Transcript Details

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Understanding Prodromal Phases in Demyelinating Diseases: Insights on MS, NMOSD, and MOGAD

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll discuss prodromal symptoms in patients with demyelinating diseases with Dr. Dalia Rotstein. She's an Assistant Professor of Medicine at the University of Toronto and also spoke on prodromal symptoms at the ACTRIMS Forum 2025. Let's hear from Dr. Rotstein now.

Dr. Rotstein:
A prodrome is a period of nonspecific symptoms that predates the typical clinical onset of a disease. Prodromes can also indicate underlying onset of the pathobiology of the disease. So we recognize today that prodromal phases are common in many different neurologic and inflammatory conditions. The research suggesting that there is a prodromal phase to multiple sclerosis, which is the most common demyelinating disease, first emerged about eight years ago. This research evaluated health service use in the five years predating the first MS attack and found that it was significantly elevated in those who went on to develop multiple sclerosis compared to controls, and those findings have been replicated in multiple studies since then. Some common symptoms that we associate with the MS prodrome include fatigue, mood disorders like anxiety and depression, musculoskeletal pain, bladder dysfunction, and sleep disturbances.

Neuromyelitis optica spectrum disorder, or NMOSD, and MOG antibody disease are two relatively rare demyelinating diseases that have distinct underlying pathophysiology compared to multiple sclerosis. The idea that there could be a prodromal phase in these two diseases was just recently investigated. My team in Ontario evaluated this separately—once in an NMOSD cohort and once in MOGAD cohort—to evaluate health service use before the first attack. What we found was that there was increased health service use in individuals who went on to develop NMOSD, but not in those who developed MOGAD. This evidence suggests that there could be a prodromal phase to NMOSD. Common symptoms in the years before NMOSD onset included sensory symptoms, visual disturbances, and pain. These findings do need to be replicated in other cohorts, but I think they are quite suggestive.

Normally, if we're talking about a definitive prodrome, we're talking about symptoms that predate the first attack by at least 30 days. But in other situations, we can have warning signs or symptoms that occur in the days or weeks leading up to the first attack. For example, with optic neuritis, which is a common first attack in multiple sclerosis, NMOSD, and MOG antibody disease, people will often develop pain in or around the eye in the days or weeks before the attack when they develop blurry vision. And other symptoms or warning signs that can occur before a first attack include profound fatigue. In the case of MOGAD, we often hear about an infection that occurs in the days or weeks before the first attack, and it's thought that the infection may actually be the trigger that leads to the disease itself.

Prodromal symptoms can differ across individuals. So we know that prodromes are heterogeneous, and what that means is that some people who develop demyelinating disease have a prodrome while others do not, and prodromes also differ in terms of their duration, their character, and their severity across individuals. It makes sense to think about age and sex with relation to the nature of the prodrome because we know that age and sex do have a significant influence on the nature and recovery from relapses in established MS.

This research is just in its infancy, but Dr. Helen Tremlett's group at the University of British Columbia investigated this in another Canadian cohort. What they found is that men with prodromal symptoms are more likely to have genitourinary symptoms; that younger individuals were more likely to have sensory symptoms and visits to an ophthalmologist with visual symptoms; and that older individuals during the prodrome were more likely to have hospitalizations for injury or for infections. So it does seem that there are likely to be some differences in the presentation of the prodrome by male versus female sex and by age.

It is very challenging for neurologists to differentiate the prodromal symptoms and demyelinating conditions compared to other diseases. The prodrome is by its very nature nonspecific, and what we see is that individuals who are in the prodromal phase of other inflammatory conditions like lupus, rheumatoid arthritis, or inflammatory bowel disease can have similar symptoms, such as mood disorders like anxiety, depression, pain, or significant fatigue. So I think the key in terms of diagnosing people who will develop MS in the prodromal phase is to pair the prodromal symptoms with specific biomarkers. Those biomarkers could include fluid biomarkers like serum neurofilament light chain or oligoclonal bands in the cerebrospinal fluid. They may also include imaging biomarkers, like white matter lesions on MRI. And I think bringing the two together will help with diagnosis of individuals in the prodromal phase in the future.

Announcer:
That was Dr. Dalia Rotstein discussing prodromal symptoms in patients with demyelinating diseases. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!