Transverse Myelitis

Symptom Management

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Krissy Dilger: [00:00:00] Hello, and welcome to the SRNA "Ask the Expert" podcast series. This podcast is entitled "Transverse Myelitis: Symptom Management." My name is Krissy Dilger, and I will be moderating this podcast. SRNA is a nonprofit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our website at wearesrna.org.

[00:00:30] Our 2021 "Ask the Expert" podcast series are sponsored in part by Alexion, Genentech, and Horizon Therapeutics. Alexion is a global biopharmaceutical company focused on serving patients with severe and rare disorders through the innovation, development, and commercialization of life-transforming therapeutic products. Their goal is to deliver medical breakthroughs where none currently exist. And they are committed to ensuring that patient perspective and community engagement is always at the forefront of their work.

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[00:01:33] Horizon is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare autoimmune and severe inflammatory diseases. They apply scientific expertise and courage to bring clinically meaningful therapies to patients. Horizon believes science and compassion must work together to transform lives.

[00:01:59] For today's podcast, we are pleased to be joined by Dr. Ram Narayan and Dr. Elena Grebenciucova. Dr. Narayan is an Assistant Professor of Neurology, Division of Neuroimmunology at the Barrow Neurological Institute in Phoenix, Arizona. He also co-directs the Demyelinating Disorders Clinic at The Phoenix Children's Hospital, which offers patient care in the areas of multiple sclerosis and related neuroimmune disorders to children in the southwest region.

[00:02:31] Dr. Narayan received his medical degree at PSG Institute of Medical Sciences and Research in Coimbatore, India, and completed a neurology residency at the University of Texas Southwestern Medical Center in Dallas, Texas, and a multi-institution neuroimmunology fellowship at UT Southwestern and The Johns Hopkins University.

[00:02:57] Dr. Grebenciucova completed neurology residency at the University of Chicago in Chicago, Illinois. Dr. Grebenciucova has been interested in autoimmune disorders of the central nervous system, including rare neuroimmune disorders, since medical school. After residency, she completed a neuro immunology

Fellowship under the mentorship of Dr. Brenda Banwell and Joseph Berger at the Perelman School of Medicine of The University of Pennsylvania.

[00:03:28] Currently, she is an assistant professor of Neurology (MS/Neuroimmunology) and neurological infections at Northwestern University in Chicago, Illinois. Dr. Grebenciucova sees patients with rare autoimmune conditions, including NMO, MOG antibody disease, transverse myelitis, and autoimmune encephalitis.

[00:03:51] Welcome and thank you for joining us today.

[00:03:53] We are starting off with Dr. Ram Narayan. So, for our first question, can you describe how the damage to the spinal cord causes the symptoms in arms and legs with transverse myelitis?

Dr. Ram Narayan: [00:04:10] Yeah. So, the three cardinal symptoms of transverse myelitis, in a nutshell, would be lack of strength or impairment of strength, i.e., weakness, number two, impairment of sensations, number three, impairment of bowel and bladder control, all these three. So, the muscles, sensations, the muscle strength, the sensations, and the bladder function are controlled by the brain and, you know, the brainstem, as well.

[00:04:49] For their signals to reach these end organs successfully, you need a very intact spinal cord. The moment there is an injury in the spinal cord at any level, these impulses, so, impulses that go from the brain to the muscles or to the sensory receptors or the bladder and bowel, they're going to be affected. All of these end organs are also constantly sending signals to the brain. That's also going to be affected.

[00:05:17] So, traffic flow in both ways is going to be hindered. And this happens to various extents, depending on the size of the lesion, how much it affects the spinal cord in the transverse level, and how much in the vertical level, and how many lesions are there, how old the patient is, depending on all of these.

[00:05:35] And what is the nature of the injury that's causing it? Is it that injury that happened over a few minutes? Or is it an injury that happened over days or weeks? So, depending on all of these, symptoms are going to differ from one patient to another patient.

Krissy Dilger: [00:05:48] Gotcha. Thank you. And our next question is, should someone diagnosed with TM continue to have MRIs periodically to monitor for possible new lesions?

Dr. Ram Narayan: [00:06:02] This is a very great, very intelligent question, I should say. The answer is it depends on what your doctor thinks about what caused the transverse myelitis, meaning it depends on the cause of the myelopathy. For example, if the myelopathy is part of multiple sclerosis, you will need an MRI on a periodic basis, every year or every six months, depending on what your physician thinks, but it's the brain MRI.

[00:06:29] This is because studies have shown that spinal cord lesions, for the most part, tend to be symptomatic, meaning the patients more often than not are likely to have new symptoms, like we just discussed before, as a result of the spinal cord lesion. Whereas brain lesions are exactly the opposite, more often than not tend to be silent lesions, tend to be asymptomatic lesions, the patient is not going to be aware of them, for the most part.

[00:07:01] So, in spinal cord diseases, like in myelopathy specifically, most of us, we monitor brain MRIs to catch disease processes like multiple sclerosis or MOG antibody disease, or neuromyelitis optica, et cetera, much earlier, based on the change in their brain MRIs. When it comes to the cord itself, let's say the physician is very convinced that this particular disease process was a one-time event in the spinal cord and this was

probably a one time, you know, vascular attack or immune-mediated attack on the spinal cord, then there is no need to get periodic MRIs.

