Rare Neuroimmune Disorders Q&A Panel

You can listen to the audio of this talk at: https://youtu.be/wRpnPFY7VSM

Dr. Stacey Clardy: [00:00:00] Okay. It looks like we have this session here. I guess we read the chat. Does that sound about right?

Dr. Jonathan Galli: [00:00:05] No. So I, I will, I have questions that I will share with you guys and I'll read them out, kind of one at a time and then we'll take it from there. And then I believe the session goes to 10:15. That's my understanding.

[00:00:22] So, I, I have the list of questions that, that our patients and families have sent. So I'll start with the first one and we'll kind of take them in order. The first question is, can I have a transverse myelitis relapse after having transverse myelitis for 23 years? This week, my left arm which was not affected before suddenly started getting that numb, pain feeling in the front of my legs and lower back, and all around my ribs had since the onset in March of 1997. Is this possible? I always had pain-free arms and total use of them.

[00:01:00] Dr., Clardy, you want to weigh in on that?

Dr. Stacey Clardy: [00:01:02] You're assigning those? Okay. Absolutely. Depending on the underlying cause of transverse myelitis, I think we'd all agree that it can relapse. And some causes can relapse, you know, five years, a decade later, depending on the cause.

[00:01:19] So generally, we take a twofold approach, right? Treat those symptoms but also try and figure out, is it a relapse or is it what we would call a pseudo relapse? Meaning the old injury is somehow becoming more symptomatic without actually acute new inflammation, or otherwise. So it's always important to reimage.

[00:01:36] And then depending, again, on the clinical scenario with all the details, we will sometimes consider retesting if the cause of the original transverse myelitis was never definitively determined. So that could include a repeat spinal tap, repeat serum testing, and other things in addition to the imaging. Mateo, you want to weigh in on that too?

Dr. Jonathan Galli: [00:02:04] He might've frozen.

Dr. Stacey Clardy: [00:02:07] For a second you all did. Anybody? How about, you know, Michael, you want to weigh in?

Dr. Michael Sweeney: [00:02:10] I agree with that. The, the risk for relapse in what we would call otherwise idiopathic transverse myelitis is really low. But, you know, in MOG positive disease, or NMO-related TM, or multiple sclerosis, but certainly you could have a relapse. So I agree that the important part is to figure out if you have evidence of new inflammation or is this a pseudo relapse or old symptoms coming out?

Dr. Jonathan Galli: [00:02:38] Okay. And then we'll move on to the next question, just so that we can try and get through as many of these. The next question is about epilepsy and transverse myelitis.

[00:02:51] And the question is, are there many people out there with both epilepsy and transverse myelitis? About one month prior to contracting transverse myelitis, I have the first two of major car crashes that I caused due to having seizures while driving. During the accident, I was hit in the back of the head by a gallon of plaster that was in the car. Does anyone think this could have added to the transverse myelitis? When I contracted it, or sorry, when I did contract it, I was misdiagnosed and told it was all in my head and that I had conversion disorder and as a release, told to get physical therapy. I couldn't walk or feel my legs.

[00:03:32] I guess I can weigh in on that and then let the rest of our panel. So, we certainly can see transverse myelitis occurring in the setting of other neurological diseases. I think, as providers, we oftentimes like to put everything under one umbrella and have an explanation for it. But I don't typically expect transverse myelitis, which affects the spinal cord, to lead to seizures on its own. Now that being said, are there processes that can, you know, cause epilepsy but also transverse myelitis? There are, but they're relatively rare. And, kind of like we talked about in the first part, as we don't have all your clinical information, it's hard to weigh in on exactly what happens.

[00:04:16] But certainly, it's something to, you know, at least wonder about if, if the two are related. That at the same time, you know, certainly we'll see patients that have primary epilepsy and then develop transverse myelitis kind of for a separate reason down the road.

[00:04:38] Does the rest of our panel have any additional thoughts?

Dr. Stacey Clardy: [00:04:45] I agree, JJ. You know, we don't maybe talk about it too, too much, but certainly there's no rule saying that you can't get more than one neurologic condition and it all sort of depends on the specific details for that situation. And, and both of those could have been post-traumatic who, you know, we wouldn't really know without reviewing the records but yeah, absolutely. I think all of us have many patients who have, carry more than one neurologic diagnoses, and certainly that's as common a combination as any.

