What to Expect Living with NMOSD and MOGAD Long-Term

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[00:00:00] **Krissy Dilger:** Hello and welcome to the SRNA, “Ask the Expert” podcast series. This podcast is titled, “What to Expect Living with NMOSD and MOGAD Long-Term.” My name is Krissy Dilger, and I moderated this podcast. SRNA is a non-profit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our website at wearesrna.org. Our 2023 “Ask the Expert” podcast series is sponsored in part by Horizon Therapeutics, Alexion, AstraZeneca Rare Disease, and Genentech. 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.

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[00:02:07] For today's podcast, we were pleased to be joined by Dr. Benjamin Osborne. Benjamin J. Osborne, MD, is an Associate Professor of Neurology and Ophthalmology at MedStar Georgetown University Hospital. Dr. Osborne is the Director of the Neuromyelitis Optica (NMO) and Neuro-Ophthalmology Clinics, as well as the Director of the Multiple Sclerosis Fellowship Program. Dr. Osborne is board certified in neurology, with concentrations in neuro-opthalmology and multiple sclerosis. Dr. Osborne evaluates and treats patients with complicated vision problems usually due to neurologic disease who are referred by other specialists. The neurological diseases that often cause such vision problems that Dr. Osborne treats include multiple sclerosis, myasthenia gravis, pseudotumor cerebri, thyroid eye disease, unexplained vision loss, optic neuritis, and papilledema. Dr. Osborne and his team participate in field testing and optic coherence tomography (OCT). He has published numerous works in journals in his fields, and is currently active in multiple ongoing research studies.

[00:03:29] Welcome and thank you for joining me today. To begin, do you mind just briefly discussing the long-term treatments available for both NMOSD and MOGAD?

[00:03:42] **Dr. Benjamin Osborne:** Sure. I'll start off with NMOSD because it's a lot easier because there are no FDA-approved therapies for MOGAD at this time. So, currently we do have three FDA-approved therapies for NMOSD. All of them are for patients who are aquaporin-4 positive and adults. So, we don't have FDA-

approved therapies for pediatric NMO yet or for seronegative patients. The first drug that was approved was Soliris, which is also known as eculizumab. This is an IV infusion that's given every two weeks. It does have a potential risk of serious side effects. So, to reduce that risk, patients have to get vaccinated to help lower the risk of getting any serious what we call meningococcal infections, which is a potential bacterial infection you can get if you go on this medication.

[00:04:31] The other two medications are inebilizumab or Uplizna, which is also an intravenous infusion that's given every six months. And satralizumab, which is also known as Enspryng. That's actually a subcutaneous injection. So, the patients can actually inject themselves at home once per month. All the drugs target the immune system. And by doing that, there's a potential increased risk of infections the longer you're on these medications. So, that's something patients should be in communication with their doctors. If they're on any of these therapies, if they develop any infections or fevers, particularly if they're on Soliris, if they develop any symptoms consistent with meningitis and they have to go immediately to the emergency room.

[00:05:11] For MOGAD, there's really no FDA-approved therapies right now. So, there's a couple strategies. So, some people, if they only have one attack, the strategy is just to watch and wait. We don't necessarily have to put them on long-term therapy if there's only been one episode of optic neuritis. However, if somebody's had a couple relapses at that point, most doctors and patients would think that it's probably prudent to go on long-term therapy to try to prevent another attack. All the data is what we call retrospective. So, it's skewed data. So, it's not the high-quality medical evidence that we like to have when I'm looking for a medication. But some of the data suggests that monthly IVIG infusions could be beneficial in preventing relapses. In addition to IVIG, some people use other non-specific immunomodulatory immunosuppressive therapy. So, it could be oral medication such as azathioprine or mycophenolate. Some people still use medications like rituximab, which is also sometimes used for an NMOSD still today. There are two major trials going on though for MOGAD. So potentially, if these trials are completed in the next few years and they pan out to show effective therapies, then we might have some effective drugs coming down the pipeline soon.

[00:06:34] **Krissy Dilger:** Yes, that is very exciting and hope to talk about that in future podcasts for sure. So, how do you, as a clinician, evaluate which treatment to use for a patient and for the NMOSD patients where there are FDA-approved medication available? Is there a benefit to choosing an FDA-approved medication over rituximab or another one that is not FDA-approved?

