Transverse Myelitis (TM)

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[00:00:00] **Angel Simpelo:** Hello. Welcome, everybody. This is Angel Simpelo from SRNA. Welcome to the transverse myelitis session and thank you so much for joining us at our symposium this weekend. This is a disorder-specific session with a talk on TM with Dr. Carlos Pardo from Johns Hopkins Medicine, including diagnostic criteria, acute treatments, and long-term effects. Please type any questions in the Q and A section. We will have time to answer questions at the end of the session. And now I'd like to introduce Dr. Carlos Pardo.

[00:00:51] **Dr. Carlos Pardo:** Good morning, good afternoon, everybody, around different states and countries that are joining the SRNA meeting. Thank you very much for joining the meeting. I'm going to be talking today about one topic that has been the focus of our activities in the past 25 years or more, is the topic of myelitis. As you can see from my title, I try to avoid the use of the term transverse. And I will focus mostly in the terminology "myelitis."

[00:01:26] My conversation today with you is going to be a little bit more on the philosophical side of defining what is myelitis, particularly because there has been a lot of progress understanding the topic of myelitis in the past several years. So, what we are going to be discussing is what is myelitis, what it's not. Again, most of the presentation I'm going to show you is based on our work at the Johns Hopkins Myelitis and Myelopathy Center. That was the first center that was established in the world for investigating what was called, in the '90s and early 2000s, transverse myelitis.

[00:02:11] I'd like to acknowledge that most of the work that we have done in the past 20 years, or more is the work of many people. Some of them are described here and the pictures right here. But this is the work of many colleagues, many fellows, many residents, many physical therapists, occupational therapists, rehabilitation doctors and colleagues have been participating in the Johns Hopkins Transverse Myelitis Center and later in the Johns Hopkins Myelitis and Myelopathy Center. And with the support of the former Transverse Myelitis Association and now the SRNA, we have enabled to collect this extensive data.

[00:02:53] The major objective of this is, again, just trying to understand the concept of myelitis versus myelopathy, and particularly to review the evolution of the concepts in the past several years. And my main goal today is to convince you to abandon the diagnosis of transverse myelitis as diagnosis and adopt an

etiological diagnosis or better diagnosis that reflects the cause of the inflammation in the spinal cord called myelitis.

[00:03:23] Let me start with the beginning. Back in the '90s, when Sandy Siegel and many of the people that have been working in the Transverse Myelitis Association and many of us who were on the medical side of transverse myelitis, back in the '90s and early 2000s, we actually put the term transverse myelitis frequently in the basket of multiple sclerosis. There were other diagnoses like acute disseminated encephalomyelitis or Devic's disease that was at that time a rare disease that presented with a spinal cord inflammation as well as optic neuritis and rheumatologic disorders. That was basically the spectrum of what was known at that time as transverse myelitis.

[00:04:12] But the reality is that in the early 2000s, there were many advances in understanding the problem. Probably the first advance understanding the topic of myelitis was the discovery by our colleagues at the Mayo Clinic, that one of those forms of myelitis that was called the Devic's disease was associated with presence of these antibodies that is called aquaporin-4 antibody, is the neuromyelitis optica antibody, that was basically the reason that many patients actually were experiencing problems in the spinal cord or in the optic nerve. What was known after that discovery is that many of those patients with the Devic's disease, neuromyelitis optica, actually had a spectrum of clinical findings that were very different to the spectrum of multiple sclerosis. And basically, it defined a new disorder that is known as neuromyelitis optica now.

[00:05:16] Later, more recently there has been more rediscovery particularly with the finding that myelin oligodendrocyte glycoprotein as an antibody is a pathogenic antibody that is associated with disorders that are mimicking myelitis, producing myelitis, and producing a wider spectrum of brain lesions and optic nerve involvement. So, this, once again, pulling us to the spectrum of the myelitis in the 20th century because we are learning more about the etiology causes of myelitis and the pathogenesis of myelitis.

[00:05:58] So what is the spectrum of myelitis in the year 2021? On one side, we have advanced clearly in understanding the cause of inflammation called myelitis in many ways. In the past several years, particularly since 2010 and 2012, we are learning more about the role of infections like enteroviral infections producing acute flaccid in myelitis in children. So, this is actually a very important development in understanding some form of myelitis and myelopathies in children. We also understand better the role of some infections and particularly post infection disorders in the presence of these inflammatory form of myelitis or myelopathies.

