What is MOG Antibody Disease (MOGAD)?

You can listen to the audio of this talk at: https://youtu.be/OBw4hjt1SY8

Dr. Sravanthi Vegunta: [00:00:00] Thanks Dr. Clardy. So I'm going to be presenting on MOG associated antibody disease. So I'm an ophthalmologist by training doing my neuro-ophthalmology fellowship this year. So MOG associated antibody disease or MOGAD.

[00:00:15] I wanted to start off with an interesting case presentation about a patient that we saw at our clinic a few years ago. So the patient presented to our neuro-ophthalmology clinic, and this is a picture of our Moran Eye Center, Eye Clinic. It's a pretty good view. Our patient came in, she was a 25-year-old woman, this is just a stock photo of a model, this isn't actually her. She came in with tunnel vision in her right eye. She had some pain with eye movements when the tunnel vision initially started. And then she said that when this initial episode happened 11 days afterwards, she lost all vision in the right eye. When her ophthalmologist saw her, who was an ophthalmologist outside of our clinic. Here she said that there was right optic nerve swelling.

[00:01:04] So this is a picture of what her optic nerve looked like. You can see the vessels coming out of the nerve. And the nerve itself you can see that it looks a little bit puffy, or sort of three-dimensional. So over the next two years she said that she had frequent pain and vision loss episodes that went through back and forth, back and forth, back and forth. She would have right eye vision, eye pain and vision loss. She would go to the eye doctor, they would tell her she had optic nerve swelling, she'd get IV steroids, and the steroids would make her pain and her vision loss better, but then she would have another episode, and another episode and so on. Eventually she started having episodes in the left eye as well. They were vision loss episodes again with pain, and they would again get better with steroids.

[00:01:46] So when we asked her “what does the pain feel like?” she said it felt like a deep, throbbing pain around the eye, like a dull ache. But also with some stabbing pain around the eye and in the eye itself. So pretty significant. When she came into our clinic, we had an exam. We calculated her BMI at 42.5, her visual acuity was 20/25 in both eyes, and so you may know that 20/20 is normal vision. This is just one line below that, so pretty good vision at least in the center of her vision. She had decreased color vision. And I thought I'd show you some pictures of eyes because eyes are cool and interesting to look at.

[00:02:22] So in her pictures of the backs of her eyes here, this is her right eye, and this is her left eye. And you can see here, even if you've never seen these pictures before, that this part of the nerve looks a little bit paler or brighter on the right side compared to the rest of it. And so we thought she had some pale optic nerves, especially on the right. The left also had a little bit of paleness, but it looked more swollen to us. So again you can tell that it's a little bit maybe coming out towards you. A little bit elevated, more pink. And when we did measurements of the thickness of her optic nerve, we found that it was in the red on the right eye, as in it's severely thin. And the left

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eye was a bit thin, but it still had some areas in the green, meaning there were still some areas with normal thickness.

[00:03:14] We did a visual field test to checking her peripheral vision in each eye individually. The right eye, the black spots actually show where there's parts of the peripheral vision missing. So this is her, almost 30 degrees of her vision centrally, and there are spots here and there that are missing in the right eye. The left eye also had a large area that was missing in the side of her vision actually. When we looked at her MRI scans that she brought in, we saw that the left eye optic nerve, and I'll point out the optic nerves right here in the middle, and right here in the middle on the left eye, looked a little bit more swollen than the right eye. So it looked, as you can see here outlined in red, that it's a bit brighter inside this circle compared to right there. So we thought that was inflammation around the optic nerve. In another view of the same scan, this is the front of the face, this is the nose, and the right eye, left eye. These are the nerves again right in the middle here, and here. You can tell there's a difference, right? Even if you've never seen these before, that the right eye, the outline of it, doesn't look as bright as the left eye. And I've outlined where it looks more bright on the left eye. And again there was inflammation around the optic nerve.