[00:07:42] In such cases, we monitor the patients clinically. So, in a nutshell, in majority of the cases with garden variety TM, we just monitor their clinical symptoms over time. We typically don't get periodic MRIs of the spinal cord. If we suspect that this is a form first of multiple sclerosis, we may monitor their brain MRIs.

Krissy Dilger: [00:08:08] That makes sense. Thank you for that thorough explanation. And then, kind of in a related topic, what types of doctors does a TM patient need to have access to, in order to maintain minimal continuing health going forward? So, obviously you just spoke about seeing your neurologist, but is there anyone else you would recommend seeing or adding to your team? And then also, if you have no major problems or concerns, do you still need periodic checkups with a neurologist and other specialists, from time to time?

Dr. Ram Narayan: [00:08:39] Again, a great question. You might be expecting that. I would say you would need a very good neuro-urologist. You would need a very good neuro rehab specialist, et cetera. Those are all important. I'm going to come to them. But I think the most important non-neurologist doctor that you would have to have is a good primary care physician.

[00:09:03] I think this is very, very important. I wouldn't expect all primary care doctors to have an interest in transverse myelitis now. That's very utopian, but I would at least have a primary care physician that is fairly comfortable with neurological patients and neurological symptoms. It's very important to have access to a good primary care doctor.

[00:09:20] The second thing is, besides the neurologist, you would need a rehab specialist. So, a neuro rehab specialist, physiatrist, or a PMNR physician, but not in all cases. I would say the majority of the cases you would need a physical therapist. This would be a physical therapist who is trained in neurological disorders, if possible, trained in MS and related disorders, if possible, with an interest in transverse myelitis. So, if you get to that kind of a physical therapist, like the one we have here, at Barrow, if you get to a physical therapist that has a specific interest in diseases of the spinal cord, there is nothing better. There is nothing better than that.

[00:10:04] I told you about a urologist. For women, I would strongly suggest that you have a good gynecologist to work with. Just have them available, have that resource available because sexual dysfunction is common, both in men and women with transverse myelitis, and, in the majority of the cases in women, we may need some inputs from the gynecologist. And this also becomes true, some of our patients are trying to get pregnant. We may have to work with the gynecologist.

[00:10:32] Depending on the presence of other immune diseases, remember, I think we, in one of our past podcasts, we talked about how there are some autoimmune diseases that are common to co-occur with transverse myelitis and, in such patients, we would recommend a rheumatologist. So, many times, as a neurologist that sees transverse myelitis patients, I'm finding myself work very closely with the urologist, with the physical therapist, an occupational therapist, depending on one's impairments, a rehab specialist, a gynecologist, if needed, and a rheumatologist.

[00:11:07] But, again, a neurologist is important. A periodic follow-up with a neurologist is important for two reasons. One, in general, a neurologist has access to resources that a TM patient might need quickly. Second, remember, this is what I tell my patients. Actually, I had one of my patients call me last week and say, 'You know, I've had this for now five years, and you said this is a stroke of the spinal cord, this is a spinal artery stroke. I don't see any reason coming to your clinic. So, why keep seeing you?' Well, the answer is they may be correct in that perspective. I may not be adding on it for each and every, you know, clinic visit. I may

not have something new to offer, but this is an area which is also going through changes. As it's evolving, we are learning more and more new things. There are new and newer research projects coming up. So, a periodic follow-up with us, even if it's once a year, even if it's once in two years, may keep patients abreast with all the developments in this area and, if there is something new about their condition, they may be the beneficiaries of that.

Krissy Dilger: [00:12:15] Okay, thank you. Our next question was one we received from a community member and their question is in patients that develop TM at a young age, such as zero to 12 months, what's the prognosis on recovery and for how long should any advances in recovery be expected?

Dr. Ram Narayan: [00:12:34] Yeah, it's very sad and very unfortunate to see, you know, young children and babies get affected with transverse myelitis. I, myself, have very few patients that are at that age group that developed transverse myelitis. There are a few. So, first of all, the so-called TM in that age group, so, let's call it myelopathy, is quite unique. The causes are quite unique than what we see in the adult group. So, in the adult group, it's mostly, the majority of our cases tend to be immune-mediated. Whereas, in that age group, in the first year of age, it's hardly immune-mediated.

[00:13:11] There are so many other things like genetic nutritional metabolic causes. There could be vascular causes, so, blood supply related problems at that age group, like a stroke, for example. There could also be conditions like folic acid deficiency, conditions like infections, like, you know, the acute flaccid myelitis that we hear about. Again, that particular age group, I don't think that there have been a lot of cases of acute flaccid myelitis reported in the first year of life, but still, in a very young age group, you tend to think about infections as one of the causes, as well, for transverse myelitis, besides the other causes I mentioned. Because the causes are very unique, the prognosis and the recovery are also going to be different than what we see in adults, depending on the cause here. For example, let's say it's a nutritional cause. Let's say it is a reversible cause. The prognosis might be better than for somebody who sustained a stroke of the cord, at that age.