[00:06:53] However, the major advance, as I mentioned before, is the understanding of autoimmune associated myelopathies and neuromyelitis optica produced by antiaquaporin-4 and myelin oligodendrocyte spectrum disorder produced by that antibody and known as a MOG antibody. But we also understand better the role of other autoimmune disorder, autoimmune myelopathies associated rheumatologic disorders.

[00:07:20] So at this moment almost 20 years after that we started using the terminology in our Center of Transverse Myelitis, we have a better understanding of what is the spectrum of this disorder that produces inflammation. We still have multiple sclerosis, and we still have the term idiopathic transverse myelitis in our terminology. But actually, in many ways we are decreasing the impetus in designing the diagnosis of transverse myelitis as the main diagnosis in the majority of patients that present with inflammatory disorders of the spinal cord. And particularly because there are more disorders that have been discovered already, discovered, or disclosed, to be associated with this spectrum of inflammation in the spinal cord.

[00:08:07] One of them is sarcoidosis, that is clearly producing a chronic inflammatory disorder in the spinal cord. And all of these disorders are basically in the spectrum of this terminology that we call now myelitis. As you can see here, I am staying away of using the term, transverse in this terminology because many of

these terms, many of these disorders that I included in this term, myelitis basically represents a very diverse spectrum of etiologies that we need to be aware as patients and we need to be aware as clinicians.

[00:08:53] Let me point out one thing that is a little bit worrisome and is that in the past several years we have included many noninflammatory myelopathies in the spectrum of transverse myelitis or myelitis. And one of those are vascular myelopathies produced by acute strokes or vascular myelopathies produced chronically by problems in the spinal cord like venous hypertension. And this is actually very concerning because unfortunately some of these patients are treated as myelitis and are erroneously mistreated with medication that sometimes may produce more harm than benefit when the etiology of this spinal cord problem is a vascular etiology.

[00:09:41] And in the same spectrum of noninflammatory myelopathies there are other disorders like metabolical disturbances occasionally associated with a vitamin deficiencies or other type of metabolical disturbances that may produce problems that mimic transverse myelitis or myelitis and also a structural myelopathy like the spondylotic myelopathies that are very frequent in our spectrum of myelopathies that occasionally are confused with myelitis and are erroneously treated as myelitis.

[00:10:20] So we need to be aware about that because unfortunately the term transverse myelitis that was coined for the first time in the mid '40s and late '40s after the discovery or description of a patient that had infection disorder and developed later a spinal cord disease was called transverse myelitis we have been basically, we have been using this terminology extensively. But unfortunately, with some erroneous connotation and unfortunately producing misdiagnoses that may lead to mismanagement and mistreatment.

[00:11:02] So should we continue using the diagnosis of transverse myelitis in our clinical practice? Should we continue the use of this diagnosis, transverse myelitis, and telling our patients, 'You have transverse myelitis?' I will attempt to answer that question in the next few minutes. And I will try to convince that we should stay away from this terminology. The rationale and support for that argument is in a study that we did, actually in the past few years. Where we went back to all our patients that had been referred to the Johns Hopkins Myelitis Myelopathy Center between 2010 and 2018 with a diagnosis of transverse myelitis. And the major focus of our study was to focus on the precision of that diagnosis and how the diagnosis in terms of the spectrum of causes of myelitis fit to define a specific treatment.

[00:12:02] And what we were very surprised is that approximately a third of the patients with the diagnosis of transverse myelitis actually they didn't have any form of myelitis or any form of inflammation of the spinal cord. And a third of the patients that were diagnosed with transverse myelitis actually had other problems like a spinal cord infarction or structural abnormalities of the spine leading to spinal cord damage or injury, or metabolical disturbances of the spinal cord rather than myelitis. It's very clear that yes, there were elements of myelitis in almost 70 percent of the patients, but it is very clear that the cause of those myelitis were very diverse.

[00:12:54] On one side, we had obviously demyelinating inflammatory myelopathies as an important cause of myelitis. We had neuromyelitis optica spectrum disorder. We have neurosarcoidosis. We have infection disorder basically producing and mimicking inflammation of the spinal cord, and we have other rheumatologic disorders. So, this is extremely important because that however reflects that myelitis is a very heterogeneous group of disorders that need to be treated specifically as the cause of the problem is.

[00:13:32] In other words it's extremely important to clarify if the myelitis that the patient is experiencing is associated with a demyelinating disorder, is associated with neuromyelitis optica, is associated with MOG spectrum disorder or is associated with sarcoidosis or is associated with a rheumatological disorder. So, this

is extremely critical and very important for the future, particularly because we are encountering more and more cases of myelitis and importantly, we are having a better understanding of the problem and we have now better medications that are able to treat the problem and are able to have better outcomes because we have a better treatments.

