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Neuroimmunology Considerations in Multiple Sclerosis

Announcer:
This Medical Industry Feature, titled “Neuroimmunology Considerations in Multiple Sclerosis” is sponsored by Novartis Pharmaceuticals Corporation.

Here’s your host, Dr Jason Freeman.

Dr Freeman:
This is ReachMD, and I'm Dr Jason Freeman. Joining us today to discuss the role of neuroimmunology in multiple sclerosis is Dr Scott Zamvil. Dr Zamvil is the Donnie Smith Chair and Multiple Sclerosis Research Professor of Neurology, and faculty member in the Program in Immunology at the University of California, San Francisco. He also serves as a Board Member of the International Society for Neuroimmunology, and is also an Advisor for the Americas Committee for the Treatment and Research in Multiple Sclerosis.

Dr Zamvil, welcome to the program.

Dr Zamvil:
Great, I'm looking forward to it. Thanks.

Dr Freeman:
Dr Zamvil, I wanted to ask about what we know about the role of the immune system in multiple sclerosis. How do the two things interact?

Dr Zamvil:
There's a cellular immune system and the humoral immune system. We're all familiar with the concept of having antibodies, but the T cells and the B cells also contribute the cellular immune system, in particular, the T cells.

In MS, we know that if T cells are targeting the myelin tissue they can cause damage. And the lesions in MS involve a predominance of lymphocytes. And some of those, we believe, maybe a small proportion, are targeting the myelin antigens. We know from models that we can transfer the disease with T cells, or clones, that are specific for myelin antigen. The B cells have important roles as well because they have a very tight association in collaboration with the T cells. The B cells can present to T cells and activate the T cells. And the T cells, conversely, can activate the B cells. And it’s the T cell that's necessary for B cell differentiation, and for B cells to start making antibodies. B cells are the antibody-producing cells. And that is important.

Dr Freeman:
What happens later in the disease, versus earlier in the disease? And is there, you know, there's a lot of talk about, out there, about neuroinflammation, is that part of this process and part of the immune response?

Dr Zamvil:
When we think of the immune system, early in disease, we think of the cellular contribution. And we know how important that is. So, early in disease, there's a lymphocytic predominance, but we know over time we accumulate neurologic damage. So, we have tissue loss. We have axonal loss from the neurons, we have glial activation, we lose tissue, we can see on MRI that we have atrophy over a period of time, and that's when we progress from the inflammatory phase of the disease to the neurodegenerative phase of disease. There's always some lymphocytes that are there.

But what happens is that they set up their own microenvironment. They set up shop within the central nervous system, and you have lymphocytes that are there behind the blood-brain barrier, and they can self-perpetuate the disease process, and you have tissue

destruction. So, one of the challenges now is treating the later phase of disease.

Dr Freeman:
Thinking about that, can you talk about the potential impact of having low immunoglobulin levels for these patients?

Dr Zamvil:
Right. So, here just to separate, we're not speaking about the immunoglobulins that are in the neuromyelitis optica where they're causing the damage to the target antigen in the brain. We're talking, here we're speaking of immunoglobulin IgG and IgM for its protective capabilities in fighting off infections, either bacterial or viral infections. And so, if you continuously deplete the B cells over years you may see drops in the antibody levels, the total IgG and IgM level. And that's something that we pay attention to.

Dr Freeman:
And why in particular is that important for patients and clinicians to pay attention to?

Dr Zamvil:
It's important because we know that antibodies, as I mentioned, can protect against, let's say, bacterial infections. But what happens over a period of time is that we may see reductions in the total antibody levels. When I say total antibody, I'm referring to IgG and IgM.

We know the IgM may go down earlier than the IgG, but over a period of time, the IgG, which is our mature antibody, may also become diminished or reduced. And when that happens, we are concerned that a patient may be predisposed to upper respiratory or lower respiratory infections or urinary tract infections, both from bacteria for the respiratory infections, but also viral infections as well.

Dr Freeman:
So just to change gears a little bit, let's talk about, maybe a patient with newly diagnosed MS. So a patient who has both brain and spinal cord lesions, as well as the finding of positive oligoclonal bands on CSF testing. Given what we just discussed, what factors do you consider when choosing a therapy for this type of patient?

Dr Zamvil:
Right, so it's very important for us to recognize early on when we diagnose MS at the earliest stage, if we can prognosticate whether they're going to have a mild or a moderate or severe course of disease. And if patients have brain and spinal cord lesions, and they have a large burden of those lesions, and some of those are active, and they also have all oligoclonal bands, which is the antibodies are produced in the central nervous system, that's the oligoclonal bands, these all portend a more severe course. We're afraid to lose tissue. So just as, you know, time is brain in stroke, it's the same in MS on a slower scale. But still, we don't want to wait.