Dr. Michael Sweeney: [00:05:15] Yeah, I would also say, you know, MOG-related disease can also present with encephalitis and have inflammation in the brain, and you could have seizures related to that. NMO, less likely, but also can cause inflammation in the brain. But I agree, it's probably pretty rare.

Dr. Jonathan Galli: [00:05:36] And then, the next question is, has granulomatous disease been explored as a possible risk factor for AFM or transverse myelitis? And Dr. Clardy looks ready to chomp at the bit. So I don't want to steal her thunder too much.

[00:05:53] I can tell you as, as her fellow, I'm sure Dr. Sweeney went through this as well, if you're not considering granulomatous disease as a potential cause for transverse myelitis, you definitely could be missing it. And so I will let Dr. Clardy weigh in on that a little bit, a little bit more. And then Dr. Sweeney, if you want to touch on, you know, your thoughts on it, in the setting of AFM.

Dr. Stacey Clardy: [00:06:18] This could really be… I've noticed actually there's a few people on here inquiring about granulomatous disease and sarcoid. We should start by saying that, that often they're synonyms. Sarcoid is a type of granulomatous disease.

[00:06:29] There are other types of granulomatous disease, some of which commonly are associated with immune deficiency, an immune deficiency called CBID. Whole separate lecture, right? But granulomatous disease in general refers to the family of conditions where you deposit little things called granulomas anywhere in your body.

[00:06:48] And, and really, they're just, sort of a good way to think of them as abnormal clumpings of white blood cells that just aren't being cleared appropriately, and over time, if they sort of stay in a little clump in one place, they can form little calcifications. Right? So one thing that we do whenever we see someone coming in with a transverse myelitis into our clinic, one of the top things for an immune-mediated cause is sarcoidosis. And so we tend to look elsewhere in the body to confirm that. We don't like to biopsy the spinal cord because that will give you lasting damage. So we start usually by a really extensive questioning of your history. We'll often get a CT scan of your chest to look and see if you have any of those little granulomas there because that's the low hanging fruit, as we call it.

[00:07:28] Many people do have evidence there. If you don't have it there, we'll ask you about your eyes, we'll ask you about your skin because really you can deposit a granuloma anywhere in your body. So we try to almost get a surrogate sort of sense of, do you have granulomatous disease? If you've already got a granulomatous disease diagnosis, you know, half the work is done here.

[00:07:45] When people come into us and say, I already have sarcoid, then we just really look at the characteristics of the transverse myelitis or any central nervous system abnormalities. And if they meet, you know, again, there's many publications on this by Flanagan, we just put one out at the U of U with our experience with neurosarcoidosis. You can find them, they're all readily publicly accessible. We look for the features, the enhancement, you know, really get nerdy about the imaging features, and, and absolutely can happen. And I will tell you the favored treatment for that now is infliximab, based on three retrospective studies: a large multicenter US one, ours at the University of Utah, and now, a European one that just came out in the last month or two. But I would, if this is the question and you feel like you're not getting an answer, this is a case where you definitely want to seek a second opinion, because the treatments vary compared to say NMO and MS and all the other things. Infliximab is not commonly used for those.

[00:08:38] So I'll stop there.

Dr. Jonathan Galli: [00:08:46] And Dr. Sweeney any thoughts on, you know, when you're evaluating a pediatric patient for AFM, is this something that you commonly see or worry about?

Dr. Michael Sweeney: [00:08:55] I would say it's, it'd be very far down the list in a, in a pediatric patient especially presenting with flaccid myelitis. It's not the usual course for a sarcoid-like presentation. Could it happen? Sure. But I think it's pretty far down the list.

Dr. Jonathan Galli: [00:09:11] Great, thanks. So the next question is, I've had some kind of issue that felt like the return of a recurrent transverse myelitis attack. The MRI was normal, but my entire thoracic spine was originally damaged. It affects my legs. My doctor said it was just the nerve damage causing symptoms. Has any doctor seen this?

[00:09:41] So one of the things that can be really tricky, both for patients and providers. And many of these, these, conditions, but especially, you know, when you have spinal cord damage from them is, am I having a flare of old symptoms for whatever reason, or is this a new attack? And it's something that can be really hard to distinguish.

