

Neuro-Ophthalmology and NMOSD

You can watch the video of this podcast at: youtu.be/io3lyhDvzz0

[00:00:02] **Intro:** “ABCs of NMOSD” is an education podcast series to share knowledge about neuromyelitis optica spectrum disorder or NMOSD, a rare relapsing autoimmune disorder that preferentially causes inflammation in the optic nerve and spinal cord. “ABCs of NMOSD” podcast series is hosted by SRNA, the Siegel Rare Neuroimmune Association, and in collaboration with the Sumaira Foundation and Guthy-Jackson Charitable Foundation. This education series is made possible through a patient education grant from Horizon Therapeutics.

[00:00:51] **Krissy Dilger:** Hello, and welcome to the “ABCs of NMOSD” podcast series. Today’s podcast is titled “Neuro-Ophthalmology and NMOSD.” My name is Krissy Dilger and I moderated this podcast. This podcast series is hosted by the Siegel Rare Neuroimmune Association in collaboration with the Sumaira Foundation for NMO and the Guthy-Jackson Charitable Foundation. “ABCs of NMOSD” is made possible through a patient education grant from Horizon Therapeutics. 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.

For today’s podcast, we are pleased to be joined by Dr. Robert Shin. Dr. Robert K. Shin is a graduate of Yale University and received his medical degree from the University of Pennsylvania School of Medicine. He completed a neurology residency and fellowships in neuro-ophthalmology and multiple sclerosis at the Hospital of the University of Pennsylvania. Dr. Shin is currently a professor of neurology at MedStar Georgetown University Hospital and Director of the Georgetown Multiple Sclerosis and Neuroimmunology Center. Dr. Shin has a special interest in health disparities in multiple sclerosis as well as visual problems associated with MS and other demyelinating disorders including neuromyelitis optica spectrum disorder. Welcome, and thank you for joining us today. To get us started, can you just explain what a neuro-ophthalmologist is?

[00:02:39] **Dr. Robert Shin:** Sure. Well, there are different kinds of physicians with different specialties. So for example, neurologists usually focus on the brain and nervous system. So that would be a neurologist. And then ophthalmologists are eye doctors. So they focus on treating eye diseases, eye conditions using medicines and surgeries to help people with eye issues. So neuro-ophthalmologists actually bridge the gap between neurology and ophthalmology.

[00:03:10] So for example, some neuro-ophthalmologists started out as neurologists and begin to learn more about the eye and then came to focus on the neurology of vision. And by the same token, some neuro-ophthalmologists start out as ophthalmologists and then they learn more about the nervous system, the optic nerves, and the brain and how they interact. So again, neuro-ophthalmologists occupy that middle ground between those two specialties.

[00:03:35] **Krissy Dilger:** Thank you. So what role does a neuro-ophthalmologist have in relation to NMOSD?

[00:03:44] **Dr. Robert Shin:** Well, neuromyelitis optica spectrum disorder, even in its name, the spectrum refers to the fact that people with NMOSD may have a variety of different symptoms or issues that bring them to diagnosis. But one of the biggest ones actually is visual issues. So when you say NMO, neuromyelitis optica, the optica part of it refers to the fact that many people with NMOSD may have visual issues. They may have inflammation of the optic nerve or nerves, which we call optic neuritis. Perhaps a little bit less commonly, they could have things like double vision or other issues like that. So actually, neuro-ophthalmologists often do become involved. Sometimes, actually, they're at the front line. Sometimes someone with NMOSD will present with a visual issue and it's the neuro-ophthalmologists that realizes that NMOSD might be going on.

[00:04:44] **Krissy Dilger:** And just a segue from that response, you said that sometimes the neuro-ophthalmologist who diagnoses or sees the NMOSD first. So what kind of tests would a neuro-ophthalmologist use to diagnose NMOSD and other disorders -- or let's just start with NMOSD?

[00:05:09] **Dr. Robert Shin:** So, a common story will be someone will just be minding their own business and will suddenly develop blurred vision in one eye or both eyes or even vision loss. So it may begin as just a subtle blurring of vision. I've heard patients say they thought they just had a smudge on their glasses, but sometimes it's very severe and they could lose vision in one eye and sometimes they lose vision completely. That will bring them to an eye doctor typically. Now the eye doctor, let's say an optometrist and ophthalmologist may do an initial evaluation looking for if you will run of the mill things, you just need a new glasses prescription, do you have a cataract or something else going on. Usually pretty quickly, the initial evaluator like wait a minute, something's going on here. The eye itself might be okay, but maybe there's a problem with the optic nerve, that's the cable that connects the eye to the brain. And that's often what will get someone sent to a neuro-ophthalmologist.