[00:07:03] **Dr. Benjamin Osborne:** Yeah. So, for NMOSD patients, I do prefer to start them on an FDA-approved therapy, mostly because they have larger trial data on the effectiveness of those drugs. We do have a lot of long-term safety data on rituximab, and we know it works fairly well in NMOSD, and I still have patients on that because they were on that prior to that era of the FDA-approved therapies. And if they're doing well on it, I haven't necessarily switched them off that therapy, but I generally use what's called a shared decision approach with my patients. So, I talk to them about the three approved therapies that are available. I look at their other medical conditions that might interfere or affect some of the drugs. So, for example, some patients have other autoimmune diseases. So, if I have a patient who has both myasthenia gravis and an NMOSD, which can happen, then I might elect to put them on eculizumab or Soliris because that's actually approved for both disease states, that's actually got dual approval for both of those autoimmune diseases. Other patients might not want to go on infusions every two weeks and so they might prefer to do Uplizna and then I have other patients who just might prefer to do injections at home. They don't want to go to an infusion site. So, they might prefer to use the satralizumab.

[00:08:25] **Krissy Dilger:** It is amazing now in the last few years, just getting those FDA drugs and having FDA-approved drugs and having different options for people who have different preferences. So, are there

concerns or things to be aware of for a patient to be on one of these treatments long-term? For example, can long-term use of rituximab cause certain negative effects, et cetera?

[00:08:56] **Dr. Benjamin Osborne:** That's a great question. So, we certainly have concerns. I think the biggest concern is the long-term risk of infections. Certainly, the drugs that deplete B cells like rituximab and inebilizumab, the longer you're on them, there seems to be a trend that you might be at increased risk for infections. So, we do track certain blood tests, we check your serum immunoglobular levels. We don't always see correlations though with patients who have infections and what the levels of their immunoglobulin levels are. That being said, we know that as patients get older, also their risk of infections might increase, and generally, whatever attacks they had that led to their NMO might increase the risk of infections.

[00:09:38] For example, somebody has just optic neuritis and NMOSD because they are aquaporin-4 positive, they might have a lower risk of infections versus somebody who had transverse myelitis. Those are quite severe, that led them to using a wheelchair, but just having the wheelchair dependence and not having the mobility is going to increase your risk of sometimes certain types of infections, having lack of mobility. So, all those factors can play a role in the long-term. So, again, I just always advise my patients if you think you're having an infection, just give a holler, let me know we can do tests to look, check for a urinary tract infection or other types of infections and treat appropriately.

[00:10:19] **Krissy Dilger:** Great, thank you. That's very helpful. Under what conditions would you recommend a person with MOGAD or NMOSD switch or end long-term therapies? How do you assess whether side effects are "bad enough to switch?"

[00:10:37] **Dr. Benjamin Osborne:** So, yeah, the side effects are mild. Sometimes with the infusion therapies, there could be mild infusion reactions. We get patients some Benadryl and some steroids and slow the infusion rate down and then re-challenge them with the infusion maybe a half hour later at a slower rate and some patients do okay with that. But if with the re-challenge, they just still have severe infusion reactions which can include tickling the throat, difficulty breathing, rashes, fevers, then we just have to stop the medication and switch. The main reason I say that people switch therapies would probably be due to potential side effects. It's not that common. They actually have breakthrough disease with these drugs. One of the nice things about all these drugs is that they're highly effective at reducing relapses. They're not cures, unfortunately. But if somebody does have a true relapse while in therapy, that would be another reason to switch.

[00:11:30] So, if somebody happened to be on Soliris and had a relapse, then I might switch them to a drug with a different mechanism of action like Uplizna or Enspryng or vice versa. If somebody's just been on the drug for a long time and just is sick of being on therapy, but they're doing well on it and they're tolerating it well, I generally don't recommend discontinuing therapy. Unfortunately, in NMOSD, we know that if your aquaporin-4 positive has a very high risk of having relapses, and that can go on pretty much the rest of your life. And if you stop the therapy, there's a risk you could have a devastating relapse afterwards, and you might not be able to recover so well from a relapse. So, the name of the game is really prevention.

[00:12:12] **Krissy Dilger:** Thank you. So, what are some of the long-term symptoms associated with having NMOSD and MOGAD? And how can someone tell if a symptom is from their diagnosis or a side effect from their medication?

[00:12:31] **Dr. Benjamin Osborne:** So, that's a good question. I'd say with NMOSD, probably the most common chronic problem that patients suffer with is chronic neuropathic pain. This happens particularly when they've had an episode of transverse myelitis. The inflammation from NMOSD in the spinal cord can

be quite extensive and even if there's partial recovery or what's thought to be a fairly good recovery, there can be persistent long-term chronic neuropathic pain that needs to be managed with other medications. The medications that are approved by the FDA are basically trying to prevent future relapses, but they don't treat the prior damage that occurred. So, the chronic neuropathic pain, which could be burning, tingling, muscle cramps, stiffness in the legs or arms, depending on the limbs that are affected, sometimes have to be managed with other medications. We could use muscle relaxants sometimes to treat those symptoms, sometimes we use medications that were originally prescribed for treating depression or preventing seizures, which we know actually work quite well for preventing neuropathic pain. Some of these can be like tricyclic antidepressants like amitriptyline and nortriptyline or anti-seizure medications like gabapentin or pregabalin, and they sometimes will help reduce the severity of that pain quite a bit.