[00:10:04] And I think, you know, hopefully we can try to clarify this a little bit. When you, when you have a, when you have a demyelinating lesion to the spinal cord, like we talked about, it's essentially like stripping the insulation off of an electrical cable or a corridor, or what have you, and you never really repair that fully.

[00:10:28] So that signal is going to be abnormal, kind of, moving forward. Now, you're able to compensate for it to some degree some of the times, but certain things can make those symptoms worse. So oftentimes, our patients with NMO or transverse myelitis, if they get sick, if they're really tired or stressed, if they're in heat, urinary tract infections are another example, those, those things can make your old symptoms kind of flare up. At the same time, you know, if we have a new patient there for, sorry, symptoms oftentimes, we will have to ask ourselves and, you know, re-examine our patients and think about repeating imaging to make sure that you don't have new lesions. But it admittedly can be very tricky to parse the two out.

[00:11:20] Do you guys have any other thoughts, comments?

[00:11:22] Okay we can move on. Here's a question I'm sure Dr. Sweeney, you get this the most. Are vaccines contraindicated after diagnosis of transverse myelitis?

Dr. Michael Sweeney: [00:11:42] So in general, no. You have to consider the acute treatments you get. So if you are treated with steroids and IVIG, plasmapheresis, in general, we don't like to give vaccines in close proximity to those treatments.

[00:11:58] One, because you won't mount as good of a response, but two, if you're getting a live vaccine, there's some danger there.

[00:12:04] So, I usually recommend not getting a live vaccine for six months after those treatments. I use best judgment when getting other vaccines.

[00:12:17] If you're going to be placed on a long-term therapy then each, each immunotherapy has kind of their own recommendations, but we try to get all of the vaccines that would be necessary for a certain age in before starting on an immunotherapy, if we can. And, try to not give, so say someone's getting rituximab, not giving a vaccine within like three or four weeks after getting dosed with that. But certainly no live vaccines during treatment.

[00:12:50] I think maybe some people wonder about, you know, the, the causation of a vaccine with transverse myelitis and would that predispose them to getting a reaction in the future. So, cases of

transverse myelitis following vaccination have been reported but are very rare. And there's no evidence, and I'm not aware of any reports, of people getting multiple reactions after vaccinations should those people go on to get additional vaccines. But that's a good question, discussion to have with your neurologist.

Dr. Jonathan Galli: [00:13:23] And then, Dr. Vegunta, we haven't forgotten about you, I promise. We're now getting down to the MOG questions. I guess, we'll do kind of a two-part piece, we'll kind of combine two of the questions.

[00:13:43] Would you recommend Solaris in MOG antibody patients? And have there specifically been any clinical trials? And what new discoveries have been made more recently in, in MOG antibody disease?

Dr. Sravanthi Vegunta: [00:13:52] That's a tough question for me, honestly. I wonder if other people in the panel could better answer that than me, because I'm much more focused on eyeballs.

Dr. Jonathan Galli: [00:14:04] I was going to say, yeah, that's okay. I just don't want… I don't want you to think we've forgotten about you.

Dr. Sravanthi Vegunta: [00:14:15] No, I'm learning a lot listening in.

Dr. Jonathan Galli: [00:14:20] Yeah, Dr. Clardy, any thoughts? I can also weigh in on this as well. I'm happy to.

Dr. M. Mateo Paz Soldán: [00:14:25] I wouldn't say that MOG... It's a new enough entity that we're still in the rapidly evolving knowledge phase of that. Because it's shared features with some of these other diagnoses that we talked about, the treatments that have been used are in analogy to those other treatments. And in particular with the long myelitis, sometimes with severe or bilateral optic neuritis, but we think a lot about whether it could be treated the same as NMO, and much of what we do to treat is an analogy to that. I'll add, though, that we know that some people with MOG associated demyelinating disease have a transient positive antibody and later goes negative.

[00:15:09] So those people might only get treated with maintenance immune therapy for a little while and then eventually come off. Those who remain antibody positive, we are, again, I'll say in analogy to NMO, thinking about it similarly. But it might be a long time between attacks, but we worry about severity of the attacks.

[00:15:30] So the list of medications that have been discussed for NMO are the ones we use. However, I think Dr. Clardy could also weigh in on this, some of the more recent trials with specific medications now FDA-approved to treat NMO, they either specifically excluded MOG antibody patients, or if they did include seronegative patients or MOG antibody patients, some medicines don't work the same in NMO as they do in MOG. So we keep that in mind as well.

