MOG Antibody Disease: Adult and Pediatric Presentations

You can listen to the audio of this podcast at: https://youtu.be/AIKKi2njDRU

Krissy Dilger: [00:00:00] Hello everyone, and welcome to the SRNA Ask the Expert podcast series. Today's podcast is entitled MOG Antibody Disease: Adult and Pediatric Presentations. My name is Krissy Dilger, and I will be co-moderating this podcast along with Peter Fontanez.

Peter Fontanez: [00:00:20] Hi. Yes. My name is Peter Fontanez. I am a member, a peer support group member with SRNA. I'm also on the board of The MOG Project. We are working this as a collaboration project to do this podcast, to ask the doctors about MOG antibody disease. I am the father of a 12-year-old girl, a daughter Isabelle, has MOG antibody disease with ADEM and optic neuritis. She's had multiple attacks. She is currently on preventatives and has been doing very well for the last four years on the preventatives.

[00:00:51] But since then, I've wanted to get involved with this, and we're doing this as, like I said, a collaboration to ask the doctors and the experts their opinions on, on this illness and get their information. Thank you, back to you, Krissy.

Krissy Dilger: [00:01:05] Thank you, Peter. 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. This podcast is being recorded and will be made available on the SRNA website and for download. During the call, if you have any additional questions, you can send a message through the chat option available with Zoom.

[00:01:32] Our 2020 Ask the Expert podcast series are sponsored in part by Alexion, Genentech, and Viela Bio. Alexion is a global bio-pharmaceutical 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.

[00:02:04] Founded more than 40 years ago, Genentech is a leading biotechnology company that discovers, develops, manufactures, and commercializes medicines to treat patients with serious and life-threatening medical conditions. The company, a member of the Roche group, has headquarters in South San Francisco, California. For additional information about the company, please visit www.gene.com.

[00:02:31] Viela Bio is dedicated to the development and commercialization of novel life-changing medicines for patients with a wide variety of autoimmune and severe inflammatory diseases. Their approach to drug discovery is aimed at providing targeted treatments for improved outcomes for the thousands of patients who have few or no therapeutic options. For additional information about Viela, please visit vielabio.com.

[00:03:00] For today's podcast, we are pleased to be joined by Dr. Leslie Benson and Dr. Michael Levy.

[00:03:06] Dr. Leslie Benson as an attending physician in the Department of Neurology and the assistant director of the Pediatric Multiple Sclerosis and Related Disorders Program and Pediatric Neuroimmunology Program at Boston Children's Hospital. She is also an instructor of Neurology at Harvard Medical School. She completed medical school at University of Colorado Health Sciences Center, pediatric training at Massachusetts General Hospital for Children, and child neurology at Boston Children's Hospital prior to a two-year fellowship in neuroinflammatory diseases. Dr. Benson is board-certified in child neurology, and her clinical work is focused on care of children and young adults affected by neuroinflammatory disease including MS, transverse myelitis, AFM, optic neuritis, MOG antibody associated disease, and ROHHAD syndrome, among others. She's involved in collaborative clinical research aimed at improving the understanding and treatment of these disorders.

Peter Fontanez: [00:04:07] Dr. Michael Levy is an associate neurologist at Harvard Medical School. He is the Director of the Neuromyelitis Optica Clinic and Research Laboratory, and Research Director in the Division of Neuroimmunology and Neuroinfectious Disease at Massachusetts General Hospital. Dr. Levy specializes in taking care of patients with neuroimmunologic diseases including multiple sclerosis, transverse myelitis, optic neuritis and neuromyelitis optica. In the laboratory, Dr. Levy's research focuses on the development of neural stems for regenerative therapy in these diseases. He uses rat and mouse models to test the survival, differentiation, and functional capacity of human neural STEM cells to improve neurological function in post inflammatory conditions. The goal of his laboratory and clinical effort is to translate the basic science STEM cell work to a human trial in transverse myelitis and other neuroimmunologic diseases.

Krissy Dilger: [00:05:03] Welcome and thank you all for joining us today. So to start us off, Dr. Levy, can you briefly define MOG antibody disease?

Dr. Michael Levy: [00:05:12] Thank you for inviting me. MOG antibody disease. MOG stands for myelin oligodendrocyte glycoprotein. And the disease is characterized by presence of this antibody against MOG. And in the clinical setting of optic neuritis or ADEM - acute disseminated encephalomyelitis - or transverse myelitis or an NMO picture, the disease has been around in a mouse far longer than we recognized it in the human.

[00:05:44] And as the antibody has been looking for the disease for over the past last 20 years, only recently has it been recognized as a separate entity. It used to be associated with MS, and then with ADEM, and then with NMO. And now more recently in the past few years, we recognize that it's an immunological attack against MOG that manifests most commonly as ADEM, optic neuritis, and transverse myelitis.

Peter Fontanez: [00:06:12] Okay. The next question is for Dr. Benson. What is the presentation for MOG patients? Are there differences in presentations for children than for adults and what are they?

Dr. Leslie Benson: [00:06:24] Hi, thank you for having me as well. I, again, you know, coming off of what Dr. Levy mentioned, there are differences in presentations for MOG associated disease. These include optic neuritis, transverse myelitis. So those are inflammation of the optic nerve, meaning that connects the eye to the brain and the spinal cord. And there's also this condition called ADEM, which is acute disseminated encephalomyelitis, which includes specific diagnostic criteria to meet that diagnosis, and that requires a presence of encephalopathy, which is a fancy word for saying sleepiness, confusion, brain dysfunction, in a global sense. And then, any kind of combination of those things. And more recently it's become clear that there's another presentation of MOG associated disease, which includes encephalitis and kind of a meningitis type pictures.