[00:06:09] Now, in terms of tests that are done, the initial assessment is often actual in examination. So I think we've all had to look at the eye chart and take a look and see if the vision is blurred or if the vision is 20/20. Other tests might include tests of visual field that might be trying to check counting fingers in the visual field or maybe doing that on a machine. We have automated visual field machines that can give us that information. The eye doctor might check color vision, for example, might take a flashlight and shine a light in both eye just like in TV. You're using a flashlight and checking the pupillary reaction. When you put all of that information together, the neuro-ophthalmologist may realize that there is in fact evidence of optic neuritis, inflammation of either one or both optic nerves.

[00:06:58] At that point, other testing may be done. I mentioned visual field testing. If any of your listeners have had to - you're like looking at a ping pong ball, you're doing one eye and lights flash and you hit a button to say whether you could see or not see a light. People may use a tool called optical coherence tomography. This sounds fancy, OCT is actually a way to look at the back of the eye and get a sense of the health or thickness of the nerve fiber layer in the back of the eye. All of that information put together again, can give us insight into whether one or both optic nerves are involved. And then at that point, really, as again, I think your listeners know specific testing for NMOSD or other conditions is going to involve some blood tests. We're going to need to think about the possibility of NMOSD to make sure that we are ordering the correct test specifically looking for aquaporin-4 antibodies in the blood.

[00:08:04] **Krissy Dilger:** Thank you. And so how would you, I guess distinguish different optic neuritis-related disorders from one another such as MOG antibody disease, MS, NMOSD, single attack optic neuritis, et cetera?

[00:08:29] **Dr. Robert Shin:** Sure. That's an excellent question. And I think it is important to remember that optic neuritis, in a way, it's simply a description. It says that there's inflammation of the optic nerve, one or both optic nerves. Now, there are many things that could cause optic neuritis. To this day, sometimes people will have optic neuritis and then it'll go away and then it never happens again. It's a one-time-only fluke, maybe it was a viral infection. I have to be honest and say sometimes you don't really know what causes an isolated optic neuritis. There is another possibility which is that optic neuritis is a common presentation or it can occur in people with multiple sclerosis.

[00:09:11] So again, I think your listeners know that there is a demyelinating disorder that affects the brain and spinal cord called multiple sclerosis. It is not the same thing as NMOSD. Although I have to say when I was training, we didn't realize they were different. We thought they were related conditions, turns out completely separate disorders. So optic neuritis can be idiopathic, meaning just its own thing. Sometimes we would say one and done you just have it and nothing else happened. Sometimes optic neuritis is a part of what turns out to be multiple sclerosis.

[00:09:41] However, we now recognize that optic neuritis in one eye or both eyes could be a sign of NMOSD, NMO spectrum disorder or can be associated with other antibodies, not aquaporin-4 antibodies, which we think of as the marker of NMOSD but could be associated with MOG antibodies, myelin oligodendrocyte glycoprotein antibodies, MOG or a condition we call MOGAD, MOG antibody-associated disorder. So all of these things have to be considered when someone presents with optic neuritis.

[00:10:15] Now, I will add, sometimes there are clues that might tip us more in one direction than another. For example, the optic neuritis of NMOSD can be more severe at times than what we might see with other conditions and is more likely to involve both eyes. So for example, run of the mill optic neuritis or optic neuritis in MS is almost always in one eye only. But if someone present and they have both eyes affected, meaning maybe they can't see at all because both eyes are affected, that is definitely going to make me think about conditions like NMOSD or maybe MOGAD more commonly.

[00:10:54] So again, little subtleties may distinguish among the conditions but it is important to remember that not all optic neuritis is NMO or MS or anything, it can be one of a variety of different conditions and then not to overly complicate things. But even though I think of it as idiopathic MS, NMO, MOG, it is also true that other conditions can mimic up or can cause optic neuritis, things like infections, things like Lyme disease, or other kinds of conditions. Now, usually, there are clues when it's one of the other disorders, but we always should exclude other mimics before we settle on our final diagnosis.

[00:11:36] **Krissy Dilger:** That makes sense. Thank you. So how does a neuro-ophthalmologist work with other health care professionals? For example, where does a neuro-ophthalmologist come in versus a neurologist, optometrist, et cetera?

