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## An Expert Perspective on RMS Progression: Key Signs & Symptoms

Announcer:

This is ReachMD, and you're listening to *NeuroFrontiers*. This episode is sponsored by Novartis. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:

Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. Jennifer Caudle, your host for today's program. And here with me today is Dr. Marin Collazo, a neurologist with a specialty in multiple sclerosis. Dr. Collazo is here to share her perspective on recognizing the early signs of relapsing multiple sclerosis, or RMS progression. Dr. Collazo, welcome to you.

Dr. Collazo:

Well, thank you so much doctor for having me today. I'm very excited, to share some of my knowledge in multiple sclerosis with you and with the audience today.

Dr. Caudle:

So Dr. Collazo, to start us off, what are some key signs and symptoms of progression for patients with RMS and active secondary progressive MS?

Dr. Collazo:

Yeah, so before I answer your question, I want to start sharing that multiple sclerosis is an immune mediated inflammatory and degenerative disorder of the central nervous system. It's one of the leading causes of disability in the young population. There are around one million people in the U.S. with multiple sclerosis. It usually presents in the ages of 20 to 30, but there are children and older people with MS and it is more common in women than in men. Multiple sclerosis most commonly present as a relapsing remitting form, which mean patients have attacks, exacerbation, relapses, or neurological symptoms with periods of remission in between.

MS can also present a secondary progressive MS, which means patient have a progressive course of disability accumulation after periods of relapses and remission. And there's also primary progressive MS, which is an insidious course of disability accumulation from disease onset.

MS consists of three phases: the high-risk phase, the relapsing remitting, and the progressive phase. I must clarify that progression refers to irreversible neurological function due to MS over time, and that active in multiple sclerosis refers to radiographic finding, new radiographic activity with new or not new neurological symptoms.

To answer your question, the key signs and symptoms of progression include worsening of gait impairment. Patient might notice that they might need an assistive device and they might transition from a cane to a walker to a wheelchair. Other patients might experience bladder, bowel dysfunction and spasticity, weakness, and cognitive dysfunction.

Dr. Caudle:

And now are there any neurological or subclinical signs of progression that might demonstrate deterioration before symptoms appear?

Dr. Collazo:

Yeah, there are a few neurological and subclinical signs of progression that might demonstrate deterioration before symptoms appear. For example, some patients might notice difficulty performing activities of daily living. They might feel more tired, more fatigue. Other patients might notice that difficulty when walking long distances, when walking upstairs, when carrying heavy objects. Other patients might notice some subtle, um, cognitive dysfunction that may manifest mainly with low performance at work or in social settings, for example.

Dr. Caudle:

Okay, and you know, now that we have an understanding of these signs, which is very helpful, let's take a look at assessment criteria. So Dr. Collazo, what are some of the clinical tools typically used to measure this progression?

Dr. Collazo:

Yeah, measuring progression in multiple sclerosis is very difficult and still an area of much interest. We don't have any specific laboratory test or an imaging finding that will be indicative of progression of the disease. However, there are different clinical tools that we can use to monitor the progression in MS.

Most commonly, we use the EDSS or Expanded Disability Status Scale score to monitor the disability in patients with MS. That score goes from 0 to 10: 0 normal neurological exam, 10 death due to MS. With common milestone or important milestone, a score of 6.0, that refers to those patients that are using a unilateral assistive device for walking, 6.5 to those that use bilateral hand assistive devices, or a score of 8.0 that refers to those who are confined to bed or to a chair. There's a limitation with the EDSS because it mainly relies on physical and ambulation function and less on cognitive dysfunction. Therefore, other clinical tools have been developed like the Multiple Sclerosis Functional Composite. That consists of different testing. For example, it includes the timed 25-foot walk to assess lower extremity function, the 9-hole peg to assess upper extremity function, the symbol digit modality test to assess processing speed, and the low contrast letter acuity test to assess visual function. Some might have developed interest in how the patients monitor their progression. What is their perception?