Krissy Dilger: [00:07:27] Dr. Levy, do you have anything to add?

Dr. Michael Levy: [00:07:32] Yeah. As Dr. Benson was saying, there are many different presentations, and I guess my area of expertise is really in the adult presentation more than in the kids. So I'll let Dr. Benson try to log back in to finish her thoughts on kids. But in adults, the most common presentation is optic neuritis by far. So two thirds of the attack are of the optic nerve. And they look pretty dramatic at first. You know, they look like really bad vision loss like you see with neuromyelitis optica, the aquaporin-4 type. And a lot of our patients will show up in the hospital with complete vision loss or near complete, just being able to see, you know, maybe a light. And for the most part, MOG patients tend to recover pretty well, but it takes a few months sometimes, and that's true in the spinal cord too.

[00:08:25] And I think in kids, kids tend to improve pretty quickly as well. And so, you know, a lot of these presentations are very, very dramatic, but then they do get better over time. And what we're worried about in the long-term is how many times can a patient suffer a damage, significant damage like that and recover each time? Our thought is that it's not infinite, that there are a certain number of attacks that eventually will lead to some sort of long-term disability.

Krissy Dilger: [00:08:57] So for the next question, what are the symptoms of MOGAD? Are there different symptoms experienced by children than there are for adults?

Dr. Michael Levy: [00:09:08] The most common symptom of MOG antibody disease is vision loss. And that's associated with pain behind the eyes; this is how it usually starts. I'll get a phone call and they'll say, you know, I have this feeling like someone punched me in the eye, that sort of soreness behind my eye. And then it evolves into pain with eye movements. So when you move your eyes to the left and right and up and down, it hurts. And then the vision loss begins. All of this can evolve over hours, but it could also evolve over days. And then as the vision loss progresses, then everyone starts to take it very seriously as a manifestation of optic neuritis. If you already have a MOG antibody diagnosis, then we recognize it.

[00:09:51] We can recognize it sooner and start treatment faster. That's how optic neuritis manifests most of the time. Transverse myelitis, it would be weakness, numbness, and most often it meant bowel/bladder dysfunction, and sexual dysfunction from attacks very low down in the spinal cord. I'm not sure if that happens as much with kids. I suspect, there's much more brain involvement with kids. Is that right, Dr. Benson?
Dr. Leslie Benson: [00:10:16] Some spinal cord involvement, for sure, and some persistent urinary dysfunction in some of the kids. I think the data is lacking a little bit there, but I don't know if it's as common as with the adults.

Peter Fontanez: [00:10:30] For a person who tests positive for MOG antibody, I know you guys have already discussed some of the, some of the diagnoses such as ADEM, NMOSD, and optic neuritis. What are some of the other additional diagnoses that can go with MOGAD that some people may not be aware of or that are still present with the illness. Dr. Benson?

Dr. Leslie Benson: [00:10:49] I don't know if Dr. Levy mentioned it, but one of the newer recognized associations with MOG antibodies is encephalitis, or sort of a meningoencephalitis picture, which can cause more seizures and brain dysfunction and look for all the world like an infectious encephalitis, except that the antibodies are present and an infection is not able to be found.

[00:11:13] And so I think that's one of the newest presentations that have been recognized and is quite interesting. Otherwise, I think Dr. Levy has probably covered all of the most common diagnoses.

Krissy Dilger: [00:11:26] Okay. Great. Thank you. This next question we got from a member of the community, says 'I tested positive for MOG and optic neuritis in both cerebrospinal fluid and blood sample at the same

time that I had a severe presentation of B. henselae. This person wants to know if this could have caused MOGAD, and is it possible to have both neuro-retinitis and optic neuritis? Dr. Levy?

Dr. Michael Levy: [00:11:57] So Bartonella henselae is a bacteria that comes from cat litter, basically. And, when cats, scratch their litter and then this bacteria lives under the skin, if the cat then scratches you, then it can travel up your lymphatic organs and infect the back of the eye, and it causes what's called a neuro-retinitis. I've only seen it once in my whole life, and it was very severe. And it's treated with antibiotics very urgently, because it can cause permanent damage.

[00:12:28] That's very different from MOG in which the problem is, it's an autoimmune attack rather than an infectious disease attack. Now, what are the chances that this happened simultaneously? I'd say that they're both very rare and that the chances of both happening are a little unusual. What I will say is I've seen a lot of cases of false positive Bartonella or of what's called an IgG, which is a long-lasting immune response, but not the IgM, which is the acute immune response. So we have lots of patients who get tested for these rare infectious diseases and they might test positive, but it's an IgG, meaning they've been infected sometime in the past, but not recent. And so I think that that's the more common presentation.

[00:13:16] And then we've also seen some positive IgMs to other infections like walking pneumonia, mycoplasma, and Lyme disease. And the question there is, does that infection stimulate or trigger a MOG antibody attack? So is it possible that if you have MOG or you're predisposed to it, and then you get an infection and that triggers an attack? It's certainly possible. It's certainly possible. Yes.

Peter Fontanez: [00:13:42] Next question. I think this is a question from the community. How come MOGAD does not show on MRIs all the time, but shows on OCT scans? Is it possible the MRI isn't the best tool for diagnosing relapsing ON or ON flare? I know that this was also a question we were discussing about as well. This is for Dr. Benson.