[00:04:28] So at this point if you've seen any doctor shows or watched House M.D., this is the point where we think about, okay what was causing her vision loss and her pain and why was it recurring again and again? So we thought it was this inflammation, so of course you know the title of my talk, but we'll still go through this just for fun. Was this multiple sclerosis, was this neuromyelitis optica, sarcoidosis, granulomatosis with polyangiitis, is it lupus, or some other unknown cause of inflammation? Was this even an infection? Because infections can also present like this sometimes, like TB, tuberculosis, syphilis, or Lyme disease, or even cancer. So we did a full workup for all these things, we did a bunch of blood tests and also her spinal tap and looked at her spinal fluid. And we didn't find anything that came back positive for any of those things on the list.

[00:05:15] So over the next four years as these relapsing episodes kept happening, she kept having flare-ups and her vision would get worse and then it would get better again while she was on steroids. We at least found that when she was coming off the steroids, if she quit taking the steroids too quickly, then the vision loss episode and pain would happen again. So we maintained her on just two milligrams of steroids, that's why the title of the talk is 'The Steroid Cookie Monster'. So I diagnosed her with chronic relapsing inflammatory optic neuritis, which is just a description of what's happening. It's also called CRION, just episodic vision loss and inflammation of the optic nerves.

[00:05:54] So while we followed her, you know, we were worried that we didn't know exactly what was going on, but you know, we didn't have any other explanation for it at this point. So, while we followed her, this was the initial peripheral field exam of the right eye and left eye I showed you earlier. Four years later, it wasn't too much worse. The right eye looks a little bit more dense in the visual field deficit here, the left eye even looked better. So thankfully she wasn't losing significant amounts of vision even though she kept having episodes. Thankfully, at some point, the MOG antibody test became available, readily available. And she got testing for it and she came back positive. So she was diagnosed with MOGAD, or MOG antibody disease.

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[00:06:36] So what is, what is MOG? MOG, if you break down the term: myelin, which is the first letter in MOG. It's actually just the insulation around our nerves. So this is the head of the nerve and this is the tail of the nerve. In order for signals to travel down the nerve, they can travel more quickly and efficiently if they're coated with something. Just like copper wires in like the electrical systems in our homes. If they're coated with a little bit of plastic, they last a little bit longer, the signals travel a little bit faster. The cells that make up this myelin coating are called oligodendrocytes, there's a picture of one of the cells here. And so there are multiple different little tendrils that these oligodendrocytes send out, to coat the nerves themselves. If we look more deeply at the myelin and say, hey what's this myelin actually made of? It's made of glycoproteins in addition to other types of proteins. So that's just a type of protein with a little sugar on it. In antibody disease MOG, or MOGAD, there are antibodies formed against these proteins within the myelin itself. This is a cross-section of the myelin.

[00:07:46] In what parts of the body do we see MOG? We see it in the central nervous system, as most of the conditions we were talking about today, so in the brain, spinal cord, in the optic nerves, just like our patient had. And why did it take so long to find this MOG antibody? I think it's kind of an interesting story. The MOG associated disease can look like multiple sclerosis or ADEM, which you've heard about or even NMO which we'll hear more about in the next topic with Dr. Galli.

[00:08:12] So initially in the 1990s when MOG was, you know, being looked into a little bit more, they thought it would be a marker for multiple scoliosis, but not everyone with multiple scoliosis has this antibody, so they kind of dropped it. And then patients with ADEM, some of them were actually found to have MOG antibodies, but again, not everyone had it. And the same thing with neuromyelitis optica, is it was thought to be a marker for it because people who didn't have a positive antibody for neuromyelitis optica but seemed to have it, sometimes had a positive MOG antibody instead.

[00:08:42] Finally we came around to understanding this disease a little bit more, understanding that it can present like any of these conditions, and we'll talk more about that.

[00:08:53] So how common is MOG? So of course it's quite rare. You can see it in this chart here. Among these other rare diseases like transverse myelitis, neuromyelitis optica and multiple sclerosis, which is not as rare, MOG is the most rare. So 0.16 people per 100,000 adults have MOG. Transverse myelitis, neuromyelitis optica, and multiple sclerosis are a lot more common.

