

What is Transverse Myelitis (TM)?

You can listen to the audio of this talk at: https://youtu.be/HkCjO_A82yM

Dr. Stacey Clardy: [00:00:00] Thank you all for joining. This is so fun. One of the silver linings of doing this virtually is that we get to see people well beyond our Mountain West community. So I have the task, as assigned to me by Dr. Galli, of talking about myelopathy and myelitis. And you've already heard of sort of two subtypes of rare neuroimmune conditions from my colleagues, Dr. Sweeney on acute flaccid myelitis, and then Dr. Paz Soldan on ADEM.

[00:00:28] And so, I'm covering, sort of backing up a step almost and going back to myelopathy and myelitis. And these are not, as many of you know, sort of the end definitive diagnoses, but really the category of condition. And so, I want to talk a little bit about this as a starting point, and what we do to help further delineate these diagnoses. So lots to cover because it's so broad. So here we go.

[00:00:52] Oh yeah, and before we totally jump in, we will have some things to talk about that are on-label medications, but we do talk a lot about off-label. But we're so excited, we have three now on-label medication for NMO. One of my other roles is doing the neurology podcast. And this podcast, in addition to the ones offered by SRNA and some of our other support groups, this is where we actually directly interview the neurologist as well. You can download that for free, if you want to hear it right from your neurologist's mouth as well.

[00:01:19] So without further ado, what is transverse myelitis? So, within our community of neuroimmunologists, we all tend to find this to be a little bit of troublesome term. It's been around. It is the term. And the diagnostic criteria are being revisited for this based on the challenges with this. Just the name of the condition itself can be a little bit misleading. And so Ben Greenberg and colleagues are working right now with everyone on revisiting this because it's sometimes neither transverse nor "itis" in the sense of myelitis or inflammatory.

[00:01:56] So this makes it confusing right off the bat, and many of you've been through this journey already. It was named sort of historically, back in the '40s, but it was referring to what the patient was describing clinically as a band-like area of decreased sensation. But, you know, when we learn about this in our training, many of us sort of think that the transverse myelitis is referring to the MRI when, in fact, it's not. So it is important to know historically how the term came about.

[00:02:26] And then the requirements to make this diagnosis, it can be very challenging within neurology, let alone sort of in the ER and other physicians who may meet someone presenting for the first time to understand, does someone meet criteria or not. Some of the definitions require bowel and bladder involvement or motor involvement, but many of you will know that sometimes it's really just a sensation that's the first sign of this. Some of the definitions limit how long you can have had the onset of a symptom and some of these definitions also exclude other things that should be included under the umbrella. So as you all know, just preaching to the choir here, that this can be confusing at the onset.

[00:03:04] One thing we do know for sure is that we have to listen very, very closely when patients tell us about the onset of their symptoms. This is where we're sort of sitting intently listening to what is said about when this first started, because if the symptoms go very, very rapidly, less than a day completely normal to abnormal and, and the worst of the symptoms within hours, we worry very much about a spinal cord infarct. And this is a rare, you know, like many of these, but even this is rare among rare condition, but so important to recognize and so important for us to be aware of because we can try different therapies for this. We can even try sort of our traditional stroke therapies like an intravenous tPA, although there's no studies, but we would want to know so that we can really throw all the resources we have at that.

[00:03:51] If you go from, you know, presymptomatic to the worst of the symptoms within one to 21 days, that's where we think about inflammatory causes like the NMO and MS. And I have transverse myelitis written here because many of you know or many of you may be in the category of what we call idiopathic transverse myelitis, meaning we're not quite sure what caused it. And finally, if there's a longer progression, more a story that you're telling your doc over a month or months or a couple years of this sort of worsening, we worry about some of these vascular causes that can be very subtle and hard to detect on imaging, or we worry about degenerative causes or a combination of the two of them.

[00:04:33] And, you know, it, it's probably not surprising to this group, but it's surprising when I give lectures to my colleagues that the, the most common misdiagnosis of myelopathy or transverse myelitis is something we call Guillain-Barre syndrome. You know, this post-infectious, sensory kind of condition that we won't get into too much detail on, but that point is it's very different. It doesn't involve abnormalities on the spinal cord imaging usually. But yet this is the most common misdiagnosis, and I think this really highlights well how we need to get better at educating everyone: the public, the physicians, everyone what to look for when trying to diagnose transverse myelitis or myelopathy.

[00:05:12] And why do I keep using those terms interchangeably? Well, because myelitis is the one we all know, but myelopathy is probably the one that we should be using because "itis" implies, again, inflammation, but we just talked about the fact that this is not always inflammatory. And so we should probably start at myelopathy, start broader and then rule in or rule out myelitis, right?