Dr. Leslie Benson: [00:14:01] So I'm not sure that this experience is consistent with my reading or my experience. I mean, I think in general, whether it's MOG associated or not, optic neuritis sometimes is subtle or difficult to see on MRI. But MOG actually is associated with I think usually more prominent changes on MRI with what we call longitudinally extensive, meaning a long segment of the optic nerve being involved. And enhancing can even cause more of an orbit inflammation, meaning that even outside the optic nerve, there can be some inflammation seen in the surrounding tissues on MRI.

[00:14:39] And so I don't know that the statement that MRI doesn't find it often is globally true, but certainly may be true for some patients' experience. In terms of OCT, we definitely see an association between MOG antibody associated disease and thinning on OCT. So what OCT is, is ocular coherence tomography, and it is a way to take a picture of the back of the eye noninvasively and look at the different layers of the retina.

[00:15:08] And with optic neuritis and MOG antibodies, we see a thinning, sometimes a rather impressive thinning of the retinal layers, even when patients can still see fairly well, particularly in children. So, I do think that OCT can show and be sensitive to attacks and further attacks, but I don't think we really know how it changes with each subsequent attack on a broad population-based scale.

Krissy Dilger: [00:15:40] Okay, thank you. And Dr. Levy, do you have anything to add to that?

Dr. Michael Levy: [00:15:46] The one thing I would add is that, at least in a lot of my patients, is that the MRI tends to improve over time. And so a lot of my MOG - and I don't know why it happens so often, it really shouldn't. But if you get the MRI too late and the healing process has already started, then oftentimes you might miss it.

[00:16:09] And that's something that we especially see in the spinal cord. We used to call it MRI-negative myelitis, but now we recognize that it happens mostly in MOG patients. Because they'll have an attack, and again, I don't know why they don't come to our attention right away. They really should be getting an MRI right away so that we can evaluate what's wrong and start the treatment.

[00:16:31] But oftentimes it's two or three weeks later, and then they get the MRI and by then it's sort of normalized, and so we miss it. That's happened a few times. In the optic nerve, the advantage with the OCT is that it shows the damage that has happened cumulatively. So if you've had an optic nerve and optic neuritis, you know, even a year ago, the OCT will still be, will still show you the damage, but MRI tends to heal, sort of pseudo-normalizes over time.

Dr. Leslie Benson: [00:17:04] That's a good point. Agree.

Peter Fontanez: [00:17:07] Thank you for that. Next question. Can you explain the difference between monophasic and recurrent MOG antibody disease? How is this determined and is it more common for children to be monophasic or recurrent? What about for adults? Dr. Levy?

Dr. Michael Levy: [00:17:21] So I think, you know, in adults, I have rarely seen a monophasic case. And I think that it's going, I suspect, that Dr. Benson sees quite the opposite, that she sees a lot of monophasic cases in kids, but I'm not sure. I would say that in, you know, once you're in my clinic, if your onset is over the age of 21, especially with optic neuritis, I think it's just a matter of time, especially if you continue to test positive for the MOG antibody. Even if the titer goes down.

[00:17:54] So let's say you were at one to a thousand on your first optic neuritis, and then you're down to one in a hundred on follow-up in my clinic. You might say, wow, maybe I'm trending in the right direction. Maybe I'm not going to have any more attacks. I certainly hope so. And I would like to see that, that the data bears that out. But we've only, we only have about two, two and a half years of longitudinal data to know whether people can even be monophasic. And so far, I am worried that people who continue to test positive are mostly going to be recurrent, but I'd love to hear Dr. Benson's answer in kids.

Dr. Leslie Benson: [00:18:33] Yeah, definitely a different experience in children. Although again, follow-up is limited, right? So one of my patients had classic ADEM, tons of spinal cord inflammation associated with it, potentially optic neuritis with it, thought she was doing great. And seven years later, she had the same triggers that triggered her first one, and she had an attack of optic neuritis.

[00:18:54] So I think there's a lot to be learned with long-term follow-up studies. But what we see is that a fair number of patients don't have recurrence. And it seems to potentially be at least in part related to whether those MOG antibodies stick around or not. The literature would support somewhere between 25 and 50% of patients have an attack rate, or have an attack.

[00:19:15] But again, that's with a limited follow-up. So I think that the rate is higher than that. The antibody piece, I think is interesting. And something that we can apply directly to patient care, at least some of the time, which is that, you know, obviously to get the diagnosis, you have MOG antibody positivity at diagnosis or at the initial event.

[00:19:35] But if subsequent, if you follow the MOG antibody, whether it's positive or negative seems to be what matters, not necessarily the titer. Then if patients no longer or have detectable MOG antibody, they seem to be at significantly lower risk of subsequent attacks. Whereas those patients who have persistent antibodies are likely at a higher risk, but in our experience, not a hundred percent for sure.

Krissy Dilger: [00:19:59] Okay. Thank you both. I guess this kind of ties into what you were just saying, Dr. Benson, but someone did ask, once you test positive for MOG, can you then test negative at a later time?

Dr. Leslie Benson: [00:20:14] Yeah. And the answer is yes. Both your positivity or negativity can change, and your titer levels can change. I would say that even when patients go from positive to negative, I tend to follow that for a little while before I'm convinced that it's persistently negative, versus somebody who might intermittently test positive, and low titer positive and negative.

