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

From Pathology to Practice: The Role of Inflammation in MS Pathology

### Announcer:

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### Dr. Freedman:

This is CME on ReachMD, and I'm Dr. Mark Freedman from the University of Ottawa in Ottawa, Ontario, Canada. And joining me today is my colleague, Dr. Ahmed Obeidat.

Hello, Ahmed. So you're going to have to have an interesting discussion today about the pathophysiology of multiple sclerosis; what we know and what we don't know. Can you tell us a bit about the role of inflammation in MS pathogenesis and pathology?

#### Dr. Obeidat:

This is a great question, Mark. And we can talk about this for hours, right? But we have very limited time today.

There are two main things in my mind when I think about inflammation in multiple sclerosis. I think about this peripheral inflammation where, in a way, when I explain to patients, I say, these are immune cells that are circulating in your blood, and then somehow, they go in and attack the brain. Maybe they're responding to something within the brain itself, and we think maybe they are, and most likely they are. So sometimes there is also the talk on what we call centrally mediated inflammation. So within the compartment of the central nervous system, there might be ongoing inflammation. There are resident B cells there. Somehow, they're doing something, attacking neurons, attacking the myelin, the oligodendrocytes, and also, there are T cells within those lesions. But also, there are other elements, like from the innate immune system. There are microglia. There's a lot of interest now in microglia in the field of multiple sclerosis, and they're kind of becoming, like, the therapeutic target.

But we know some of the therapeutic targets are B cells, T cells, the communication between B and T cells, that is imperfect, and also in the central nervous system. So these are some of the things when I try to summarize inflammation in a way. But there is way beyond to this. It's more and more and more complex than this.

But I will challenge you a little bit. I'm going to ask a question. Is multiple sclerosis a primary inflammatory disease? And I know maybe it is, but I will challenge that. So I don't know what you think.

#### Dr. Freedman:

Oh, I think the pathologists have been arguing this for decades now. Is the inflammation secondary to another process that began, or is it primary and inducing the process. So the old chicken-and-the-egg story here. But clearly, addressing the inflammation has shown us that we can control the disease and change the course of disease. So something about the inflammatory component is important.

Of our current therapies that we have, do they get into the brain, and are we able to target that other cell, the microglia?

Dr. Obeidat:

Some of them do, and some of them don't. Now, the current approved therapies, we know that there are some that get to the brain because they're small molecules, but we don't know if they're affecting microglia. Now we know that in development, there is this class of medication called BTK inhibitors, or protein tyrosine kinase inhibitors, that are thought to maybe modulate the function of microglia in a way, and these are also medications that can get to the brain, and they are in experimental stages and some of the data has been released. Maybe they slow down some of the aspects of progression in MS in certain patients.

So there is some hope there that if, maybe if we can get to the brain, modulate those cells, maybe we're going to get something beneficial to our patients there. But more to come, I think, and we have to look more at these data more carefully, too.

# Dr. Freedman:

So all our therapies currently are approved on the basis of relapse rate reduction, which is, I guess, the clinical manifestation of this peripheral inflammation, right? Going in the future, we are looking at something called PIRA, the progression in the absence of relapse activity. And that's not thought to be driven by the peripheral inflammation, right? So we need something that's going to drive at that. Is that going to be the only way we're going to hit PIRA?

## Dr. Obeidat:

That would be one way. But I think, to hit PIRA, too, I think there is many ways including also, controlling comorbidities, nutrition. Making sure that we are doing brain health-related issues such as exercise, eating healthy, avoiding smoking. All these kind of aspects that can help protect the brain may actually influence PIRA. And I think this is interesting, but targeting this compartmentalized inflammation may be one way to also maybe modulate this. But I think more to come and the concept is interesting, but we need to learn more about it.

## Dr. Freedman:

Yeah, I love your important point about the holistic approach in taking all of the patient into consideration.

Well, this has been a great discussion. It's small compared to what we need to talk about, but thanks everyone for listening.

## Dr. Obeidat:

Thank you. Thank you so much.

# Announcer:

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