[00:14:18] So the bottom line here is myelitis as a disorder is a heterogeneous group of spinal cord diseases produced by different causes, etiologies. And it's extremely important to understand that if we take a look at our retrospective experience, we have misdiagnosed almost 30 percent of the cases as TM when they don't have any clear cause of myelitis except that they have all the etiologies like vascular myelopathy.

[00:14:48] So it's extremely important to keep in mind that because where we are listening to our patients as a physician and when our patients are telling us about the problems that they are experiencing, we need to keep in mind that we need to recognize clearly what are the major clinical presentations of those myelopathies for understanding and establishing a better diagnosis.

[00:15:15] So as a clinician, the first step for evaluation with a patient with suspected myelopathies are recognizing the symptoms of the myelopathy. And for the patient, the most important aspect for telling their clinicians what is going on is to identify the symptoms that are associated with the spinal cord disorder, mostly weakness, sensory abnormalities like numbness, tingling, problems with bladder dysfunction like increasing urinary frequency or gait disturbances that produce lack of balance or unsteadiness.

[00:15:51] And it's extremely important that the clinician and the patients identify the temporal profile of evolution of those symptoms. It's extremely important that the patient discuss with the clinician what is the temporal profile, meaning the onset of symptoms and the plateauing of the symptoms, and the evolution of those symptoms in terms of a temporal profile. This is extremely important for the clinician, for the patient, particularly for understanding the cause of the problem.

[00:16:29] So when we are dealing with spinal cord disorders, and we are trying to identify myelitis and the cause of myelitis. That equation, that actually involves several factors. It's not only the MRI. It's not only just one term of a symptom. It's basically an analysis that you need to identify what is going on with the patient, what is going on with the temporal profile of the lesions, what is the result of the neurological examination to identify the etiological factors.

[00:17:03] So this is an equation that involves several factors, the client profile, the age of the patient, the localization of the problem in the spinal cord. And with that approach, we are able to associate a better diagnosis and more precise diagnosis. So, we, as clinicians, need to pay attention to all of those elements, temporal profile, localization, evaluation, by clinical exam, evaluation by MRI and put together that information along with the spinal fluid analysis, blood testing and other elements that will allow us to establish a better diagnosis and a better precision of the diagnosis.
[00:17:45] So spinal cord disorders are very well evaluated not only clinically but also with the spinal cord MRI. And a spinal cord MRI requires a very careful assessment of the pattern of involvement, not only in the spinal cord to determine what is the involvement of the gray matter versus white matter, what is the extension of the lesion, what is the patterns of the inflammation that may be reflected by enhancement, or what is the evidence that if there is any abnormality in the brain MRI or there is not. So, all of those elements are actually going to tell us importantly in the more precise diagnosis of myelitis.

[00:18:31] The same with the spinal fluid analysis. A spinal fluid analysis is extremely critical for establishing a better diagnosis in myelitis. Identifying the presence or absence of oligoclonal bands, doing a study for viruses or immunological assays that make up 25 specific disorders, like MOG associated disorders or

neuromyelitis optica, evaluating other elements in the spinal fluid in the future will help to understand the potential outcome of the injury in the spinal cord.

[00:19:06] Now let me give you a view of what we are doing for understanding diagnosis and improving precision. And this is a study that was published by our group back in 2018 in the Journal Neurology that represents an analysis of more than 400 patients with a diagnosis of transverse myelitis that later we were able to dissect and clarify if they were really myelitis or vascular abnormalities related with a stroke or chronic vascular abnormalities related with dural AV fistulas.

[00:19:42] And what we basically introduced as an analytical approach was the factor, the different factors that influenced the precision in the diagnosis of myelitis versus a stroke, or myelitis versus chronic vascular problems of the spinal cord. And what we found for example is that in the case of differentiating myelitis versus a stroke, the presence of autoimmune disorder was mostly in favor of myelitis, and the presence of a temporal profile that was hyperacute was actually in favor of the diagnosis of vascular abnormalities of the spinal cord.

[00:20:21] So when we had patients that had neurological symptoms that evolved in a matter of minutes to few hours, and we called this hyperacute, that actually was a factor that influenced more to our diagnosis of a vascular ischemic damage of the spinal cord or stroke rather than myelitis. And the presence of a more subacute and chronic evolving symptoms was mostly in favor of the myelitis. Very interesting that in the clinical profile of a patient with a stroke, the acute onset of excruciating back pain either in the upper back or lower back actually was a factor that was an important factor to identify patients with acute onset of a stroke or vascular myelopathies.