Peter Fontanez: [00:20:36] Great. Thank you for the answer, Dr. Benson. How often should testing be done to check MOG levels per reoccurrence? Does the level of MOG correlate to the severity of disease, such as the title level? Dr. Levy?

Dr. Michael Levy: [00:20:49] The titer level. So the amount of antibody that you have does not correlate with the severity of disease, it correlates with the reliability of the diagnosis.

[00:21:01] So the data coming out of the Mayo Clinic, where they test most of the MOG antibodies is that if your titer is one to a hundred or higher, meaning you dilute the serum a hundred-fold and you still detect the antibody. If you can do that and still detect the antibody, then the likelihood of MOG being the correct diagnosis is better than 95%.

[00:21:26] If you have lower titer, so less antibody, like one to 40, one to 20, or one to 10, which is measured at Quest, then your chance of a false positive is higher if you have MS. So if you have MS or they think you have MS, and you tested very low positive for MOG, and you have a bunch of brain lesions, then we think you sit somewhere between MS and MOG, but it's not clearly MOG antibody disease.

[00:21:53] If you have MS, and then you test positive for MOG with a high titer, then you convert, you come to my clinic and we change your diagnosis code. So that's how we use the titer of the antibody.

Peter Fontanez: [00:22:07] And how often should they be tested for the titer levels or MOG tests? How often in frequency?

Dr. Michael Levy: [00:22:13] We use it just to make the diagnosis. So if there's an uncertainty, like let's say you test low positive once, or even negative, then it might be worth rechecking if you're maybe considering a more aggressive MS treatment and you want to make sure it's MS instead of MOG or something like that. It's only useful for clarifying the diagnosis to retest.

[00:22:38] The other situation is where you want to know if there's going to be a relapsing disease. So let's say you've only had one attack, and you want to know if you're going to be monophasic or not, or if you're going to start treatment, then it's worth re-testing. I usually do it at the six-month mark, and then every year after that for three years, and if you're persistently negative, then I would call you negative, but I'd still keep an eye on you.

Peter Fontanez: [00:23:04] Anything to add Dr. Benson?

Dr. Leslie Benson: [00:23:07] Yeah, I think that in the pediatric world, we do tend to follow the titers more, but perhaps that's driven by the fact that some of our patients, more of our patients are monophasic and the, again, the kind of relapse assessment piece. I would add as well that I've seen some literature that titers correlate with severity of the attack.

[00:23:23] So during the attack, the higher titers may be associated with more severe attacks, but I would also point out that the positive titer - over one to a hundred or lower, I guess is... Well, I agree with Dr. Levy's statement. I don't think that the titer itself is predictive of whether you will have a relapsing course in the, you know, in follow-up. What I've seen most and what is probably easiest, because different points in time are gonna vary, right? When you check your antibodies. So for studies, it's likely that those earlier time points that are untreated that are more likely to be easier to interpret when you're studying them.

Krissy Dilger: [00:24:03] Okay, thank you. And Dr. Benson, what are some of the long-term issues pediatric patients may have, for example, behavior or psychological changes, learning difficulties, seizures, or any other residual symptoms?

Dr. Leslie Benson: [00:24:20] That's a great question. And I think it's a really understudied question with MOG. There's one paper looking at academic difficulties following MOG associated disease. And they clearly found an association between, a diagnosis or the presentation of ADEM, a presentation under 10 years of age, and those who had lesions that involve the deep gray matter. So the kind of in the middle of thalamus and basal ganglia parts of the brain. That seemed to increase the chance of having academic difficulties associated. But there aren't detailed neuropsychological testing that have been published so far. And I think it's a, it's a great need.

[00:25:04] Certainly patients may have seizures associated, although I would think that's the minority. And if you don't have full recovery, certainly leftover vision loss from optic neuritis, or as we were talking about earlier, bladder and bowel dysfunction from transverse myelitis, weakness and things can be present, although at least in children, most of them seem to recover their physical functions quite well overall.

Peter Fontanez: [00:25:30] Thank you for that. Dr. Levy, a similar question. What are some of the long-term issues adult patients may have? For example, blindness, visual loss, or any other residual symptoms that they may have.

Dr. Michael Levy: [00:25:41] Most of the residual symptoms are vision issues, light sensitivity, visual acuity problems that are not necessarily correctable with glasses. That happens often. And those who've had attacks in the spinal cord will have sometimes some persistent numbness or weakness or bladder issues. So it could be incontinence, it could be retention. I did say earlier that most of my patients recover well, and that's the truth. But residual problems are almost always present when, especially when a patient becomes ill or feverish or exercising or another way their body temperatures increase.

[00:26:24] That's when we see a lot of the symptoms re-emerging, and it can impair day-to-day function. I also have a couple of patients who have permanent visual impairment from just repeated attacks over and over again. I think what we're doing is, we're mostly comparing to aquaporin-4 NMO, where the recovery is horrible in a lot of cases. Compared to that, MOG recovery is good, but still I feel like there are many more residual, neurological problems that result from MOG.

Krissy Dilger: [00:26:54] Thank you, Dr. Levy and Dr. Benson for that. The next question: has hearing loss been linked to pediatric or adult MOG patients? Dr. Benson?

Dr. Leslie Benson: [00:27:06] You know, in my experience, I have not come across patients who have had hearing loss associated with their MOG associated disease. I see in the literature, there have been kind of some case series and case reports of an association.

[00:27:19] And I can understand how, if you had a brainstem lesion that was in the right location, that you might end up with a problem with your hearing related to that lesion. I don't know if Dr. Levy has seen it personally though. I have not.