[00:11:52] **Dr. Robert Shin:** Sure. Well, I already hinted at the fact that often patients with a visual issue would see their local eye doctor first, a general ophthalmologist or optometrist because there's a blurred vision, they need to see what's going on. It's often the eye doctor, the optometrist, the ophthalmologist who will realize, wait a minute, this isn't a problem of the eye itself. It's not a lens problem or the cornea or the surface of the eye or glasses, this is an optic nerve or brain problem. And they'll make that referral to neuro-ophthalmology.

[00:12:25] Sometimes it goes the other way. For example, sometimes as you know people living with NMOSD, maybe they don't have any visual issues, maybe they had weakness or numbness or some bladder symptom,

maybe they had more of a spinal cord presentation. However, once a diagnosis of NMOSD or MOG has been made, MOGAD, their neurologist may say, I want you to check with the neuro-ophthalmologist just to see if the vision has been affected at all or to get a baseline examination for future reference. So as I said, we lie in the middle between neurology and ophthalmology there. There are actually not a lot of us who are a very small specialty. But I like to think that we do have an important role, particularly in a condition like NMOSD that can cause a lot of visual issues.

[00:13:17] **Krissy Dilger:** Thanks. And can you briefly just go over what acute treatments are used for optic neuritis in NMOSD?

[00:13:29] **Dr. Robert Shin:** Well, it's interesting because, for a long time, we weren't sure what the best way to address optic neuritis was. Again, people, commonly, young people would have vision loss and often there's some discomfort, pain on eye movements that can occur. We could recognize that there was inflammation of the optic nerve, but it wasn't clear the best way to address it. And this now goes back many decades, but there was an optic neuritis treatment trial where different treatments were studied.

[00:14:01] One of the arms of the study was placebo, meaning actually there was no treatment and this was the comparator arm. One group of individuals received lower dose oral steroids, prednisone. And then a third group received higher dose steroids through the vein, intravenous corticosteroid, methylprednisolone. There's a brand name Solu-Medrol that may be used.

[00:14:26] The interesting result of that study actually was that all three groups had the same ultimate outcome and people don't realize this, that actually all three groups did well, meaning that 90% of the time vision returned, whether they were on a placebo or receiving steroids of either type. Now having said that, the group that received the high dose, the intravenous corticosteroids did have a faster recovery. So they recovered more quickly, but everybody ended up in the same place. Now that led to a period of time when sometimes we would say, well, if you have mild optic neuritis, maybe I don't even have to treat you. The outcome is going to be the same.

[00:15:12] And the other, I guess finding in the optic neuritis treatment trial was the recognition that often optic neuritis was a first presentation of what ultimately became multiple sclerosis. And that led to a lot of research into what we call clinically isolated syndrome in the MS world in terms of early MS. Having said all of that, although it is more rare, we now recognize that NMOSD and MOGAD can be associated with very severe optic neuritis. And I have to say, I think most of us feel that it is important to treat those forms of optic neuritis early. And with a, if you will, a relatively strong treatment, like maybe using those intravenous corticosteroids.

[00:16:00] And again, as your listeners may be aware in attacks of NMOSD, we may go to things like plasma exchange which is washing the blood. And so, I guess our lessons are that we should still take optic neuritis seriously, especially when severe. Certainly, in the context of NMOSD or MOGAD, I would say for the most part, we don't want to leave that untreated. But the tools are as we reviewed them, things like corticosteroids, whether by mouth or perhaps more commonly intravenously at higher dose, or things like plasma exchange or PLEX a technique, again, if you will, wash the blood of any inflammation as best we can.

[00:16:49] **Krissy Dilger:** Thank you. And so when people unfortunately experience visual loss or visual issues following an attack, is that vision loss permanent or is there hope for recovering it?

[00:17:07] **Dr. Robert Shin:** Well, I will say that it's going to vary by the individual. So I mentioned with - I don't even have a good word for this, regular or typical optic neuritis. Again, the optic seen in the optic neuritis

treatment trial. Again, 90% or so of individuals had their full recovery of vision. Having said that, full vision visual recovery means the vision returns to better than 20/40 which is driving vision if you will. But often individuals could compare and they'll still know that the optic neuritis eye was not quite as good as their other unaffected eye. So that's always been the case.

[00:17:46] With NMO spectrum disorder, a more rare condition, the optic neuritis classically has been felt to be or observed to be more severe and sometimes not associated with good recovery. In fact, that was a signal for us if somebody had optic neuritis and they did not recover their vision well, we were like, wait a minute, that's a little bit unusual. Maybe we should check for a condition like NMOSD.