Dr. Stacey Clardy: [00:16:00] There are a couple of multi-center prospective MOG trials in the works. You know, I know we've been contacted. We also were sort of trying to push these. There, it does behave differently as Dr. Paz Soldán said from aquaporin-4, and I think that's very important to remember. And when you're talking with your physicians, be certain that they're aware of that if

they're not seeing a ton of this all the time. That aquaporin-4 and MOGAD, one thing that is clear right now, is that they should not be treated the same.

[00:16:40] Right? You can't lump them as one condition. The pathophysiology is different. We already have early data suggesting that treatment response is different. So the three medications that were recently approved for NMOSD were approved, as Dr. Galli covered, for aquaporin-4 positive NMOSD.

[00:16:58] And the reason those companies went for that indication is, one, because they studied majority aquaporin-4 positive patients. But perhaps, are also maybe getting a signal in those two trials that enrolled seronegative patients that, that maybe the medications aren't as effective. And, and, you know, there'll be different breakdowns of MOG in that component, but we need prospective trials for MOG and for MOGAD basically.

Dr. Jonathan Galli: [00:17:22] And then, Dr. Paz Soldán, there was a question about, just have to find it now. Yeah. Has anyone or their child not fully recovered from ADEM? Um. My daughter has nerve damage throughout her lower body and no one seems to be able to give us an answer. If you wouldn't mind touching on, kind of, some of the long-term outcomes, if you will, in relation to ADEM.

Dr. M. Mateo Paz Soldán: [00:17:41] Yeah, I did mention when I was speaking about ADEM that most children, more so than adults, but most children do recover quite well, but not everyone does. And if, you know, unfortunately, a child falls into that category where symptoms don't completely recover, then really any other cause of spinal cord injury would be similar to symptoms that can come and go based on various things. It's been mentioned already in this discussion here, that infections is a common reason for symptoms to be aggravated. And, and really what we need to sort out is, do we think that there's still inflammation? Or whatever the pathology was that caused the problem, is it still active?

[00:18:34] Yeah, because then repeating acute therapies might be important. Or is there no longer any active pathology, no longer any active inflammation? And then we focus on treating the symptoms. We unfortunately don't have medicines to repair damaged nerve fibers in the spinal cord.

Dr. Jonathan Galli: [00:18:47] Thanks. We'll move on to the, another question. If a patient who is aquaporin-4 seropositive, has had one attack, which was the initial one and is attack-free for seven years, can it be treated as a monophasic NMO?

[00:19:11] And this is a, this is a great question. And this is actually something we get asked in clinic quite often. You know, I had my attack, and everything's been quiet for years, do I have to go on, you know, this immune suppressing therapy? And, and the answer is that there are probably some cases of neuromyelitis optica that are monophasic in the sense that they've had one relapse. But my question is always, until when? When we look at the kind of the natural history and things like that, back in the previous studies that have been done, we definitely can see patients go years without a relapse, but you're always at risk for one when we actually look at the natural course of the disease.

[00:19:50] And so in that case, I would still, you know, in my patients we're still recommending indefinite treatment based on the long-term risk of relapse. I don't know if you guys have any other, you know, I learned under Dr. Clardy, so a lot of this she hopefully agrees with, but I don't know if her, Dr. Paz Soldán, have anything else to add to that?

[00:20:15] Okay. Alright. And we'll move on to the next question. With the current pandemic, is it still okay to receive rituximab?

[00:20:30] We can, Dr. Clardy, I don't know if you want to weigh in first to see?

Dr. Stacey Clardy: [00:20:36] I'm happy to address that one. Yeah, I think, you know, we all worry and, you know, as docs, we've, we've really been concerned throughout this because almost all of our patients are immunosuppressed or immunocompromised. So far, at our University, many of our patients are doing quite well. They don't have the option to stop their immune suppression, you know. We don't take the decision for people on these medications lightly. So, yes, certainly we've had a few patients, both in our clinic and the rheumatologic clinic, on rituximab and similar agents get COVID and recover. So we've been fortunate, I think. It's a case by case basis, though, for sure. And it does depend on the other comorbidities that we all hear about in the press, you know, hypertension, obesity, lung disease, severe asthma, those sorts of things. And, I would say, you know, it's a, it's a personal decision you discuss with your physician and we've discussed it with each of our patients. Lots of messages going back and forth, understandably. But you know, when you're looking at conditions, like for example, aquaporin-4 positive NMOSD, the stakes of having an attack off of therapy are just too high. And, you know, we don't, we don't like to scare our patients, but certainly all of us have seen an untreated aquaporin-4 positive NMOSD attack.