There has been other tools that we can use based on patient perception. For example, the Patient Determined Disease Steps, which is the PDDS, which is very similar to the EDSS as well goes from 0 to 8; 0, normal tasks, and 8 on patients basically bed bound. Also, the Multiple Sclerosis Impact Scale, which consists of 29 items; 20 of them assessing physical state, and 9 of them psychological state. The score goes from 0 to 100, with 100 worse disability status.

Dr. Caudle:

For those of you who are just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Marin Collazo about recognizing signs of RMS progression.

You know, as we know, biomarkers play an important role in identifying mechanisms of progression. Can you tell us about some of the clinical markers being used to measure progression in relapsing forms of MS?

Dr. Collazo:

So yes, biomarkers play an important role in identifying mechanism of progression in multiple sclerosis. Between few of them, we have the serum and cerebrospinal fluid, neurofilament light chain. Neurofilament light chain is a neuro-specific cytoskeleton protein that is released into the extracellular fluid after axonal injury. An axonal injury or loss is the hallmark finding in MS and disability. One must be aware that neurofilament light chain can be elevated in other neurological disorders like ALS, Parkinson's, Alzheimer's, and traumatic brain injury. Some studies have found that neurofilament light chain, or NFL, seems to be a reliable indicator of prognosis and treatment response in patients with MS. It has been found higher in patient with progressive MS than those with relapsing remitting MS as well baseline NFL. And, over time, tend to correlate with the prognosis in those patients that have higher risk to transition from relapsing remitting to secondary progressive MS.

Other biomarkers commonly used for progression include the oligoclonal bands. The IgG, CSF, oligoclonal bands are mainly diagnostic, but the IgM oligoclonal bands seems to be on higher levels in those with relapsing remitting than in those with progressive MS. GFAP, glial fibrillary acidic protein which is highly expressed on the cytoskeletons of astrocytes have also been found to be higher in those with worse disability and progressive MS than those with lower disability.

Dr. Caudle:

Thank you for that. And based on your clinical experience, Dr. Collazo, what are some challenges preventing us from identifying clinical and subclinical signs of RMS progression early?

Dr. Collazo:

So some of the challenges in preventing us from identifying clinical and subclinical signs of progression in MS is that we don't have established criteria for secondary progressive MS. We have a criteria for relapsing remitting, we have a criteria for primary progressive MS but not for secondary progressive MS.

However, it is widely accepted to diagnose somebody with secondary progressive MS after at least six months of irreversible worsening of neurological function after a course of relapsing remitting phase. Also, the fact that the diagnosis is made on retrospect presents a challenge with the diagnosis. Sometimes we take into consideration the patient-reported symptoms which sometimes cannot be that reliable and cannot be confirmed. We do a neurological exam or with MRI findings for example. Also, the fact that there is no definite

imaging or laboratory test to confirm progression in patients with MS.

Dr. Caudle:

And before we close, I'd like to discuss patient-centered care. What are some strategies that we can use to ensure that our management and treatment options take into consideration the unique needs of our patients?

Dr. Collazo:

Yes, when evaluating a patient with multiple sclerosis, it is recommended an individual case approach as every patient with MS is different. Their symptoms, their progression, their radiographic finding, the treatment response. I usually recommend also to consider a multidisciplinary approach to be able to evaluate all the physical and non-physical symptoms and to consider conventional and non-conventional approaches, because every patient is different, and having in mind their age, their comorbidities, their disability, and first of all, patient preferences.

Dr. Caudle:

Well with those insights in mind, I'd like to thank my guest, Dr. Marin Collazo, for sharing her valuable perspective on recognizing the signs of RMS progression. It was great speaking with you today, Dr. Collazo.

Dr. Collazo:

Same here. Thank you so much for having me, um, today. Hope that everyone have a good day today.

Dr. Caudle:

Thank you.

Announcer:

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