[00:18:14] I do want to reassure your listeners, however, that people who are living with NMOSD actually can have good recovery of vision. And in my experience, I've had individuals who have been completely blind, but thankfully have responded well to treatments if we figure it out early and get them on treatment quickly and had good recovery of vision especially early on in the disease course. So it is maybe harder to recover in someone who's had many episodes of optic neuritis and has already begun to lose vision. But these days as you increase awareness of this condition. I like to think that we're diagnosing it more quickly and more accurately and allowing individuals to access the high-efficacy therapies that are available now. And as a result, the outcomes can be better.

[00:19:00] So this idea that, well, if you have NMOSD, it's going to be so severe, you're absolutely going to lose vision and have difficulty walking. I don't think that's true anymore. I think with early diagnosis and use of effective therapies, basically the recognition of the condition, I think we can do a good job of preserving vision and ambulation and other symptoms. So, it's really all about awareness and getting people on highly effective therapies as early as possible.

[00:19:32] **Krissy Dilger:** Thank you. Finally, is there rehabilitation for optic neuritis? Anything someone can do to help after an attack or even supplements that help?

[00:19:47] **Dr. Robert Shin:** It is a good question and I do get asked that a lot and different individuals may provide different answers. So I'm just going to give you my opinion. As I said, to me, the key is early recognition and early application of effective treatments. And I think that's really the best thing we can do to try to ensure or encourage a good recovery. And really to prevent other episodes from happening in the first place, I mean, that's always the best outcome is if we can prevent additional episodes of optic neuritis or transverse myelitis or any brain or brain stem or spinal cord episode.

[00:20:26] But what if an episode has occurred or maybe this was your first episode and you wanted to come out? Well, I would say that I don't think that things like vision therapy and those kinds of techniques are necessarily effective. Now, again, there may be differences of opinion. I do know that there are providers out there. A lot of optometrists or neuro-optometrists may be believers in vision therapy to try to bring vision back. But I actually really just can't endorse that from my own training or practice, if it benefits you, that's fantastic.

[00:21:01] But the tricky thing is that as I hinted, there is the potential for optic neuritis to improve with time and with treatment on its own. So it may not be a therapy that fixed it, it may have been time that helped to fix that. Now, I will say that sometimes if vision loss is severe and there has not been good recovery or if the vision loss is affecting both eyes and thus, you don't have really a good way to compensate for it. There are forms of low-vision therapy. This is really adaptive therapy that can be helpful.

[00:21:34] And so like neuro-ophthalmologists, low vision specialists are not as common. But if you have access to them, if you can find them or be referred to them, they have lots of either training or technology

like microscopes that can help or special cameras that can magnify images that you can read or watch television. And I do recommend that type of evaluation for those who do have significant visual impairment.

[00:22:05] **Krissy Dilger:** Thank you. Those are all the questions that I have, but I wanted to open it up in case there is anything you'd like to add or anything you think the listeners would like to know.

[00:22:16] **Dr. Robert Shin:** Well, I really salute you and others who are making the effort to get the word out and to educate the community as well as providers about NMO spectrum disorder. The reason I say this is because as I hinted, we thought we understood optic neuritis back in the 1990s and early 2000s because again, a condition like multiple sclerosis is maybe more common or more familiar to many individuals.

[00:22:43] But since the early 2000s, once we were able to definitively show that NMO spectrum disorder is a distinct condition that requires different treatments and has a different outcome, I think that our field is out to rethink. But what if someone shows up and they have optic neuritis, maybe I shouldn't assume that it's something like MS, I should consider the possibility of NMOSD. And people need to understand how that is tested. I'm sure you've covered this in another podcast in terms of the importance of using a cell-based assay to check for aquaporin-4 antibodies or MOG antibodies as well.

[00:23:24] So that mission to maybe educate the community of providers as well as people living with NMOSD, it's really just so important. In a way, we're in the infancy of the period of time of treatment of NMOSD. Currently, three different FDA-approved treatment options for NMOSD. Each one I believe to be highly effective, but they're not going to work if we don't give them to the correct patients and figure out an NMOSD as early as possible. And so, these kinds of programs are just really so important. So, thank you for letting me be a part of this.

[00:24:02] **Krissy Dilger:** Well, thank you so much for joining us and volunteering your time to answer questions. I know our community members really benefit from these podcasts. So thank you so much and have a great rest of your day.