[00:22:04] And it's not something we're willing to risk. We know we can generally support people through any infections they get. Coronavirus is just the newest flavor there. Yeah, but certainly have the discussion with your doctor, I would say, absolutely to, to assess your specific risk factors. You know, we monitor our patients, their immune systems in general, what's their IgG level look like? What does their lymphocyte count look like? All of that. And then, you know, for COVID especially, the best, you know, prevention right now is being cautious. Certainly, we're all doing this on your behalf as well. I haven't had a haircut in decades, you know, it feels like. Sort of staying out of public and avoiding unnecessary risks is really the best thing to do.

[00:22:53] And I think a lot of us have it dialed in on how we can do that well. I, you know, I don't go out without a mask, any of it, mostly for my patients at this point. So I would say discuss with your specific doctor, your situation, but by and large, we are recommending that all of our patients that needed immune therapy before COVID are still on it because they need it.

Dr. M. Mateo Paz Soldán: [00:23:14] Okay, I'll weigh in as well. And reemphasize what Dr. Clardy said that when we choose to put a patient on these medications, we're really balancing the risk of the disease activity with the risk of the medicine. But I'll add that, specific to medicines like rituximab, you know, we're talking today about neuroimmune diseases and so we don't have experience directly with these, but we do have experience with these medicines treating other more common diseases. And in particular, multiple sclerosis medicines like rituximab, these B-cell

therapies are used. And there's a registry in Europe, there's a registry in North America where neurologists across the country at neurology centers can add information if they unfortunately have a patient taking these B-cell therapies who contracts Coronavirus. And we know from the North American registry, where there's almost 900 people taking various immune therapies that have been added to it, that the risk of longer illness and more severe illness is what we see with medicines like rituximab.

[00:24:11] So if you're taking those, you should for sure, should be cautious about doing all the things to keep yourself safe.

Dr. Jonathan Galli: [00:24:20] And I would just, I would echo all of that. And we'll, sorry, we're getting a little bit close on time and I'm going to try to take some questions out of the chat as well.

[00:24:32] Dr. Paz Soldán, this, I think would be a good question for you. For the ADEM presentation, MOG is not mentioned as a possible cause or in relation. And so the question is, is ADEM not affiliated with MOG anymore? And, I think, if you wouldn't mind, just kind of differentiating the two a little bit as far as kind of from a diagnostic standpoint.

Dr. M. Mateo Paz Soldán: [00:24:58] Yeah. You know, actually, Dr. Vegunta actually had a good slide in her presentation where she was showing sort of the history of what we thought MOG told us or didn't tell us about various neuroimmune diseases. And, it's a, it's a low percentage, but, you know, people with multiple sclerosis, some of those test positive for MOG antibody, ADEM, et cetera. Early on, we were testing MOG in children presenting with ADEM because we thought that that gave us some idea about what to predict about their future, whether we thought it would be monophasic or they'd be at risk for recurrence. And as we've learned more about MOG, really, you know, it's similar to ADEM as the first presentation of multiple sclerosis. ADEM can be the first presentation of MOG antibody associated demyelination. And so if we see that antibody, it's not so important that the initial presentation is ADEM. We really just take the antibody positive result and follow that forward and think about treatment in the context of MOG antibody associated. Rather than maybe they presented with optic neuritis first or a myelitis first or an ADEM type of a picture. It's the antibody that we're trying to learn more about and that guides our treatment moving forward.

Dr. Jonathan Galli: [00:26:22] Great. Thank you. Unfortunately, we, we are all out of time for this question session. I really appreciate all the great questions and I apologize. I know there were, there were many that we didn't get to. Before we go, I just wanted to thank everyone who submitted questions and then, of course, all of our speakers from the first session: Dr. Clardy, Dr. Vegunta, Dr. Sweeney, and Dr. Paz Soldán for their time, for helping answer these questions. And with that said, we're going to transition from the sessions area over to the stage, and we're going to talk more about symptom management in these various conditions.