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Autoantibodies in MG: Their Role in Diagnosis and Treatment

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Silvestri:
This is CME on ReachMD, and I'm Dr. Nick Silvestri. Here with me today is Dr. Chip Howard. There are a number of autoantibodies that are clinically associated with generalized myasthenia gravis. They are, of course, important diagnostically. Do they also provide guidance on both treatment strategies and likely prognosis?

Dr. Howard, can you please speak to this topic?

Dr. Howard:
Thank you, Nick. There are multiple different serologies in myasthenia, most commonly is antibody to the acetylcholine receptor seen in about 85% of our patients. There's another 8%-9% of patients who have antibodies to muscle-specific kinase, MuSK, if you will, about 1% or less to LRP4. And then there are a number up around 10% of patients where we've yet to identify antibodies that are causal in myasthenia.

It's critically important to identify the serology of myasthenia because it impacts our ability to treat or what we should be treating with. For instance, patients who have MuSK antibody are often allergic or insensitive to cholinesterase inhibitors. They do not respond to complement inhibition because they're an IgG4 antibody, whereas those to AChR are IG1 and IG3. Similarly, it's been found that they do not respond to surgical thymectomy. So it's important to provide the patient with the appropriate therapeutics, and serology plays a key role.

The seronegative population is a changing field. Back in the mid '70s when I started, if you didn't have the AChR antibody, you were seronegative. When MuSK was identified, then we talked about double negatives. We now talk about the triple negatives, and I'm sure there are others out there. What we don't have a good handle on is the ability to detect antibodies using commercial assays. My belief is that they're relatively insensitive. There are technology or tools using cell-based assays that will give us another percentage of positivity, particularly with AChR, but it's not readily available.

It's also important to recognize that the antibody assay differs among laboratories. And there are some laboratories that are much more sensitive than others, and we've all clearly seen false negatives and even false positives by one lab that are not borne out when they're sent to a second lab. So that has to be kept in mind.

The third point to make is that if one sees the patient very early in the course of the disease, within the first 6 months, their antibody is an IgM type, and around 6 to 8 months, it converts over to an IgG type. So if one is seeing the patient who's had symptoms for a few weeks and they're antibody negative, it behooves you to retest them at 6 months, 8 months, somewhere in that time frame to see if they indeed have become seropositive and have converted.

The MuSK population is interesting because, in the US, these individuals tend to be women, they tend to be of African American descent, but in other parts of the world, they're predominantly Caucasian. And why that difference, I don't understand.

And so the bottom line is that there are multiple antibodies, I'm sure we'll find more, that if they're negative early, please retest.

Dr. Silvestri:
Thanks very much, Chip. That was a very comprehensive discussion. With that, our time is up. Thank you for listening. We hope you found our perspectives useful.