[00:09:20] And when you look at, among these diseases like multiple scoliosis, NMO and MOG, when patients first present, how many of them actually present with optic neuritis or inflammation of the optic nerves, with eye pain and vision loss? 20% of people with multiple scoliosis present with this vision loss and eye pain and color vision loss and such. 64% of NMO patients present with it, and MOG, I found a range of values, so 44%-64%, so a lot of patients present with this specific pattern of symptoms, like our patient did.

[00:09:58] So what other kind of symptoms can patients also have? So in a study that was published just last year out of the UK, 252 patients were looked at who ended up having MOG antibody positive. And they found that among those patients, 31% had optic neuritis in one eye, 24% had it in

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both eyes, 18% actually had ADEM, as you learned is acute disseminated encephalomyelitis, it can present with seizures, confusion, and swellings. And then, 9% presented with both vision loss and transverse myelitis episodes. And some people presented with longitudinal extensive transverse myelitis, which means multiple different levels of the spinal cord were involved. And, a small, the smallest percentage presented with just transverse myelitis, that was the, the short version, or just one spinal cord level or two spinal cord levels involved.

[00:10:52] So how bad can the vision loss be from MOG antibody disease? So patients can present with severe vision loss, so like our patient, she actually lost all vision in her right eye at some point. On average, patients can lose vision to the level of count fingers, meaning that they can't read the eye chart, it's way too blurry, but when you hold fingers up to their face, they can count the number of fingers that are there. But they oftentimes have really good recovery. So like our patient, she was just one line away from perfect when we measured her again after her recovery. A lot of these patients, the majority of them have recurrent episodes of optic neuritis. And then, if they're going to present with other neurological symptoms like ADEM and transverse myelitis related symptoms, that usually happens within two months after their vision loss episode.

[00:11:42] I wanted to show you some more brain scans of what their brain can look like with MOG that affects the brain, like in ADEM for example. As you saw earlier in Dr. Paz Soldán's talk, is a lesion of the brain, this is the front of the head, this is the back of the head, and you can just tell it looks a bit brighter here. And then here on, as Dr. Clardy showed in transverse myelitis, you can have a bright area in the spinal cord. So again the top part is the head, this is the front of the neck, back of the neck, these are the vertebrae, and the spinal cord should just look all like this diffused gray up here, but the circled area shows you that there's some lightening or whiter area here. That's inflammation.

[00:12:28] So I wanted to also talk quickly about why, or how MOG is different from NMO or neuromyelitis optica. Because that can also present with optic neuritis. And Dr. Galli will talk more about neuromyelitis optica, but I just, in terms of at least presentation and vision issues, I wanted to talk about that.

[00:12:45] So patients usually present around the same age, but usually a little bit younger in MOG. More women are affected in NMO than men. Sorry in NMO than men are. And then in MOG associated diseases, it's more even, but still more women than men. The vision loss is more commonly bilateral, or in both eyes in MOG, versus NMO is usually more likely to be unilateral, one eye. The severity of vision loss can be pretty bad in both conditions. So they can lose vision completely, where they can't even see light, or they can count fingers, like the picture that you saw earlier. But in MOG, thankfully their vision recovers very well. In NMO, not so much. The spinal cord can be involved in both conditions but more commonly in NMO.

[00:13:33] Briefly about the treatment, just like we saw in many of the other conditions, we start with IV steroids, plasma exchange, if they keep having recurrent episodes, we try to do a prolonged steroid taper instead of cutting off the steroids quickly. We add on other treatments like immunosuppressants. You make have heard of azathioprine or cellcept, mycophenolate,

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methotrexate, IV immunoglobulin is something we also try. And if those don't work, then we can also try like long-term steroids, again with rituximab, which is an inhibitor of a certain immune cell.

[00:14:06] So, the last thing I'm going to talk about right here is, last slide, is in the health outcomes of these patients, 50-80% of patients have some sort of disability after a condition like this. But most commonly, it's not because of vision related issues, it's most commonly because of transverse myelitis related issues such as weakness of their arms or legs.

[00:14:33] So I'll take questions at the end in the question and answer session, and I'd like to present Dr. Jonathan Galli next. He's the Assistant Professor in the Division of Autoimmune Neurology at the University of Utah, and he's going to present on neuromyelitis optica spectrum disorder and optic neuritis.

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