[00:13:45] For MOGAD, I don't think there's as many long-term side effects that we've seen in that disease except-- again, there might be chronic neuropathic pain if somebody's had severe transverse myelitis from that. Sometimes they also have chronic bladder dysfunction that can persist. That could be urinary urgency, urinary incontinence, urinary frequency. Even once the damage to the spinal cord is done, the nerves that control your bladder control actually travel through the spine. So, if there's a transverse myelitis from NMOSD or MOGAD, you might have persistent bladder symptoms and bladder dysfunction. And also, sexual dysfunction could be erectile dysfunction or other sexual dysfunction that persists. Most of the times, those symptoms are due to the disease itself and not the medications. There are some side effects you do have to watch out for. So, with Enspryng for example, you can get injection site reactions at the site where you're injecting the medication because that's a subcutaneous injection. Some doctors will recommend monitoring your cholesterol levels because there can be a bump in the lipids from Enspryng. That's another potential side effect. And then as I mentioned earlier, there's a potential increased risk of infections with all these drugs. So, if you do develop any infections, that's probably more of a side effect of the drug than maybe the NMOSD itself.

[00:15:07] **Krissy Dilger:** Thank you. So, what effect, if any, does living with NMOSD or MOGAD have on aging? Are patients more prone to other disorders or higher risk of negative health conditions?

[00:15:24] **Dr. Benjamin Osborne:** So, I think we have more information in NMO because our understanding of MOG is still evolving. They just published this year in 2023 the first proposed diagnostic criteria for MOGAD. So, it's a disease and evolution as far as our understanding. I think though with NMO, we definitely know that there's a higher risk of other autoimmune diseases. So, many NMO patients might, like I mentioned earlier, have myasthenia gravis, Sjögren's disease, lupus, autoimmune thyroid disease. And so, all of that will have an added effect of causing further health complications as the patient ages. They might have to be on multiple drugs to control their multiple autoimmune diseases. And those drugs might increase the risk of opportunistic infections. Those are the types of infections when your immune system is weakened by these drugs.

[00:16:17] With NMOSD itself, the risk with aging is also that it can increase morbidity and mortality, especially there's a lot of data before we had highly effective therapies to treat the disease that patients had a higher risk of passing away or dying particularly from respiratory failure. If there's a severe attack of inflammation in the brain stem, where the nerve centers for the brain that control our breathing muscles are located, that's an increased risk for dying from complications of that or, again, if there's been a long, extensive transverse myelitis and the patient's paraplegic or quadriplegic, they could have aspiration pneumonia, decubitus ulcers, or skin breakdown. And these infections could also lead to increased risk of hospitalizations and other complications. I think now that we have highly effective therapies, I think we're going to see a change in that. I have many NMO patients where you never know they have NMO. Like they had an attack of optic neuritis, they have pretty good recovery, and they're walking around working full time. Some of them work full time jobs at hospitals nearby, and you never know they had NMO just looking at them. So, I think because we have these highly effective therapies and we're going to be starting people after their first attacks more

rapidly, we're going to see less morbidity and less mortality in the future.

[00:17:38] **Krissy Dilger:** That's really great to hear. And I think even just in the last 20 years or so, the thinking has changed on that particular topic. It leads me into my next question about the prognosis for someone with NMOSD or MOGAD. Does the age of onset severity of attack, number of attacks, or any of other factor into prognosis? And can it affect your lifespan, or can it not affect your lifespan? And I think you already answered this, but can the disorder itself cause death, or is it more like an effect of an attack causing death?

[00:18:25] **Dr. Benjamin Osborne:** Yeah. So, the NMOSDs can be highly variable. So, some factors that appear to be poor prognosis is patients who are African American seem to have higher rates of disability, morbidity, and mortality from these diseases. I'm not sure we clearly understand the mechanism of why that is if it's socioeconomic issues, or systemic racism in medicine, or maybe some other genetic factor that increases their risk. But it's also more common in African Americans, and people from the Caribbean and Africa compared to Caucasian. They say that the first attack, how well you recover is a good prognostic sign or a bad prognostic sign. So, if you have a severe transverse myelitis and you end up using a wheelchair and you can't walk again after that attack, obviously, that's a poor prognosis. Whereas some patients, if they have an area postrema syndrome, they recover well from that or optic neuritis, and they might do quite well once they get on a highly effective therapy and actually have minimal long-term disability from the disease.