[00:14:12] Now that said, so, part of the prognosis depends on what the cause is. Part of the prognosis also depends on how young the child is. So, many times, that is also the time that the nervous system is going through the myelination and maturation. So, if the nervous system is hit at that young age, it may have an impact on prognosis. So, I am unable to comment on it's going to be good versus bad without knowing more details about what caused it and what resources are available for the child, in terms of rehab, et cetera.

Krissy Dilger: [00:14:49] Gotcha. Thank you so much. And this question also came in from our community. This person wants to know, does the inflammation ever go away completely? And how do you know if the lesion is inflamed or not?

Dr. Ram Narayan: [00:15:03] Let me answer the second part of the question. How do you know that the lesion is inflamed or not? Two ways. In general, if there is inflammation in the cord, that tends to be swelling. And if there is swelling, many times people have symptoms, number one. Number two, the other way we know about inflammation, there are other two other ways. One is the MRI. So, that's probably the most important thing that we are looking at as clinicians, to see if there is active inflammation going on or not. And we see that on a contrast in MRI sequence where we see there is an uptake of contrast. So, this is a lesion that's going to light up with a contrast called gadolinium that is given with the MRI.

[00:15:46] There is a third way we know if there is an inflammation or not in the spinal cord and that is by testing the spinal fluid. If the spinal fluid has white blood cells, meaning a higher number of white blood cells, and a higher amount of protein, then it is likely that the lesion in the spinal cord is going through inflammation.

[00:16:06] Does the inflammation ever go away completely? Now, in most instances, depending again, depending on what caused it, the inflammation usually goes away. So, in other words, if we're talking about, again, if you're talking about garden variety transverse myelitis, which was a one-time inflammatory event of the spinal cord, usually we should expect the inflammation to subside in about one to three months. So, beyond three months, if a lesion is persistently enhancing on contrast, meaning if it's persistently inflamed, we get concerned about it. For example, there are some conditions that can do that. Is the sarcoid? Sarcoid is a condition that causes chronic inflammation, meaning long-term, longstanding inflammation, but to a lower grade.

[00:16:53] So, is it that kind of a myelopathy? Is it myelitis or transverse myelitis caused by sarcoid? So, that's a concern. The other concerns we have are is just not even inflammation to begin with? Are we missing something like a lymphoma of the spinal cord, a tumor of the spinal cord? So, again, in a few sentences inflammation in garden variety transverse myelitis almost always goes away.

Krissy Dilger: [00:17:21] Okay, thank you. That was a great explanation. Next question we have is about aging with TM. So, this person wants to know, do you find that some patients progressively get weaker over the course of years or experiencing a worsening of symptoms? And, if so, will it continue to progressively get worse? Is there anything that can be done to stop or slow down or worsening symptoms as a person ages?

Dr. Ram Narayan: [00:17:49] Again, a very interesting question. And this is also a question for research. So, one of my mentors at Johns Hopkins, Dr. Carlos Pardo, who is very well known to the SRNA group is, you know, is interested in aging, the aging phenomenon of the spinal cord, in itself, and he used to teach us about that.

[00:18:08] So, spinal cord, just like all other organs, just like the brain, itself, also undergoes an aging process. How do we know that? So, the same transverse myelitis process, if it affects a younger person at 16 years of age versus somebody at 50 years of age. Let's say the cause is the same, it's an immune mediated attack on the spinal cord, one time, post-infectious, immune mediated attack on the spinal cord, just once. A 16-year-old is going to bounce right back and be almost back to normal. Whereas a 60-year-old may not almost always return a hundred percent back to normal.

[00:18:45] This, itself, shows that the reserve that the spinal cord has, by the way, the spinal cord does have reserve. It does have some plasticity. So, that is lost with aging. So, if you find that there is transverse myelitis that is diagnosed at a particular age, there are a few patients, as mentioned in this question, where they are stable, you know. Let's say they have some walking impairment, they are not able to walk well, they do therapy, they get well, but then they're more or less stable. They're not getting better, but they're not also getting worse. After a particular age, there is a chance that they might slowly start declining.

[00:19:24] There is one particular term used to describe this. And this is called solitary progressive sclerosis. Some people think of it as a variant of multiple sclerosis. This is a very rare condition, and this typically happens in, as the name suggests, single lesions of the cervical spinal cord. Patients, they are impaired, in terms of the strained sensations, to begin with. They improve with therapy, they stabilize with therapy, and, after a few years, they may slowly start declining. So, when that happens, there are a couple of things that people need to remember. One is, are you still getting therapy or not? Because if anything can put the break to that kind of a decline, it's going to be physical therapy. Regular physical therapy can still potentially slow down that process.

[00:20:10] Two, are we missing any other disease process? Is this not just transverse myelitis, but rather a part of another condition, like multiple sclerosis, for example, which is getting worse. So, these are two

things. If somebody with transverse myelitis, after a certain period of time, is getting worse, you need to make sure that they are not de-conditioned, they're getting therapy, and we also need to make sure that we're not missing any other diagnosis.

Krissy Dilger: [00:20:35] That's very helpful. We do get a lot of questions about worsening symptoms over time and aging with TM. So, I think our community will find that answer very helpful. Our next question came in from someone in the community asking what suggestions do you have medication-wise for patients with TM that do not want to feel cloudy or doped up? This person is asking mostly about spasticity in the abdomen, tinnitus, and random hammering pain throughout the extremities. This person was on gabapentin, but it left them too cloudy and did not help mitigate the pain. Any suggestions?