[00:05:32] We call that differential diagnosis in medicine, and we want that to be very broad. We try to be very broad when we first meet a patient so that we don't miss something. We don't want to have tunnel vision right out of the gate and then not catch some of these other less common cause of spinal cord symptoms. Because this affects how we treat, this affects the prognosis. You know, if we start from a shaky foundation, everything else is not going to be optimal. And so, how do we sort this out? Well, if we're starting with a suspected myelopathy, spinal fluid and MRI imaging are really the mainstays. These are very important. And not just obtaining them, but obtaining them correctly. Checking the right things in the spinal fluid and getting the right imaging from the MRI and then really pouring over those images in the different cuts that we get to make sure that we're not missing any subtle clues to the cause.

[00:06:26] Many of you've been down this journey. Many of you may still feel like you're in it, right? And so these are sort of things to pay attention to. You know, all of you know you need to advocate for yourself. We're here to teach you how to advocate for yourself and for your care. So in the spinal fluid, if it's noninflammatory, meaning we check the white blood cells, oligoclonal bands, the protein levels, all of that, and it all is completely normal, not even a little bit outside of normal. That may start to make us think about the metabolic or vascular causes for your symptoms and less of the inflammatory NMO, MS kind of ones. If on the other hand it is inflammatory, if you have some extra white blood cells, it doesn't have to be a lot. You know, the cut of white blood cells in spinal fluid is often a level of like five or something. Many of our patients will just have a level of 10, but that's enough and it's abnormal.

[00:07:17] Same thing with proteins levels and stuff like that. If we get those hints, then we start thinking about multiple sclerosis, NMO, MOGAD, infectious causes, and neurosarcoidosis. So this is just sort of some clues, things that should be sending off flags to us to make sure that we don't rule things out too quickly. Likewise, even if we find an inflammatory cause, sometimes we'll still go back and look for things that can aggravate it as well as a comprehensive approach to spinal cord health. So even if I know someone has NMOSD, I'm still going to check their vitamin B12 levels because low B12 can sort of weaken or make your cord more vulnerable. Things like that. So a really comprehensive look. Constantly revisiting it at every visit.

[00:08:02] I want to talk to you about two large studies that were done by members of SRNA. This one is by Carlos Pardo out of Hopkins. And they are, you know, like many of us, a referral center for questions of not clearly diagnosed myelopathy or transverse myelitis. So in this study they looked at 457 patients that were referred to them with a presumed diagnosis of transverse myelitis and the really important conclusions from this study. I couldn't have said it better here than he does, so I just pasted it, right. "The temporal profile of the symptoms serves as a clinical biomarker in the differential diagnosis."

[00:08:37] So like we just said, listening to your story, it turns out is not shocking, but so often, you know, not completely done. Listening to your story and how quickly it happened or how slowly it happened and what happened in between. Was it stuttering? Was it a really clear dramatic course? This is probably the best biomarker we have to start us off to figure out your cause, right? And then, they also stress here, "The establishment of a definitive diagnosis requires critical analysis of MRI and the spinal fluid," right? The clinical analysis piece here is very important. For example, in our group, whenever we have a questionable diagnosis, we present it to the entire group with our neuroradiologists. So you don't just get one of our opinions, you get the opinion of all 15 or 20 people who are in that room looking at the images and listening to the story.

[00:09:27] And finally, of all the predictors, the temporal profile - I put it here again in red - contributed the most to discriminating different causes. So I think this is so important. And hopefully, you're experiencing that this is being looked at in, in your presentations as well.

[00:09:43] Here's another similar study that came out at a similar time from our colleagues at the Mayo. And they looked again for 226 patients that were sent to their center for idiopathic, meaning not clear cause, of transverse myelitis and they tried to see, could they sort out what the cause was

in some of these cases? And what did it look like? So again, back to our point about misdiagnosis, you'll see on this slide, actually 27 of these patients didn't actually have a transverse myelitis or myelopathy. So this is a tricky thing to really pay attention to, to look at.

[00:10:19] Even in their hands going over this in incredible detail, 41 of these patients still ended up with an unclear cause of the myelitis or the myelopathy. And then you can see all the other sort of ones that we're more familiar with here down below including, you know, the ADEM, that you've already heard of and the MOG and NMOSD and neurosarcoid, you'll hear about later today.

[00:10:39] Not to be forgotten here, they sorted out 53 of these patients. They said, "You don't have transverse myelitis. You have a myelopathy." Meaning it wasn't inflammatory. And the, the causes are listed there: spinal cord infarctions, compressions, nutritional deficiencies. And just sort of hammering this home again, for those of you who aren't certain that you are confident in the cause or the diagnosis or you've been told so far that we can't figure it out, again, these are things that we are looking for. Did you have a complete loss of spinal cord function? Well, you can have an acute sort of discompression that causes something like that or a trauma, right?