[00:19:30] MOGAD again is so variable. It's hard to say. I think with MOGAD we really have to differentiate. There's MOGAD that affects children and pediatrics where we see more of something called ADEM or acute disseminated encephalomyelitis. There might be more of a risk of that being what we call monophasic disease with less risk of recurrences. Whereas in adults, it's still, there could be people who are monophasic and then some people who have relapses, and we're still trying to sort out how to predict who will get those relapses. But I think with MOGAD, the same holds true. If you had a really bad relapse with poor recovery, then that's a bad prognostic sign. I don't think we see much or have enough data yet to predict effects on mortality in MOGAD. My general impression is that it doesn't affect mortality as much as NMO. I think NMOSD has a worse prognosis overall than MOGAD. The people with MOGAD in general have better recovery from the relapses when they get steroids. Sometimes they have to be on steroids for a very long time, but they tend to have a more robust recovery versus NMO patients. They could have good recoveries but more often than not, they sometimes have permanent disability after an attack.

[00:20:40] **Krissy Dilger:** Well, good to know. Thank you. So, finally, we do get a lot of questions from people looking to improve their long-term quality of life. So, are there any known treatments, supplements, vitamins, lifestyle practices, diets, et cetera that someone with one of these diagnoses can use to try and improve their long-term quality of life?

[00:21:05] **Dr. Benjamin Osborne:** That's a great question, also. I think to supplement whatever medical therapy you're on, it is a good idea to investigate other ways to improve your quality of life and your overall health. The problem is we don't have a lot of great data to support the evidence for this. Much of this is extrapolated from what we know about multiple sclerosis, which I think is kind of true. That's like how NMO was initially-- we thought it was a variant of MS. So, probably the most common vitamin supplement people take is vitamin D. But even in MS disease, we know a lot more about in many respects. There's great evidence that vitamin D deficiency is much more common in MS. And it seems to be more common in NMOSD, also. But there's not great evidence that by taking supplementation, you're going to have a benefit long-term or impact on the disease, relapse rates, or disability. That being said, if your doctor finds you're vitamin D deficient and prescribes your vitamin D, I would recommend taking that. Some people like to take supplements so they can take over-the-counter vitamin D and a multivitamin. But again, there's not a lot of rigorous, well-controlled trials, showing a benefit to these vitamins. As far as diets are concerned, again, there's different diets that

have been bandied about a low salt diet was a big bad in multiple sclerosis for a while. It was thought that too much sodium and high salt content could cause damage to the central nervous system in people had autoimmune diseases like MS. And it might be true in NMOSD again. So, I think in the United States, at least our diets are already well-saturated with a lot of sodium. So, making sure you don't have a high-sodium diet might be beneficial. A lot of people look into the Mediterranean diet, which is also a healthy diet lifestyle in general, regardless of whether you have NMO or MOGAD. But again, there's no data that has an exact benefit on these two diseases. But in general, it seems to be a healthy diet and lifestyle.

[00:23:00] I would definitely say that if you need to get it, getting physical therapy and if you don't need physical therapy, just making sure you exercise regularly would be very important. So, making sure that you’re mobile will help keep your body healthy in the long term and your mind decades in the future. So, making sure that you are not a couch potato and getting up, and exercising. It doesn't have to be super vigorous exercise. It could be 3-5 days a week, 30 minutes a day, or a session of an exercise and whatever you enjoy. If it's walking, that's fine. It doesn't have to be high-impact exercise or cardio. Some people might like yoga, whatever you find fulfilling. I’d definitely say quitting smoking is definitely an important thing. We know it's clear cut in multiple sclerosis that tobacco use actually aggravates and makes MS worse. And I suspect the case is the same with NMOSD and MOGAD. So, talk to your doctor about ways to try to quit smoking if you do smoke. And I think that's about it that I can think of.

[00:24:28] **Krissy Dilger:** Well, that's all-great suggestions, great advice. I would say just as a disclaimer if you do try any supplement or new rigorous exercise, it might be a good idea to check in with your physician just to make sure.

[00:24:26] **Dr. Benjamin Osborne:** Definitely.

[00:24:26] **Krissy Dilger:** Thank you so much for joining me. I think this is all great information and we're so happy you were able to join us. So, thank you.

[00:24:34] **Dr. Benjamin Osborne:** It's my pleasure. Thanks for the invitation.