Dr. Ram Narayan: [00:21:18] Don't know if I got the question, right. So, if I'm getting the question right, is it that somebody is spastic because of transverse myelitis or they're in a lot of pain from transverse myelitis? They are put on medications to treat that and, as, probably as a result of that, are experiencing this doped up feeling, the dizzy feeling, the sleepy feeling, the brain fog feeling, et cetera? I think that's what this question is alluding to. If that is the case, this is a very common problem. We see in patients who have transverse myelitis, very common. There are a couple of approaches that I have used. And, again, there is no standardized approach to this.

[00:22:01] So, each of us do it in a different way. Believe it or not, many times, there are issues pertaining to the autonomic nervous system that affects transverse myelitis patients. For example, that is a condition called POTS, postural orthostatic tachycardia syndrome. These are patients who, when they stand up, get a little dizzy, they're lightheaded, they're, you know, they have some cognitive symptoms, their processing speeds slow down, they have some brain fog, et cetera. And a lot of these patients who get diagnosed with POTS are those that are very sedentary and are not involving themselves in regular physical activity, aerobic, physical activity.

[00:22:43] And this happens because of deconditioning. Now, deconditioning can happen because of various other conditions, but, again, transverse myelitis can be one of them, as to why you're deconditioned. So, it's important, again, that pushing on the therapy side of things, exercise side of things may help restore some of the blood, you know, the blood flow to the brain and can alleviate some of these brain fog symptoms.

[00:23:06] Now, this is the less common part of the question. The meat of the question is how do I deal with these medication side effects? Well, one thing is, if possible, try and avoid medication and use lesser medication. Let me give you a few ways to doing this. Let's come to spasticity. I aggressively push for Botox injections. The reason is Botox injections can not only help, it's, of course, it's an FDA approved treatment for spasticity. But the great thing about Botox, which I love, is you're able to go off your baclofen, and your tizanidine, and your clonazepam, which can relieve your side effects because Botox does not have those symptoms.

[00:23:53] It does not have those side effects. It just is given in the muscle, and it stays in the muscle. It's not a medication that causes sleepiness or sedation or anything like that. So, that's one. Number two, baclofen when it's delivered through a pump, in what we got intrathecal baclofen, when it's delivered through the pump placed in your spinal canal, at one hundredth of a dose and much less sedative side effects, can cause a significant improvement in your spasticity. This is what I meant when I said that try and avert medications or reduce the dose of medications. Majority of the patients are on high doses of baclofen by mouth, or gabapentin, or combination of all of these medications. When you do this kind of a combination, I mean, it's no surprise that you're sedated, and sleepy, and brain foggy all the time.

[00:24:52] If you can try and avert some of these by using Botox injections, baclofen pumps, there are some patients whom I know, for example, for the bladder, people go on medications like oxybutynin, which is by and large, it's probably the most commonly prescribed medication for neurogenic bladder. Partly for, you know, insurance related reasons, as well. Now, oxybutynin at a high dose can cause cognitive impairment. It is an anticholinergic, so it can cause a cognitive side effect. Again, one trick that I use is I use medications like oxybutynin, which selectively work on the bladder without causing cognitive side effects. It's also one of my areas of interest, but the problem is these are also expensive medications and then most patients may not have access to that. But, if possible, a smarter use of medications, these ways, can help alleviate some of those cognitive symptoms.

[00:25:50] The last thing I would say is it's important for some of our patients with transverse myelitis to establish care with a comprehensive, integrated pain clinic. So, this would be a pain clinic, for example, that would just not work with medications, but would also provide acupuncture, would also provide, you know reflexology, meaning it's a form of a therapy that's offered by electrical stimulation. So, you can do that, chiropractory, and these are some of the other ways. So, I've even had some of my patients get hypnosis, et cetera. So, there are so many other nonconventional approaches, which we technically are not very good at most of the times. There are some dedicated pain clinics that offer this integrated approach. These are some ways where you can be successful at, so you can come down on some of these medications that tend to cause side effects.

Krissy Dilger: [00:26:42] Gotcha. Thank you. So, okay. Our last question is I experienced symptoms such as a ring of stiffness and pain around the waist and lower back, like as if someone has carried you off the floor, holding you at the waist, what type of medication is usually prescribed for minimizing these symptoms?

Dr. Ram Narayan: [00:27:02] I think what this person is referring to is something called banding pain that we see in conditions like transverse myelitis, multiple sclerosis, neuromyelitis optica, et cetera. It's usually a tight band like pain or a gripping pain around the waist or around the trunk. It might be a difficult symptom to read. So, let me acknowledge that at the beginning, but there are some medication options for this. There are medications like Tegretol, also called carbamazepine, baclofen, clonazepam, tizanidine. These are some commonly used medications to treat, and even gabapentin, Lyrica. These are some commonly used medications to treat that banding, grip-like pain.

Krissy Dilger: [00:27:46] Great. Thank you so much, Dr. Narayan.

[00:27:49] We will now be joined by Dr. Elena Grebenciucova. So, our first question comes from someone in the community who asks, do patients with idiopathic TM of the cervical spine have allodynia and itching on scalp, neck, and trunk? What symptom relief would you prescribe?