Dr. Michael Levy: [00:27:33] Just had that one case that we, I think it's been published now. Just one so far, but, I think, you know, we've seen that more often actually with patients who have overlapping lupus diagnosis, especially with aquaporin-4. So if there is hearing loss, I'm always suspicious about lupus overlying it.

Peter Fontanez: [00:27:56] This next question I think is going to be for both of you. We'll start off with Dr. Levy. Fatigue and pain has been a noticeable symptom. Is this more common in adults or in children, or MOG overall?

Dr. Michael Levy: [00:28:08] I have heard some pretty dramatic stories about fatigue in MOG antibody disease, and it's not necessarily associated with a relapse.

[00:28:18] It's like profound fatigue that just impairs patients for months at a time and then goes away. It's almost like its own type of relapse. And then for the most part that it can go away, just kind of on its own. And so I'm not really sure what that is. Is that a, is that some, you know, MOG reactivity going on in the brain, is it amenable to treatment with steroids?

[00:28:40] Is it from damage that was done? We don't know. We also see it in patients with transverse myelitis. These are folks who have a single attack in the spinal cord. And you don't think of energy and fatigue as being localized to the spinal cord. We think of mental and fatigue and sleep issues being mostly a brain issue.

[00:29:00] But why would we see it with transverse myelitis? I don't know. But it seems to be in common with multiple sclerosis and transverse myelitis and neuromyelitis optica.

Peter Fontanez: [00:29:10] Dr. Benson, anything with the pediatric side with pain or fatigue?

Dr. Leslie Benson: [00:29:14] I don't know. I can't think of any dramatic problems with fatigue.

[00:29:18] Although I think overall, patients can be very irritable and very unwell during clear attacks. I have had a fair number of patients complain about stomach pains and headaches and things during recovery phase as well. And I don't know if that's directly related or sort of secondary. The pain piece. You know, we certainly, there's definitely an association between like myelitis and pain in NMO, particularly aquaporin-4 NMO. I have seen a little bit of pain associated in my patients with MOG, but it hasn't been, a majority. It's a minority of patients who have struggled with that.

Krissy Dilger: [00:29:54] Thank you, both Dr. Benson and Dr. Levy. We have a lot of questions about treatment, so we'll move on to those for now. First question is, what are the acute treatments used for a new attack? Is it the same for children and adults? Dr. Benson, do you want to take this one?

Dr. Leslie Benson: [00:30:13] Sure. I think likelihood is that the treatments are the same between kids and adults for the most part, but certainly Dr. Levy can comment on that. Globally, a first line treatment for an acute attack, regularly is going to be steroids, and usually that's an IV steroid. We may dose it different in children because we dose by weight.

[00:30:32] But it should, it's likely the same steroid. And so usually it's an IV steroid followed by an oral steroid that slowly tapers over time. We also, in patients who don't respond sufficiently to steroids, think about using

things like IVIG, which again is an IV infusion medication, or plasma exchange, also called plasmapheresis, where it's a process of filtering the blood, usually with a large catheter, which may be a little bit more complex of a consideration in a small child than an adult. But the catheters are used to take the blood out, filter it, and then replace the blood basically, and it sort of filters out antibodies and other inflammatory mediators.

[00:31:16] And those are really the, three treatments that get used most commonly in acute management of not only MOG, but many of the conditions we treat.

Krissy Dilger: [00:31:25] Okay. And just to follow up, are there any major differences for children and adults or any treatments that are considered unsafe for children?

Dr. Leslie Benson: [00:31:35] We use all of those treatments pretty frequently. I don't know if Dr. Levy uses anything else in adults.

Dr. Michael Levy: [00:31:41] No, but I have been pushing more than steroids because I don't like how my patients get biologically almost addicted to the steroids, such that it's hard to wean down without triggering a relapse. So I prefer much more to use IVIG, even acutely.

Dr. Leslie Benson: [00:32:03] We tend to treat all of our MOG... once we know they have MOG, we tend to give them IVIG.

[00:32:07] And sometimes we give them IVIG for a period of time. So I think we have the same sense you do.

Peter Fontanez: [00:32:15] With you talking about the IVIG, Dr. Benson, what are the most common long-term preventative treatments for adults with MOGAD and for children? For example, some studies specifically suggest medications, like IVIG having better results for pediatric patients.

[00:32:29] Can you add to that, I guess, for both of you, but starting off with Dr. Benson?

Dr. Leslie Benson: [00:32:33] Yeah. Sure. So there are more and more studies of what patients have been treated with. They're all retrospective, no perfect trials to give us super clean data. But the same types of treatment get used in kids as used in adults.

[00:32:47] To start with IVIG, since we're on that topic, and it's again, an infusion of immune globulins. And it can be given upfront as sort of a double dose to calm inflammation. And it can also be used as what we call a maintenance therapy or a preventative therapy, where we give a single infusion every three to five weeks, approximately. Usually we use four weeks, but it does vary. And that can then keep the inflammation down and calm things. There is some data and some new data this year, that's suggesting that IVG maintenance may work better in kids than adults, but the numbers are super small.

[00:33:23] We're talking about like, five patients in the cohort showing us that. And there are other data there, but there does seem to be a trend in the treatment studies suggesting that IVIG may be particularly useful in MOG associated demyelination. So we are definitely using that. Other treatments that get used are very similar to those used in aquaporin-4 NMO.

