Castro:

Exactly. I mean, I've used a lot of videos—pictures and videos. I tell them—and obviously from that point on, they are taking 1,000 pictures of the poor kid like every second, but it's very helpful, because you can tell them to give me a picture in the morning, at noon, and at night and show me different scenarios or activities. With the little ones, right, with, I would say, 10 and below, it's one that I ask

more, because it makes life easier.

But yeah, I think this part, in terms of the diagnostic and also kind of how do we measure the response to therapy, becomes very hard with the younger patients. You have to be a little more specialized to treat these patients.

So before we wrap up, let's talk a little bit about the key takeaways. For me, it's very important that, one, we have to use the antibody testing. You use a lab that it's a good lab that has the history of doing antibody testing. Let's say, like you said, there are new antibodies that are coming. Right now, most of the times I send for acetylcholine receptor with reflex to MuSK and LRP4. If they are negative, they will check for those 2. Electrophysiologic testing, would do it as needed, if it's really, really needed. And then what I was just saying about the tools, right? I think I feel comfortable with the tools we have, 10 or above. But 10 below, it becomes harder, so videos it is for me. What about you?

Dr. Strober:

Yeah, I mean, I agree with the antibodies, of course, because having some definitive test that really lets you kind of forget about the diagnostic journey, like move on from that and kind of then get to the treatment part. And, like we said, sometimes you need to repeat the test. If you get a negative, don't just rule out myasthenia. You really need to kind of think about it. If it's really something, maybe you'll broaden your differential a little bit and think about things a little bit more, but always have that on the back burner, and maybe come back to the antibody testing and keep trying, because sometimes kids will seroconvert, and sometimes you'll get a positive result after they've been negative for a while. So I think that's super important.

And then I agree with the testing is just really hard because the younger kids, the cooperation is different. Kind of their ability to do certain things is different. So getting that history from the parents and from the kid.

And the kid may have a hard time explaining what they're feeling, right? I think that's the other thing we always forget is these kids will use words that like, "I'm just tired—I'm just tired all the time," instead of saying, "I'm fatigued."

And I think we always grapple with that adult patient, even with "I'm weak" versus "I'm fatigued," right? Muscle weakness, fatigable weakness—like we use all these words, and they kind of mean something a little different to us, but a lot of people out there will use them for the same thing. And so I think also kind of honing in on what they really mean. What are you experiencing? Tell me what it is that you're experiencing without using those words. Like always ask my patient, what do you mean by fatigue? And they'll be like, "You know, I'm fatigued." And I'm like, okay, somebody's been using that word and you're hearing it, but you don't even know what you're saying. So come up with other terms, and sometimes you can have a good conversation and get them to really explain what it is they're experiencing. And sometimes it's just really hard in this population.

Dr. Castro:

So that's our time. I would like to thank you, the audience, for tuning in. And thank you, Jonathan, for joining me for this conversation. I love always—it's great to have these shared perspectives. You practice one way, I practice very similar, but these are little things. I love your point about retesting. That's an extremely important point.

So thank you for having us today, and we hope you enjoyed.

Announcer:

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