Dr. Elena Grebenciucova: [00:28:09] Yes, absolutely. So, people who have lesions that cause transverse myelitis, if the lesion is located high in the cervical spinal cord, it is in the similar area that innervates, that parts, the scalp. So, people can definitely have symptoms that are similar to what we call occipital neuralgia, where there is a distribution of the occipital nerve, that kind of innervates the dermatome, the area of the scalp that's kind of like up above your neck, right, and towards your ear.

[00:28:45] So, people with transverse myelitis with a lesion in that area definitely can experience abnormal sensation in the skin of the scalp exteriorly, behind the ear. In terms of management, I think, in the acute phase, you know, it's always worthwhile to kind of wait and see for a few, at least a few months to see if these sensations will naturally improve.

[00:29:10] If the sensations are really bothersome, like it's itching or burning, or tingling, or if the sensations are making it difficult to focus or sleep, then yes, absolutely, a treatment is necessary. And the treatments are really symptomatic treatments, meaning that these are medications that reduce the intensity of these sensations and, hopefully, can, well, control it. And there are different options that we utilize for that. Those are gabapentin, also known as Neurontin. There is also pregabalin, which is Lyrica. There's a medication called duloxetine, Cymbalta, and there are some other medications that we sometimes use, like amitriptyline, nortriptyline, to try and help that. Among them, I think that, you know, different patients tolerate these medications very differently.

[00:30:03] And it's a matter of time to find what works for you and, importantly, what dose works for you, right? So, a lot of times, your doctor will start with a low dose of a medication and then we'll adjust the dose, based on your response. And it is true that sometimes one medication doesn't work for everyone. So, then you can try something else. Occasionally, we use combinations of those medications, if the sensations are really, really bothersome. I think that non-pharmaceutical means of pain control can also be utilized.

[00:30:35] Sometimes I know that people can do acupuncture and derive some benefit from it. Sometimes there are some relaxation techniques, and even cognitive behavioral therapy, and biofeedback that can be done to sort of reduce how hypervigilant, you know, someone is experiencing the symptoms, how strong those symptoms are, right? So, you kind of like read why are you experiencing those symptoms.

[00:31:00] So, there's a number of techniques ranging from medications to biofeedback, sometimes, you know, relaxation techniques, cognitive behavioral therapy. And so, it's just a matter of time of finding what works for you.

Krissy Dilger: [00:31:12] Okay. Great. Thank you. The next question came from someone who asks, 'Are unilateral hypertonic quad contractions common during a pseudo attack, four years after thoracic LETM? And what kind of therapy or medication would you prescribe for that?'

Dr. Elena Grebenciucova: [00:31:34] Even though we see it rarely, yes, people can have tonic spasms after experiencing transverse myelitis. They're particularly, you know, common in people who may be having an infection or maybe they recently had some sort of maybe a UTI, maybe they got a cold, or maybe they're in hot weather. So, anything that can put an additional stress in the system where there has already been damage can provoke tonic spasms and chronic spasms are best prevented. So, there are certain medications that can be used, and mitigations include baclofen, tizanidine, which are muscle relaxants. In people with severe tonic spasms, these medications may or may not work.

[00:32:29] In those instances, for tonic spasms, we use a medication called carbamazepine. And carbamazepine tends to be more effective, but it all depends on the unique situation, and I think every patient's unique in their response to medication. So, you should always discuss with your doctor what is the best option for you. Sometimes carbamazepine can be combined with baclofen or tizanidine, so it's just a matter of finding the right combination.

[00:32:57] Occasionally, for severe sort of dystonia or severe cramping, whether it be, you know, the arm or the leg kind of gets stuck in that position. Occasionally in some patients, it can be so severe that Botox injections actually can be of help to try and reduce the pain associated with it and discomfort. Physical therapy, of course, is very important. Stretching, passive or active stretching of the limbs is very important. And, most importantly, making sure that you're adequately hydrated, that you have enough electrolytes. Sometimes we even tell patients to take a small dose of over-the-counter magnesium, around 200 milligrams, which should

not be done if somebody has kidney issues like a kidney dysfunction. And, you know, while this is general advice, before taking any new medication, you should always check with your treating physician.

Krissy Dilger: [00:33:55] Great. Thank you. That is great advice all around, but very thorough answer that I definitely think will help. Our next question is this person was diagnosed with idiopathic TM, almost 20 years ago. They still have feelings of electric currents and want to know if this is usual and if anything can be done about it.

Dr. Elena Grebenciucova: [00:34:17] Yes. I think that, you know, when somebody has transverse myelitis, ultimately there is an area that's been damaged, right? The area in the spinal cord. And every one of us is so unique in our ability to regenerate. And that's why some people, they actually improve significantly over a few months or over a few weeks and some people have residual symptoms that last for a very long time. And in some instances, they are going to last potentially throughout your lifetime. And so, the reason behind it is because there is a damage in the area that transmits nerve impulses that are responsible for, you know, providing you with normal sensation.