[00:11:18] You know, we... there's all kinds of things us neurologists worry about, the, you know, the trampolines, and, and, you know, with sort of hitting the spinal cord. Or surfers can bend back and get a myelopathy by having their back hyperextended. You know, this is why we're paranoid folks sometimes as neurologists [laughs], but we look at these causes, we ask these questions. I frequently say to my patients, if it's not a clear cause, "Hey, are you a horseback rider?" "Have you ever been thrown by a horse?" "Have you ever been in a car accident?" I ask them all these questions and they kind of look at me funny, but it's really to try and tease apart these possible vascular or traumatic related causes.

[00:11:54] And what other symptoms go with it, right? It's so important to know, you know, beyond the numbness or the weakness is there bowel and bladder involvement. You know, is there, you know, abnormal sweating? Is there, you know, visual loss going along with it? Is there something that indicates to us that it goes up beyond the spinal cord? All these questions are so, so important.

[00:12:17] So I'll give you a couple of quick samples in the very few seconds I have left. Here's an example of a vascular. Again, timing matters for this. And the treatment is totally different. You can have vascular cause being stroke or you can have vascular cause being abnormal vessels feeding and then that's not as traumatic, but feeding in and around the spinal cord. And these... this is so important to know because if you get plasma exchange or steroids with this, your symptoms could very well get worse.

[00:12:45] Here's an example of a compressive myelopathy. I want you to take away two things. Yes, we should look at this. This is usually apparent on imaging. But also, many of us have more than one thing going on. You could have an NMO, an MS or a sarcoid, and if you also have degenerative disc disease in your neck, that may be where you get your inflammatory lesions, right? So there's no rule saying you can only have one cause of your symptoms. We frequently see folks who have a disc, you know, that's degenerating in that area and then they get a sarcoid lesion or an MS lesion on top of that. So keep that in your mind. That's important to remember.

[00:13:20] We'll talk more about sarcoidosis, I think, later, but very important clues that can be found when looking in, critically at the imaging with contrast enhancement patterns. And even sometimes PET scans can give us a clue to a neurosarcoidosis when we need to do that. NMOSD, you'll get a separate lecture on this as well. But again, this presents when we look at the sagittal images compared to the axials. You have a you know, you're a lot more likely to have half of the cord involved and that helps us sort it out. And more likely to have these other clues here, right? You might have Sjogren's, lupus, myasthenia, these other autoimmune conditions, either personally or in the family. So we ask about it: nausea, vomiting, hiccups common in our NMO patients as are these other things. So important that you're asked about these when we're trying to sort these things out.

[00:14:11] And then the newer myelopathies. Next, after me, we'll have a talk just on MOGAD. This one's new, emerging. It's where aquaporin-4 positive NMOSD was 10 to 15 years ago. So we've got a lot of work to do on MOGAD right now. PFAP, we didn't talk about this too much. This is one more of our autoimmune paraneoplastic class of myelopathies and myelitis. And again, important that this at least is considered somewhere in the back of our heads when we're trying to do the diagnosis. Acute flaccid myelitis, you already heard a little bit about this morning from Dr. Sweeney. You'll hear more about it this afternoon as well.

[00:14:45] Treatments are evolving. Acutely, they're very often the same. People choose from IVIG, IV methylprednisolone, and plasma exchange or mixtures therein. And then we have targeted therapies. You'll see several times on here, I think we need trials. There are multiple papers on each of these, but for neurosarcoid, for example, and for MOGAD, we have no prospective trials at all yet. So this is what we still consider low quality data, but things are evolving rapidly there. Most important, for all at the bottom is aggressive rehab and symptomatic management, especially pain, right? Pain in this sort of trauma, figuring everything that goes out can fall down the list. It should never fall down the list. We need to address this early and often: spasticity, pain, bowel, bladder, and aggressive rehab.

[00:15:32] So overall, we have to start at myelopathy, then figure out if it is transverse myelitis. Make sure it's not some of the other causes. We don't ever want to delay treatment, but we need to be sort of suspicious and always revisiting it. At each visit, I revisit how confident am I in the diagnosis? Sometimes I'm 100% confident. Sometimes I'm 80% confident, and we revisit. If it's anything less than 100% confident in the diagnosis, each time I revisit, each time I go back over. We look at the new data or new antibodies or new testing that's come out.

[00:16:03] I always do say, if somebody's doing repeated spinal taps and trying to continue down this diagnostic journey, you must insist that they save that spinal fluid for you so that, you know, they're not doing another one just because we forgot to get something the first time. It's very easy to just save it and test it later and test it in sort of research assays.

[00:16:23] Make sure that your neurologists are the types who are not afraid to consult, who are supporting you in second opinions if they're necessary, and listening to you, especially about the course of your illness, and as time goes on which symptoms are the most bothersome. Here's a quick shot of our new rehab hospital I'm incredibly excited about. I encourage you to watch the video. The things that we are able to offer for our spinal cord and neurologic patients now are just amazing.

And so I'm so excited that we've opened this facility. That's all I have. I want to introduce to you next, my colleague, Dr. Sravanthi Vegunta, a neuro-ophthalmology fellow at the Moran Eye Center.