[00:21:16] In the spectrum of chronic vascular myelopathies, actually the chronicity, as well as the involvement of areas of dysfunction like bladder dysfunction or bowel dysfunction, and particularly the worsening with exercise were factors that tilted toward the diagnosis of vascular damage rather than myelitis.

[00:21:45] Age is an important factor and is extremely important because, for example, a majority of demyelinating disorders present in the spectrum of age that is a young age, frequently between 20s and 40s. And this is interesting because neuromyelitis optica spectrum disorders may have the same distribution, but also there is a bit of presentation to our age that is a little bit older, 60s.

[00:22:15] And spinal cord strokes and vascular abnormalities have potential by modal presentation including patients that are very young and patients that are adults over age 60. So, this is important to keep in mind because the strokes and acute or chronic vascular abnormalities may present in a different spectrum of age. Spondylotic myelopathies, those that are associated with spine degenerative disease is frequently a disorder that is after age 50. So thus, it's important to keep in mind.

[00:22:53] So we have identified that the spectrum of temporal profile and the spectrum of age is important for identifying different categories in diagnosis of hyperacute symptoms, identifying acute vascular myelopathies and acute flaccid myelitis in children. Acute symptoms are frequently associated with myelitis or inflammation associated with myelitis in different spectrums. Relapsing and remitting symptoms are frequently associated with myelinating disease or neuromyelitis optica spectrum disorders. And inflammation of the spinal cord associated with sarcoidosis is frequently a chronic, evolving process. So, this is important because we can use all of those elements to improve the precision in the diagnosis of those myelopathies.

[00:23:46] Now, in terms of using MRI and using diagnostic tools to improve the diagnosis of myelitis versus a stroke, it is very clear that the MRI, particularly where the MRI has evidence of beryllium enhancement

or when the MRI show lesion that are particularly localized in the posterior region of the spinal cord, those are elements that help in the diagnosis of myelitis. In contrast, vascular or stroke are frequently extensive, but they don't have enhancement and they tend to have a more gray matter involvement rather than white matter involvement.

[00:24:27] And importantly, the spinal fluid is a very good element and a very good factor to classify diagnosis because the spinal fluid analysis frequently shows with evidence of increased white blood cells, increase of oligoclonal bands or the presence of oligoclonal bands. And this is actually a very important determiner for establishing a very precise diagnosis of myelitis versus vascular etiologies.

[00:24:54] Now, let's go back to one of the concerning aspects of the initial finding that I described to you, and it is that a very important percentage of our patients, almost 32 percent of our patients had other etiologies that were not myelitis, like the spinal cord infarctions or vascular abnormalities. And this is important because if we take a look of the figure that I showed you before, it appears that approximately 30 percent of patients actually represent all of the etiologies, vascular etiologies, metabolical myelopathies, and structural myelopathies.

[00:25:32] So it's important to keep in mind that because the clinician needs to be aware about those etiologies before committing to a diagnosis of myelitis. And the reason is, vascular etiologies may have a different way to be treated. And unfortunately, the major problem that we have is that vascular myelopathies don't have a golden standard for diagnosis.

[00:25:58] We attempted to define arbitrarily vascular myelopathy to those in which we have excluded other etiologies, like inflammatory or autoimmune etiologies, in which the addition was following a vascular distribution, there was good evidence by risk factors known for a stroke like presence of hypercoagulable disorders or presence of other factors leading to stroke to be able to establish that diagnosis. But the reality is that we are still struggling to establish a very good and precise diagnosis of vascular myelopathy because we don't have good criteria to define those by clinical or by neural imaging or spinal fluid studies.

[00:26:51] Now why it's important to keep in mind the differential diagnosis. It is important to define what is inflammatory myelopathy versus an ischemic myelopathy because if we are dealing with inflammatory myelopathies, we have the opportunity to treat those specifically with treatments like IV steroid treatment, plasma exchange. And in that way, we are able to protect the spinal cord from inflammation.

[00:27:20] The problem is that if we erroneously misdiagnose a patient with ischemic myelopathies and treat patients with plasma exchange or other immunosuppressive treatment, we are not helping those patients. We are actually exposing those patients to a higher risk of harming and producing other complications like opportunistic infections or more damage to the ischemic injury that they have experienced already. So it's really important to keep in mind of this because if we have a patient that has an ischemic myelopathy, we need to identify the risk factor that led to the ischemic myelopathy to protect those patients in the future from other damage of the spinal cord or injury associated with ischemia.