[00:34:57] So, when there's damage and that damage is permanent and hasn't been repaired by your body well enough, then it is definitely possible to experience those symptoms long-term, chronically. And a lot of times, you know, stress, or exhaustion, or dehydration, or hot temperature, a lot of times can kind of like make you feel the symptoms are worse. Luckily, it's transient and once that you cool down, or you're less stressed, or you no longer sick with something, things should get better. But, for those people who continue to experience burning, tingling, I think, like what I mentioned in my previous answer, there are medications that can help with that, such as gabapentin, pregabalin, duloxetine, also amitriptyline or Triptyline. There's a biofeedback type of approach, cognitive behavioral therapy, relaxation techniques, and, for some people, acupuncture actually, as well, aquatherapy. So, every patient, you know, it takes time to find a unique approach that helps the symptoms.

Krissy Dilger: [00:35:58] Gotcha. Thank you so much. Our next question is, 'My TM event happened in 2018. I fatigue easily. Is fatigue, a common result of TM, or can it possibly be caused by medications? And will physical therapy help after two years of limited recovery?'

Dr. Elena Grebenciucova: [00:36:18] Well, fatigue is such a, you know, it's such a ubiquitous concept, meaning that fatigue can be so multifactorial. I think that there's also a difference between fatigue and fatigability, like fatigue that you experience overall versus fatigability of muscles when you start walking or trying to do something with those muscles. So, it's very common. Patients who have had transverse myelitis feel fatigability of muscles, meaning that even though they may have recovered some strength and they can use their limbs, they get tired very quickly when trying to walk or do things. And, yes, that is a part of the, you know, post transverse myelitis sort of recovery. In some people, it is chronic, particularly if there is a substantial degree of weakness. And, yes, physical therapy could help with that.

[00:37:15] Having said that, as you mentioned in the question, yes, some medications can definitely worsen and bring along the fatigue. There are some medications like, you know, gabapentin, for example, or even baclofen, you know. When used at high doses or when used in people who are just very, sort of sensitive, yes, those medications sometimes can worsen fatigue. That is very true. And there are many other medications that can do that, but I think whenever you feel fatigue, it's very important to think about the following things.

[00:37:46] The question that I would ask myself is, 'How is my sleep?' You know, because, if your sleep is less than adequate and you're getting less than eight hours of sleep at night, and if you're awakening multiple

times at night, you really need to think about, you know, and see a sleep medicine doctor or discuss with your primary care doctor or neurologist because, as long as the sleep is impaired or less than perfect, fatigue is going to persist.

[00:38:11] The second question that I would ask myself is, 'How am I doing? How am I coping with stresses in my life? Is there any chance I might be depressed?' Right? Because people who have gone through formidable sicknesses, and a neurological diagnosis, and treatments, they become stoic, and they internalize the stress. They internalize their struggles. Often, they don't feel like there's anybody that understands them or anybody that they can talk to, and that can lead to burnout and depression.

[00:38:43] And sometimes people are not even aware that they are depressed. They feel sad. They sometimes feel almost helpless, like they don't have anybody to talk to or nobody's listening and this is important. If you ask yourself a question about those things and you feel that way, depression sometimes can lead to pretty serious fatigue. In fact, fatigue, fatigability is one of the criteria for the diagnosis of depression. And so, if you've answered yes to any of the questions I just asked, it's good to talk to your primary care doctor, to talk to a psychiatrist or a psychologist, or talk to a therapist, or even seek some feedback from the transverse myelitis community, other patients, and all of us.

[00:39:29] And other causes of fatigue can include a low thyroid function, vitamin deficiencies, so, for example, B12 deficiency, vitamin D deficiency, which is very common, is one of the common culprits of fatigue. And, you know, many medications that somebody could be on. An additional thing is chronic caffeine use. So, while an occasional cup of coffee can give you energy, people who are chronic consumers of caffeine and they drink multiple cups a day, tend to have a little bit of that chronic fatigue. So, in that instance, caffeine may actually work in reverse. Instead of giving you energy, it actually maintains you in that chronically exhausted type of place. And so, for those patients, I would say that the best approach would be to try and very gradually cut back on caffeine consumption over many weeks or sometimes months, depending on the amount you would take of your caffeine intake. And, of course always discuss with your neurologist or your primary care doctor what is the best way to do this.

Krissy Dilger: [00:40:32] Okay. Great. Thank you. Those are some really great suggestions. And I also think it's important to think about how these different symptoms interact with one another. So, as you mentioned, sleeping's so important. Maybe, if you're having stiffness or pain in your legs and that's keeping you up at night, treating that could actually help alleviate your fatigue, in the long run. So, definitely having that comprehensive lookout.

Dr. Elena Grebenciucova: [00:40:58] Yeah. And the same thing with bladder, right? So, if somebody has incontinence or a lot of urgency or pressure in the bladder, painful sensations, and they are having to go so often throughout the night, that's, you know, your sleep is interrupted. You cannot possibly feel energetic if that's the case.

[00:41:14] And that's where we ask our patients to see urology doctors to try and come up with a better plan to help you sleep better, to help your bladder control. So, that's definitely one of the very common situations and pain control for pain management, through working with your physical therapist, with your neurologist, is absolutely so, so, so important, in this instance.

Krissy Dilger: [00:41:36] I agree. So, this next question is more about treatment options. This person asks is Rituximab or IVIG ever used as a treatment for TM beyond the first stages? Or is that really only for other disorders such as NMO or MOG?