Dr Freeman:
If we consider another patient this time, maybe someone who's, you know, long been diagnosed with relapsing-remitting multiple sclerosis, but having continued relapses and evidence of new disease on MRI despite, you know, compliance with therapy, how do you then go about making your treatment decision at that stage?

Dr Zamvil:
So, this is where we follow and monitor patients both for their clinical activity and their activity on imaging as well. We're afraid to wait too long, because we know that we have to protect against tissue loss.

Dr Freeman:
Do you have greater concerns about their impact on the overall immune system? Or is it really a matter of the clinical effects outweighing that impact on the immune system, and in particular, on immunoglobulins and risk of infection?

Dr Zamvil:
Right. So, efficacy and safety are equally important. You have to, but you have to have efficacious medications.

And if you have concerns, you know, with some of the medications that we have, we have to be aware what the risks might be.

We just have to be aware that it predisposed to a viral infection in patients that had had in a latent infection with one of the viruses. And we can now monitor. If they don't have experience with that virus, they've never seen it, we know they haven't been infected, and that's the only concern, their particular concern with that medication. We can use it. But if they then become exposed to the virus, then we can no longer use it, and we have to discontinue its use.

B cell depleting therapies are very potent. But nevertheless, we have to follow just as we do with the immunoglobulin levels over a period of time that may become reduced.

Dr Freeman:

Thank you. Obviously, we're still in the midst of the COVID-19 pandemic. And I wanted to know how that's impacted your own practice and the way you factor your concerns for immunologic function into both treatment decisions for patients but also thinking about things like vaccination and both if one is to be vaccinated, but also the timing and use of vaccinations?

Dr Zamvil:
So, let me first point out that because the COVID-19 situation has changed dramatically since March of 2020, and seems to evolve, we have to be on top of things. We really have to be on our toes, because we have to adapt ourselves as well.

Early on when we didn't know at the very start, my patients that were on certain therapies, we were concerned whether they should be on a B cell depleting agent. And what we did at that point is that patients who were on those therapies and needed to be on, we monitored their B cell counts and we delayed the therapy. But we found very quickly that some of the patients have very active MS and we couldn't do that. So, I recognize that for each individual patient you have to take as its own case, and some patients continued on therapy, as if COVID was not, it did not exist in that sense. It was not a factor, I should say. Obviously, they were wearing masks and social distancing, but they had to continue their therapy. In other patients, we were able to delay.

Dr Freeman:
And one other thought was about the way in which you are seeing and having access to patients. So, lots of neurologists have - have gone to the use of telemedicine visits, to see and follow up with their patients. How has that impacted your own practice? How has it impacted your ability to make a firm diagnosis and/or to make treatment decisions for patients?

Dr Zamvil:
Well, for me, it's had a huge impact. During the year, I, within a week was using exclusively Zoom. And so, the Zoom and telemedicine has had - for everyone, has been important because much of what we do is managing our patients' symptoms and their medications and ordering lab tests and evaluating the results. Unfortunately, I can't examine a patient and tap on their reflexes or examine their eyes or do a 25-foot walk from video.

Dr Freeman:
Got it. And what are some of the benefits that you may have seen? I'm assuming that some patients actually prefer to be seen by Zoom, especially those who may be more established patients. That – does that really help make it easier for them?

Dr Zamvil:
Well, my patient in Ramallah and my patient in Frankfurt, et cetera, makes them happy that we could do it by Zoom. It made it easier because nobody could travel. So, I think there's been a benefit to the patient. I feel that our visits even now and going forward, I would say at least 50 to 80 percent of our follow-ups could be done by Zoom, and especially for those patients that are at a distance, whether they're on the East coast to the West coast or Alaska or whatever, we - we will use that. They don't replace the in-person exam. It is a challenge to have a new patient by video. It still can be done. It's not optimal.

Dr Freeman:
Well, these have been some great insights for us to take with us. As we continue to think about multiple sclerosis, its treatment, the role of the immune system, and certainly the importance of immunoglobulins as we think about the different treatments that are currently available.

And with that, I want to take the time to thank my guest today, Dr Scott Zamvil, or updating us and helping with our understanding about immunology and multiple sclerosis. Dr Zamvil, it was great speaking with you today.

Dr Zamvil:
It was a pleasure. Thanks.

Announcer:
This program was sponsored by Novartis Pharmaceuticals Corporation. If you missed any part of this discussion, visit ReachMD.com/Industry-Feature. This is ReachMD. Be Part of the Knowledge.

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