[00:28:06] But if we have identified the patient with an inflammatory myelopathy or myelitis, clearly, obviously the options for treatment are very clear. We have the opportunity to use B-cell depletion therapies. We have the opportunity to use complement inhibition therapies that are basically the most important development in the past few years in the treatment of inflammatory autoimmune myelopathies. We have the opportunity to treat with other therapies like TNF-alpha inhibitors in the case of sarcoidosis associated myelitis, or we

have the opportunity to use cytotoxic or immunosuppressive regimens to minimize the inflammatory damage of the spinal cord.
[00:28:52] So it's important then, that when we diagnosis myelitis, we attempt to clarify the myelitis is associated with demyelinating disease, is associated with NMO spectrum disorder, or MOG-related disease because then we will have the opportunity to use all of these therapies, and we may have the opportunity to help patients in a better way and accomplish better outcomes and be able to recover much of the neurological function that patients have lost during the inflammatory injury.

[00:29:30] Now, if we are talking about myelopathies and we are talking about the inflammatory myelopathies, in addition to those pharmacological approaches to treat the myelopathy, we have also to keep in mind that the most important way for recovery is to use the strategies with physical therapy, rehabilitation, occupational therapy. And after that, actually, we need to keep using physical therapy and occupational therapy and rehabilitation. And after that as well, we need to be using the same. And after that we need to be using the same.

[00:30:08] So don't forget that it's not only what you are using in terms of medications like B-cell therapies, like rituximab, like ocrelizumab, or the new medications that have been introduced in recent years, or the use of complement inhibition therapies for NMO, or the use of TNF-alpha inhibitors, we need to keep in mind that it's extremely important to associate those medications or the use of those drugs together with the strategies with physical therapy, rehabilitation, and, the most important, resilience, and, the most important, a very good vitamin P.

[00:30:48] And you are going to be asking me, "What is vitamin P?" I will answer that in the question and answer session. But I'd like to leave a message here is please stop using the diagnosis of transverse myelitis. Let's start identifying the cause of the myelopathy before we establish a better treatment for patients that are affected by myelopathies. Thank you very much for your attention.

[00:31:28] **Angel Simpelo:** Thank you so much, Dr. Pardo, for that very helpful and valuable information. We are just about at our end time right now. But if we could take a moment to answer a question, please? Julie asked, "I was diagnosed in 2008. They did not do any anti-MOG testing." She's not sure why they would test for that, and she asked, "Should I have an anti-MOG test?" And she adds that if she had a vascular myelopathy or stroke in the spinal cord is the treatment different?

[00:32:11] **Dr. Carlos Pardo:** So, Julie, the answer is back in 2008 there was not an antibody testing for MOG. The MOG antibody actually has been developed and improved in the past few years and the validation of that process actually took several years. So, if you think that you may need to reassess the diagnosis in 2008, the most important aspect is share with your neurologist the clinical records and re-evaluate the clinical profile of presentation of your problem. I already gave you some clues. If you think that your symptoms evolved dramatically between a few minutes and a couple of hours or three hours, that is a concern for vascular ischemic lesion of the spinal cord or stroke versus myelitis. If you think that your symptoms evolved over a few days, few weeks, it's very possible that you have inflammatory myelopathy myelitis, and it's important to reassess if there is evidence of antibody, either aquaporin-4, or MOG, or any other rheumatological disorder marker to determine if you are in the right treatment right now.

[00:33:35] **Angel Simpelo:** Okay, thank you so much. Perhaps we could move forward a little more. Another question from T. Scott, "For idiopathic TM, if my MRIs have shown no active inflammation in the past seven years, diagnosed nine years ago, are there any medical treatments I should consider to improve my symptoms?"

[00:34:02] **Dr. Carlos Pardo:** Very good question. So many patients like you actually have that profile that present what we call monophasic myelopathy or monophasic myelitis. If originally at the beginning of your problem there was not an identification of etiological factor, the answer is yes. You may have an idiopathic form of myelitis.

[00:34:20] Some of those idiopathic forms of myelitis were forms that possibly were related with a post-infection disorder, were related with an infection, or were related with some transitory dysregulation of the immune system that produced the myelitis. And that is, unfortunately, we call idiopathic because in the medical term, we were not able to identify a clear cause of the problem.