Dr. Elena Grebenciucova: [00:41:58] Well, I think that, when somebody presents with the first event of transverse myelitis, that is negative on workup, meaning they are not positive for aquaporin-4 antibody, which would give them diagnosis of NMO. They are not positive for MOG antibody, which would give them that diagnosis of MOG associated demyelination. When there is no definitive answer and this is just an idiopathic transverse myelitis and there's no evidence of prior attacks, there is no evidence of lesions in the brain, or other lesions elsewhere that would make you think they have MS, in the instances where there is just one, isolated transverse myelitis that is deemed idiopathic, Rituximab does not have a strong role.

[00:42:46] However, as we've talked in our first webinar, the typical acute treatments for inflammatory transverse myelitis include steroids and either IVIG or plasma exchange, depending on the amount of response to steroids initially. And as you sort of mentioned in the question, Rituximab is typically a medication that we use for recurrent transverse myelitis, off-label in multiple sclerosis, in neuromyelitis optica, in MOG associated disease, and in some inflammatory diseases where you see relapses, right? So, it's not just a one-time event. But, initially, no, there is no strong role for Rituximab at the time of the first event.

Krissy Dilger: [00:43:33] Gotcha. We got several questions about pain management. So, this person asks, they've had pain for several years, they've tried gabapentin and some other, and baclofen. Is there anything new in pain management in recent years? Or is it kind of just the same it's been for a while?

Dr. Elena Grebenciucova: [00:43:56] Well, I think that beyond baclofen and gabapentin, remember, there are other medications that could be tried, right? I mentioned duloxetine, amitriptyline, also topiramate, nortriptyline, pregabalin. Other than that, you know, people with severe pain that is completely unresponsive to anything, to the point where even, you know, people are either sort of stuck on opioids, which is never a good thing, but, unfortunately, some people need to use opioid medications, right, if the pain is severe? And that's completely understandable. We could try to avoid it as much as possible, due to side effects. And, of course, you know, and dependency on opioid medications.

[00:44:37] The other thing that we also utilize is spinal cord stimulators for pain control and that is something that you would typically see your surgeon for. So, you would get a referral from your neurologist or a pain management doctor to see if you would be a good candidate for a spinal cord stimulator to help with pain.

Krissy Dilger: [00:44:57] Great. Thank you. So, this question is kind of in the rehabilitation realm, but this person wants to know when someone that has become paraplegic and regained some of their movement after a TM diagnosis, does this mean they have regenerated some myelin? Can the body repair the missing myelin in the spine by making more?

Dr. Elena Grebenciucova: [00:45:19] Yes, absolutely. And that's what I hinted at earlier, during some of my answers, is that first and foremost, each one of us is unique genetically and some of us can do a little bit more repair and remyelination than others, right? Sometimes it's age dependent, sometimes it's not, but I think that every case of transverse myelitis is different, right, based on the entity that's causing it. So, for example, people with transverse myelitis from multiple sclerosis often have a little bit more remyelination and faster recovery.

[00:45:55] In some cases of transverse myelitis, there's a little bit more damage that is more difficult to recover from, but, yes, absolutely, most humans do display some ability to remyelinate, to heal. And that's why we say that, after acute stage of transverse myelitis, you really have to give yourself at least six months to see how much you improve. That's precisely because, you know, it takes time for inflammation to calm down and it takes time for your body to try and do a little bit of self-care and remyelinate, if the damage has

been not too severe. Because, in some instances, if the damage has been very severe, it's very challenging to remyelinate. But, again, everybody's different and, from the get-go, it's very difficult to say who will remyelinate to which extent.

Krissy Dilger: [00:46:48] Gotcha. Thank you. We did get a few questions about vaccinations. The first one being, do you recommend that someone with TM receive a COVID-19 vaccine?

Dr. Elena Grebenciucova: [00:47:01] Well, I think that, generally, remember, if you get COVID itself, it's going to stimulate your immune system so much more. So, for people who are worried about, 'Well, what if, you know, vaccine stimulates my immune system too much?' I understand the concern, but, at the same time, if you catch COVID, not only is it going to stimulate your immune system tremendously more, so any side effect that you're worried about, anything you're worried about, it's going to be so much worse if you actually get COVID. But, most importantly, you know, if you catch COVID, the risk of secondary side effects of COVID infection is pretty tremendous, right? And it's significantly higher than any of those exceedingly rare risks with the vaccine.

[00:47:47] So, people who have a history of idiopathic transverse myelitis, as long as they've been following with their neurologist, they've had serial MRIs, they know that it was truly, it remains an idiopathic transverse myelitis, they haven't formed new lesions to make us think that they have MS, they have been appropriately tested for NMO, for MOG, they haven't had recurrences, and they're really idiopathic, then, yes, these patients, just like anybody else with a history of inflammatory disease, these patients should get vaccinated because the risk of vaccine is significantly lower than the risk of actual infection. Infections are a much more powerful stimulator of the immune system.