[00:33:44] So things like, mycophenolate mofetil, azathioprine, and rituximab are treatments that also have clear effect and can reduce how often the relapses are happening. And we have used, all three of those medications get used in children as well. I think there may be some emerging therapies that have been used in adults that I haven't necessarily seen used in kids, like Tocilizumab.

[00:34:10] And so Dr. Levy may have more experience with those.

Dr. Michael Levy: [00:34:15] I agree with you that IVIG is a wonderful treatment on the prevention side as well for MOG. I would say that maybe the treatment failures that I've seen with IVG have all been that the lower dose. And the ones that are successful are on the maximum dose, which is two grams of IVIG per kilogram of ideal body weight. On that higher dose, I have rarely, if ever, seen a relapse, and it's the higher dose we use for the acute treatment as well. IVIG is a pain. It's several infusions every month. And the infusion schedule is difficult. It causes headaches. It's not easy to use.

[00:34:57] And so for the majority of patients, I would say most are still not on IVIG even though it's wonderfully effective. I would say most are on more convenient treatments like mycophenolate -that's CellCept - and rituximab. And rituximab has sort of a mixed picture. There are some people who seem to respond very well to it and then many who do not. And I'm not quite sure what the difference is between those two populations. If you respond well to rituximab, that's great.

[00:35:26] It's easy to use in long-term, very safe. But I don't know who would respond to it. When they step into my clinic, I don't know if a patient is going to be rituximab responsive or not.

Krissy Dilger: [00:35:38] Okay. Great. Thank you. We've been hearing a lot about new potential treatments for aquaporin-4 positive NMOSD patients. So can you tell us about potential treatments that may be available in the future for MOG patients, whether they be pharmaceutical or tolerization? And is STEM cell treatment something to have hope for? Dr. Levy, do you want to start off?

Dr. Michael Levy: [00:36:03] Yeah, we are working with two companies on future trials in MOG that are pharmaceutical. So one is - and I can't announce them yet, and the companies don't want me to name them because they haven't formalized anything yet - but one is working on the mechanism of IVIG, that's based on the mechanism, and would be a subcutaneous infusion, which would be a lot, lot easier than IVIG. And another company has the pill, that seems to be very effective in MS, and they're interested in developing it for MOG. There are so many drugs already available for MS, and MOG has nothing. They see this as a potential unmet need, and they would like to develop that. So MOG is now, under the attention, they've got the attention of, of industry, and that's very good.

[00:36:59] STEM cell treatment is something to hope for. I would not say that MOG patients are the most needy of them because MOG, like I said, MOG patients do heal well. There are some who have, you know, residual disability and maybe STEM cells are a potential treatment for them. The more severe demyelinating diseases like NMO and some patients with transverse myelitis who have no function below the lesion, I think those are the ones where STEM cells will be developed first. And then over time as they demonstrate their safety, I think they'll be used for other diseases like MOG.

Peter Fontanez: [00:37:40] This question comes from the community, I know you guys have already touched on treatments, but this comes directly from the community. I am on 20 milligrams of steroids, started with 60 milligrams, January 2020. I tried a combination of CellCept and Rituxan, but every time I go below 20 milligrams of steroids, I get optic neuritis.

[00:37:57] I still experience some pain, but it doesn't increase day by day. I feel better at 22.5 milligrams of steroids. I recently started Imuran. Are there any other treatments that the patient could try, and also is this indicative of steroid dependency that tends to be more prominent in MOG patients? Dr. Benson?

Dr. Leslie Benson: [00:38:15] It certainly sounds like steroid dependency, and some patients really have a hard time getting off steroids. And I don't know that it's because they get addicted necessarily, but just that they have a high amount of inflammation, and end up on long, long courses of steroids. I think she has already identified one option, which is Imuran, or azathioprine, which would be a rational, additional thing to try to get off steroids. And then, as we've been talking about, we're fans of IVIG. And so if it's accessible to patients, given the need for infusions and the cost, I think it's something to certainly, that we're certainly optimistic about. And in, at least in pediatrics in general, try to do everything I can to get patients off of, off their steroids long-term and find something that maintains them off of steroids.

Krissy Dilger: [00:39:05] Thank you. The next question also came from the community. I know we already talked a little bit about rituximab, but this person specifically wants to know if it works on MOG patients and how effective it is in preventing relapses. And then also, how long can a person safely stay on rituximab? Will it decrease in effectiveness over time or cause any adverse side effects? Dr. Levy.

Dr. Michael Levy: [00:39:34] We put together a study with something like 20 other centers worldwide in adults who are using rituximab. And we found that the efficacy somewhere between 35 and 40% in terms of being able to prevent every relapse and not failing even once. So by that high standard, Rituximab maybe is not as effective as IVIG. But for the few patients, for the, 35, 40% where it's perfect, it's really wonderful. And we've had patients come off of rituximab and relapse. So we recognize that your rituximab certainly seems to be helpful in some patients, but we don't know in advance who those will be. I would say that for those of you who are on it and seem to be responding and have not yet relapsed, I would stay on it. And how long you can stay on it? People have been on it for 15 or even 20 years now. And there are long-term issues that need to be monitored over time. So, in general, again, Rituxan tends to be safe. We even use it through pregnancy. We use it in kids. We use it in older folks.

[00:40:47] And so, if it works for you, great. If it doesn't, there are the other options we talked about.

Peter Fontanez: [00:40:53] Dr. Benson, do you have anything to add to that from that the pediatric side?