[00:34:49] If you have remained stable and the myelitis hasn't experienced an exacerbation or reoccurrence of the disease, that means that you are going to be relatively fine in the rest of your life. What is probably important for improving your symptoms is that you have an evaluation by a rehabilitation specialist to direct you in the identification of the deficit and direct you in strategies with physical therapy, occupational therapy to improve some of those problems that you may have, or you may be experiencing right now.

[00:35:27] I always think that the best ally of patients with myelitis and myelopathies is not only the neurologist, it is the best ally person and provider, is your rehabilitation doctor, your physical therapist, occupational therapist that should be helping you to keep a good physical stamina to keep very good physical condition. And remember that by doing physical therapy sessions for six weeks, that is not going to be sustainable if you don't continue doing that. But the reason I emphasize in my previous slides that you need to keep doing PT, and after that you need to keep doing PT, and following that you need to continue doing PT.

[00:36:10] **Angel Simpelo:** Thank you so much. Perhaps we could answer two more questions quickly, thank you. From Tony, "Time profile of appearance of the symptoms seems to be a key part of diagnosis. What are the symptoms that should be considered when evaluating the time profile?"

[00:36:32] **Dr. Carlos Pardo:** So, time profile is very helpful. Particularly to identify what are the symptoms presented at the beginning, when was the time to nadir or plateauing of the symptoms? Because if you have, what we call hyperacute symptoms, meaning from minutes to couple of hours or three hours, that is going to be very helpful for the clinician to investigate the possibility that this is a problem that is a vascular cause of this spinal cord disorder and not necessarily myelitis.

[00:37:15] The period of a few days is basically the period of, a few days to a week, is mostly those autoimmune disorders in the spectrum of NMO, in the spectrum of MOG, that actually are very helpful. And if you have a clinical profile that extends more than several days and weeks and basically is somewhat evolving. That actually is something helpful to say, okay this may be a demyelinating disease in the spectrum of multiple sclerosis, or maybe another type of chronic evolving, or subacute chronic evolving inflammatory myelopathy.

[00:37:59] Or even it's not necessarily a myelitis and may be another type of problem, like those that happen in vitamin deficiency for example. So, dissecting that temporal profile is one of the elements of a better and precise diagnosis. It's not going to be the only one but it's going to be very helpful for the clinician for helping the patient to identify the cause of the problem.

[00:38:27] **Angel Simpelo:** Thank you. And finally, from Janel, "Are there more testing options for individuals who are diagnosed as TM but test negative for MOG, NMO, and other diagnoses?"

[00:38:44] **Dr. Carlos Pardo:** Janel, it's extremely important that once you are diagnosed with myelitis or myelopathy and at the beginning there is not a clear definition of the cause, you keep basically checking

with your neurologist. I frequently advise my patients in which we are not able to identify at the beginning of the spinal cord disorder the cause of the problem, I actually I encourage my patients to return to my clinic in which we are going to say, "Okay, we are going to test for MOG in three months, and we are going to check for NMO in three months, and we are going to check in six months later, or even one year later."

[00:39:26] Or even sometimes we need to check for demyelinating diseases, and occasionally demyelinating diseases show up as a form of myelitis that remains quiet for two, three years and then show up as a form of demyelinating disease with brain lesions or optic neuritis. So, there is always a need to keep alert to the onset of new symptoms or to keep a very good conversation with your clinician to stay alert to the possibility that another disorder may be unmasked later.

[00:40:02] Rheumatological disorders occasionally behave in that way. I mean rheumatological disorders like lupus, or Sjögren's disease, or even sarcoidosis or neural sarcoidosis. So, you need to establish these continuous follow-ups just to be alert to the identification of other factors. If you have remained stable for more than five years and none of those other disorders that I mentioned are diagnosed, I think that you are safe. You can continue being alert but not necessarily extremely anxious that you are going to have another attack or another problem.

[00:40:38] **Angel Simpelo:** Thank you so much. Unfortunately, I don't believe we have time for any further questions. But we will be publishing answers to the questions that have been posted at a later time. Thank you so much, Dr. Pardo, for joining us. We're very pleased that you could join us today. And we're very happy that everyone else could be here with us.

[00:41:06] We invite you to join us for the following talk that's coming up. It's live right now in the stage area, "Acute Treatments at Onset and Relapse" with Dr. Eoin Flanagan. We're going to be moving on now, this is the end of this session. We hope to see you at the next session on this stage. Thank you so much.

[00:41:37] **Dr. Carlos Pardo:** Thank you.