[00:48:32] So, when you worry about, and you say, 'Well, could a vaccine trigger me to have another attack?' We're not really seeing that. But what I will tell you is that, if you're, you know, wondering about that, I would say that it would be an extraordinarily low risk, but if you get the COVID, an actual infection, that risk would be significantly higher because it's a more powerful stimulator of the immune system. So, yes, patients should get vaccinated, but they should also discuss with their neurologists, you know, what is the appropriate timing for them, are there any other concerns.

[00:49:11] For people with transverse myelitis who ended up being diagnosed with something like multiple sclerosis, or MOG, or neuromyelitis optica, yes, vaccinations are recommended for these patients. In fact, the vast majority of my patients with a history of transverse myelitis, with a history of MS, NMO, and MOG antibody demyelination have been vaccinated very successfully, and have done very well.

[00:49:38] And remember that, after every vaccine, just like after every infection, somebody who has a history of transverse myelitis would have transient, mild return of all of those old symptoms or even exacerbation of all those old symptoms. And that's normal because, when your immune system is activated and it's responding to a vaccine, you've got a little bit more inflammation. So, those areas that have been damaged long time before, they are put under a little bit more stress, so they become a little bit more symptomatic, we call this pseudo exacerbation, pseudo relapse, meaning that it's not that your disease is getting worse. It's not that you are having another attack. It's literally a transient event. You're transiently symptomatic from the old scar tissue.

[00:50:26] We see this very commonly with any infection and sometimes post vaccination. So, if you are a patient with transverse myelitis who gets vaccinated tomorrow, and you asked me will you get a headache, could you potentially have a few days of like worsening tingling, or maybe feeling really, really off and weak

for a couple of days, absolutely, that can happen. And that's normal and expected. You should always let your doctor know and, if that still keeps going on for more than a few days, you should see your doctor.

[00:50:57] But I think it's almost like an expectation that somebody could potentially experience headache and fatigue. And, if they have a fever, just like any fever from any infection, people with a history of transverse myelitis can have transient, you know, return of their old symptoms. That's common. It's not something to be afraid of. But, as long as it's kind of gets better and resolves within a couple of days, you're in the clear, but you should always communicate any new symptoms to your doctor and check in with them. So, yes, the answer is you should get vaccinated, but always discuss with your doctor the appropriate timing, the appropriate vaccine, and if there are any specific considerations in your specific clinical scenario.

Krissy Dilger: [00:51:39] Great, thank you so much. I think that's really important for people to hear and I'm glad we were able to touch on it. I think we're almost at the end of our time, but if we have time for one more?

Dr. Elena Grebenciucova: [00:51:50] Yes. Yes.

Krissy Dilger: [00:51:51] So, it's just one last symptom management one and we kind of answered it, but, if you have anything else to add, this person just asked could you please comment on drugs that are used to treat long-term symptoms of the burning and stiffness in legs?

Dr. Elena Grebenciucova: [00:52:05] Yeah. I think burning is considered to be like a nerve related neuropathic pain and, as I mentioned, we utilize medications like amaphenten, duloxetine, pregabalin, amitriptyline, nortriptyline. We also utilize non-pharmaceutical approaches, such as biofeedback, sometimes acupuncture for some patients can be helpful.

[00:52:27] We also, you know, suggest that patients are well hydrated, that their sleep is improved because insomnia and anxiety or depression infamously will make you experience any symptoms at a greater level of magnitude, right? So, people who are anxious, or sleep deprived, or very stressed, any sort of burning or tingling is going to be present in an amplified manner.

[00:52:54] So, I think ensuring good sleep, good hydration, good stress coping techniques, and appropriate medication management with physical therapy, maybe acupuncture, also aquatherapy really can make a major difference in somebody's neuropathic symptoms. For stiffness, we tend to utilize physical therapy, stretching, passive or active, you know, a good amount of hydration, and medications that have muscle relaxers, such as baclofen, and tizanidine, and sometimes cyclobenzaprine.

Krissy Dilger: [00:53:28] Great. Thank you. And, just to close out, is there anything you would like to add or kind of reiterate to the community?

Dr. Elena Grebenciucova: [00:53:35] Well, I think it's a very scary time for everyone right now, but I think it's really, really important to discuss with your physician your questions about the vaccine and ultimately get vaccinated, unless there are some specific contraindications in your specific scenario. I think that the good news is that, you know, I have a very large practice of patients with both transverse myelitis and neuromyelitis optica, and MOGAD, and MS, and, like I mentioned, most of my patients have been successfully vaccinated and everybody has done extremely well. I have not had anybody who relapsed after a vaccine.

[00:54:14] So, if people of wondering about that, I can be the witness of how well people actually do. So, I do strongly encourage you to get vaccinated, talk to your physician about the vaccine, the timing of the

vaccine, depending on whether you are on a specific immunosuppressive medication. Ask them questions about advocacy and, of course, we here are also available for you for any questions that arise. And I wish everybody to stay safe, to continue, you know, following CDC guidelines, and maybe being even extra careful and cautious beyond that. And I wish everybody to stay safe and healthy. And thank you so much to SRNA for everything you're doing for the TM community.

Krissy Dilger: [00:54:57] Great. Thank you so much. We really appreciate it and, hopefully, we can do this again sometime. Have a great rest of your day. Thanks again.

Dr. Elena Grebenciucova: [00:55:05] You too. Bye. Have a good day.