Dr. Leslie Benson: [00:40:58] I think it gets at the next question as well, but it would say that we, we do see some patients responding to rituximab, sometimes in part or fully with no relapses or less frequent relapses. How long you can stand rituximab as a child, I think is an open question, and really depends on how well your body is tolerating it. As Dr. Levy alluded to, there can be long-term effects on the immune system. So those two things tend to be low levels of a white blood cell called your neutrophils or low levels of IgG, that antibody. And so we watch for those effects and try to transition to a different therapy if we see signs of those effects influencing a patient.

[00:41:43] And so I think we don't really know how long you can stay on as a kid, but we certainly use it for years in some conditions when we need to. And we also think about when somebody is well controlled on rituximab or something, how well are they tolerating it? And is there an easier therapy or a safer long-term therapy to change to. And sometimes we switch patients from rituximab to something like CellCept or azathioprine once they're stable.

Krissy Dilger: [00:42:13] Okay, thank you. The next question also comes from the community. This person has been on eculizumab a little over two years and is doing very well. They had a meningococcal shot before starting eculizumab. And their question is if they will need a booster? Dr. Levy.

Dr. Michael Levy: [00:42:33] Okay. So first of all, eculizumab is not indicated for MOG. It's only indicated for

aquaporin-4 where it was studied. So if you have the MOG antibody and you've been on eculizumab, please contact me because I want to know what your story is and if this is information that needs to be disseminated out into the, into the scientific community. Please do let me know if you're MOG antibody positive and doing well on eculizumab. If you were aquaporin-4 positive, the approach for vaccination is you're supposed to get it at the start of treatment.

[00:43:10] And then, there are several different vaccine types. There's several different ones. Two of them require boosters, two of them don't. The boosters are either six months or five years later, just depending on which type you use, but that's all in the label. She can look up, or again, if you, if you are MOG positive, please do email me and I'm happy to answer your booster question if you tell me your story.

Peter Fontanez: [00:43:33] Dr. Benson, this question comes from the community. My daughter is 16. Her first attack of optic neuritis was at age five. At the time, doctors were unaware of MOG, and there was no test available. She had a second attack at age 14 of ON and TM, and she had tested positive for MOG.

[00:43:48] She had a bad reaction to both azathioprine and CellCept. Her last two MOG tests were negative. She suffers from bouts of extreme fatigue. Is this usual? And is there anything that would help?

Dr. Leslie Benson: [00:43:59] I think this question brings up several points. One is, this is an excellent example of how MOG can go nine years and quiescent between attacks. And it brings up a point that I really want to emphasize. At least within the pediatric community, we do not recommend treating everybody who has MOG antibodies with long-term treatment. We treat patients with relapsing disease with long-term treatment, and even some with relapsing disease with infrequent attacks, we don't necessarily put on preventative treatment.

[00:44:29] And I think that may be something that's very different from the population Dr. Levy sees, and I want to make that clear. My colleagues would not be happy with me if I made an impression that we treat everyone with long-term therapy because we do not. So I think that's question number one is whether this patient even needs a preventative therapy. Certainly, there are other options for treatment.

[00:44:49] If she does need a long-term preventative treatment like the IVIG that we've been talking about, or rituximab, which might work better for her. The other piece, which is she's asking about the bouts of extreme fatigue, which we talked about earlier. And it sounds like this may very well be a part of MOG that we don't yet have data or literature to tell us if these bouts of fatigue respond to immunotherapy or other interventions.

Krissy Dilger: [00:45:17] Okay, great. Thank you. And then, Dr. Levy, have there been any studies on dietary changes that may benefit someone with MOGAD? And, we also got a question about if gluten can trigger an attack?

Dr. Michael Levy: [00:45:31] I don't know the answer to that, but I would like to know. Dietary studies are very difficult because you can imagine the ingredients that go into all different kinds of recipes, even at home and certainly when you eat out. They're so complicated, there's so many, and you don't know necessarily what you're eating or how much of any particular substance you're eating. Add to that the complexity of the gut microbiome, where you have over a trillion bugs, and they're all living in some sort of symbiosis with your immune system.

[00:46:07] So the diet combined with your microbiome combined with your own immune predisposition is so complicated, it's mind boggling. I think only computers will be able to figure this out for us, and we don't know how to program them yet to do that. So, I don't have any studies to rely on for dietary changes.

[00:46:26] I would always advocate for just a moderate, balanced diet, low fat, you know, lean meat, that type of thing, and reduce your sugar intake. Dr. Benson, do you recommend anything for your kids?

Dr. Leslie Benson: [00:46:39] I don't. I think we have the same challenges. I have not seen any associations between diet, and certainly not gluten, with the disease. And I would just add that even in pediatric MS, which we've known about for longer and been diagnosing longer, it took years and national collaboration to come up with any data on the influence of diet on that disease. So I think it's, like you've mentioned, a very complicated question to answer, with no answers yet.

Peter Fontanez: [00:47:07] Thank you for that. One last question that we have from our podcast, before we dive into the questions that are being asked online. A recent study suggested that, though very rare, dual positivity for MOG and aquaporin-4 is possible. Has this been confirmed, and what other implications may this have for presentation, symptoms, and diagnosis? Is this specific to one demographic such as adults or pediatrics? Dr. Levy.

Dr. Michael Levy: [00:47:32] I hear about these things from my colleagues at the Mayo Clinic. Again, they're the largest testing center for the MOG antibody. And of course they also test for aquaporin-4.

[00:47:42] And the last I heard is that there were 10 cases of overlap where the MOG antibody was detected, only at a low level, 1 to 40 or less. And the aquaporin-4 antibody was very high level, and the disease, for all intents and purposes, looked like aquaporin-4 disease. And so we're calling those aquaporin-4 NMO, and we don't know why the MOG antibody is there, but it does not seem to be playing a role.

[00:48:11] So we don't take it too seriously if the MOG antibody level is low and the aquaporin-4 level is high, and we've never seen the reverse yet.

Krissy Dilger: [00:48:18] Okay. Thank you. We've gotten several questions coming in. And they all kind of just relate to long-term preventative treatment. And I know Dr. Benson touched on this a few questions ago, but they just want to know how can you tell whether it's time to end your preventative treatment if you haven't had a relapse in a long time? Dr. Levy, do you want to touch on this?

Dr. Michael Levy: [00:48:47] It's really a tough call. I have some patients who've had, you know, two or three attacks, but they're in a cluster over a year or two, and then they go silent with treatment. And they're curious to know how long do they have to go? Two, three, four, five years.

[00:49:03] How many years until we feel comfortable taking them off of the preventive treatment? And there's no way there's no right answer. There's no wrong answer. And I would say that if your MOG antibody converts to negative and you're in remission and you haven't relapsed in a long time, I would feel comfortable taking you off of treatment as long as you have my cell phone number and my email, and that if anything comes up, we can bring you back in and, and start treatment right away.

[00:49:32] And if you don't want to stop treatment and you're comfortable using whatever you're using on a regular basis, I think that's reasonable too. And until we have the right answers, I would say that it's really an individual decision. You know, it might be based on whether you can afford the drug. It might be based on whether you want to have kids and you don't want to expose the fetus to the drug.

[00:49:54] There are many, many decisions that go into this. But again, there's no wrong answer here.

Dr. Leslie Benson: [00:49:59] I think from the PEDs side, I would just comment that, echo that it is an individualized decision. We may think about it more often in the pediatric side, given the potentially lower rate of relapsing disease. I would say that all of the things you mentioned go into the consideration, usually in a patient who has relapsing MOG-associated disease.

[00:50:23] We wouldn't think about taking them off before at least two years of being kind of in remission. And then things like, how well are they tolerating their current therapy? What's going on in their lives? Did they respond well to steroids when they did have their attacks? Do they have residual disability and are high risk if they have another attack? All of those things come into consideration when we are having those discussions with individual patients.

Krissy Dilger: [00:50:51] We only have a few minutes left. We have gotten several questions coming in, asking if there is any indication that MOG positive individuals have had an increased risk of COVID complications. Dr. Levy, I know you worked in a COVID-19 ICU, so I'll let you respond first.

Dr. Michael Levy: [00:51:12] I did work in a COVID clinic. It was in the outpatient setting, not in the ICU, but even in that clinic, I didn't see many cases of MS or NMO or TM or MOG. These diseases did not seem to predispose to either getting the infection or to having a bad outcome from the infection. There are studies published in China and Italy, and it doesn't seem to be a significant risk factor.

Krissy Dilger: [00:51:44] I was just going to see if Dr. Benson had the same experience?

Dr. Leslie Benson: [00:51:48] Yeah, I don't have any data or experience to suggest that it increases the chance of disease. In fact, most of our patients are younger that have MOG and younger, just like the general population, younger kids seem to be doing better and be more resilient with COVID.

[00:52:03] We just tell our patients that there's always the chance if they were to acquire the infection of both recrudescence of old symptoms, meaning return of old symptoms, which does not mean a new attack. And then also any infection may trigger another attack. And so, I would expect it would be the same with COVID, although I have not seen that happen so far, knock wood.

Peter Fontanez: [00:52:24] Is there anything else that you guys would like to add about MOG, Dr. Benson or Dr. Levy? Any closing points that you guys would like to make?

Dr. Michael Levy: [00:52:32] I would just add that there are other companies - I didn't mention this - there are companies interested in treatment for MOG antibody disease, but we're also working with companies that are interested in tolerization to get the immune system to relearn that MOG is not foreign. It doesn't need to be attacked itself, and it should be preserved. And there are companies interested in that approach as well. So I think that there's a lot of potential here.

Krissy Dilger: [00:53:00] Great. And Dr. Benson, anything, last thoughts?

Dr. Leslie Benson: [00:53:03] I think we've covered things really well. I think just as a kind of overarching thought is that I think, you know, there's a lot of, a lot, a lot of new data coming out about this disorder all of the time. And so it's an exciting area, and I think we will be continuing to learn more and have more to share with the patient community as time goes on. Overall in kids, I think it's a very, most of the time, a very treatable condition. And I would like to end on a positive note that, you know, most of our patients, and at least our children, really do well long-term, even those with a relapsing disease.

Krissy Dilger: [00:53:42] Okay. Great. Thank you. And I think that's a great message. And I just want to thank both of you for joining us and giving us your time.

[00:53:49] I think this went really well and it's also opened up discussion for future podcasts. We've gotten a lot of questions, so I think a whole other hour could have been filled. And also, thank you to the MOG Project for your collaboration on this podcast and Peter for co-moderating and submitting some questions for us. And, hopefully we can do it again.

Peter Fontanez: [00:54:10] Thank you for having us.

Dr. Michael Levy: [00:54:11] Thank you both. Thanks, Leslie.

Dr. Leslie Benson: [00:54:13] Thank you.