What is Neuromyelitis Optica Spectrum Disorder (NMOSD)?

You can listen to the audio of this talk at: https://youtu.be/WtDMB_7UOaU

Dr. Jonathan Galli: [00:00:00] It's good to see you all back again. And so thank you to our presenters so far. It's been great. I hope our patients and their families have felt the same. Today I'm going to talk about neuromyelitis optica spectrum disorder, or NMOSD. I have no personal financial disclosures. But we'll be talking about off-label use of some of the medications towards the end of this presentation. So the objectives of this talk today are really to talk to you guys and inform you a little bit more about what is NMO. And so we'll briefly talk about the epidemiology of the disease, the pathophysiology, how patients present as well as touch on treatment. What is it neuromyelitis optica? So this is a disease that's classically associated with antibodies against aquaporin-4 receptors in the central nervous system. And we'll delve into that a little bit more and how that affects the nervous system.

[00:01:05] There are some patients who do not have these antibodies and are called serum negative. And falling into the spectrum is also the MOG antibody associated disease, although that's starting to kind of become its own thing. And we're not going to touch on today because we are just had a great talk on it. NMO is more common in females, about an eight to nine to one ratio, compared to males.

[00:01:29] The average age of onset is about 40 years old. Now that being said, the actual range of ages of onset is much broader and can be all the way down to young pediatric patients and upwards of patients that are, that are much older and into their elderly years. NMO is also a rare disease. It's got a much lower prevalence, especially compared to multiple sclerosis, estimated at about four in 100,000, at least in the United States.

[00:02:00] And I think of note, there are higher rates of NMO in Black patients. It's also very commonly associated with other autoimmune diseases, such as lupus or Sjogren's. So what is NMO? In some of the patients that we have, who were diagnosed with NMO a while back, you may hear the term Devic's Disease, or you may have read about this, and this was, it's kind of an old verbiage, back when this was thought to be a variant of multiple sclerosis. Now, the more we found out about this and the discovery of the aquaporin-4 antibodies has really taught us that it's completely different than multiple sclerosis, both in the path of physiology, as well as the treatment. It's an inflammatory disorder that affects the central nervous system and primarily affects the optic nerves and the spinal cord.

[00:03:00] And it's caused by these antibodies, which are immune proteins that bind to aquaporin-4 receptors. Aquaporin-4 is a water channel that's actually located not on the nerves themselves, but on supportive cells called astrocytes. They're there to kind of keep some of the nervous system healthy and well supported.

[00:03:26] This is a very busy slide that I borrowed from Dr. Weinshenker's paper, and we're not going to get into this into too much depth, but I think it does a really nice job of kind of laying out how this disease works. So the immune system, for whatever reason, reacts with the aquaporin-4 receptors, not in the nervous system, but actually in the rest of your body and triggers T cells, T helper cells, kind of to transform and then activate the B cells of the immune system.

[00:03:58] And the B cells are really important cells, because these can actually create antibodies. In the processes of NMO when you're developing it, these B cells then turn into plasma cells, which start to produce these immune proteins against aquaporin-4. These immune proteins, then go from the... your kind of blood in your, just in your body, enter the nervous system and then bind onto the foot processes of those astrocytes.

[00:04:32] That binding of the antibody then bind to the other immune molecules called complement. And this has a downstream effect of damaging the astrocytes and the loss of that supportive astrocyte leads to direct damage to the myelin, which is again, that insulation around the nerve fiber, but also the cells that help make the myelin.

[00:05:01] And so what does this look like clinically? And it really depends on the location of the attack. Certainly the most, you know, obvious and I think severe onset is usually the transverse myelitis. And this is when a spinal cord becomes involved, and the spinal cord lesions can cause paraplegia, quadriplegia, bowel, or urinary incontinence, and certainly a significant amount of pain and spasms in the long-term.

[00:05:27] If it affects the optic nerves, that will typically present as a painful vision loss, both visual acuity and color vision, and interestingly it can also, less commonly, affect the brainstem and then a particular area called area postrema. And patients can come in with severe and tractable vomiting as well.

[00:05:51] If left untreated, this can relapse in the future, but it doesn't really have the same progressive course that multiple sclerosis does. And so if we can prevent any further relapses, oftentimes our patients won't have any further progression, at least when we look at it and compare to multiple sclerosis.

[00:06:13] So evaluation. When we test your blood, the big thing we're looking for is that aquaporin-4 antibody. It's important that we test this correctly based on a cell-based assay, which for us patients isn't necessarily something to remember, but it's certainly something that we teach our trainees.

[00:06:34] And as Dr. Clardy had alluded to with transverse myelitis, especially it's important to rule out other diseases, MOG, you know, multiple sclerosis is important to rule out as well, as other infections or inflammatory diseases. Some of you who have been evaluated for this might've had a lumbar puncture.

[00:06:55] And while this isn't necessarily a single diagnostic test, it can help us evaluate between NMO and MS. With your spinal fluid results being a little bit differently and interestingly, we don't

really look for the aquaporin-4 in your CSF because it doesn't really give us much more diagnostic value.

[00:07:18] From an imaging standpoint, MRI is a very important part of your workup. Classically, spinal cord imaging will demonstrate what we call longitudinally extensive lesions. And that's just simply more than three spinal cord segments in length. So if you look to your right, you'll see the spinal cord imaging. And I'm not sure if you can see my mouse, but this is of the cervical spine. And the spinal cord is this dark structure here. In the middle of the bones, surrounded by the white spinal fluid. And there's a big, bright lesion that goes down probably at least four or five spinal cord segments along there.

[00:07:57] That's pretty classic for what we see in neuromyelitis optica. If we do specialized optic nerve MRIs, we can also see enhancement of the optic nerves and in adults, the brain is not frequently involved. And so if we see a lot of brain lesions, we oftentimes have to check ourselves and make sure we're getting the diagnosis correct. The exception to that is in pediatric patients, which those patients present with more demyelinating lesions in the brain. This, table is borrowed from Dr. Weinshenker's NMO paper out of Neurology Journal. And this is not something that any of you should feel the need to memorize, but this just kind of shows the diagnostic criteria that we, as your providers, will follow when making the diagnosis.

[00:08:50] And importantly, it really helps us decide if somebody has seronegative neuromyelitis optica. So in the first part of the table, you'll see diagnostic criteria for NMO and that's with aquaporin-4 antibodies. So essentially if you've had one clinical characteristic, which is either presenting with transverse myelitis, optic neuritis, or area postrema syndrome among some other symptoms, with those being the three classic ways. If you have that, plus the cell-based assay for aquaporin-4 that's positive, we can be pretty confident in the diagnosis. If it's negative, then we have to say that you need at least... that's when things get a little bit more complicated, and that's when we like to see at least two different attacks or two different areas involved.

[00:09:39] And that's why some of you who have had this diagnosis, it's a little bit trickier and can take more time to get to the diagnosis. And most importantly, if we're going to give somebody the diagnosis of seronegative NMO, we certainly have to exclude other diagnoses. And that's when the workup becomes, you know, pretty elaborate at that point.

[00:10:00] So what do we do for patients with NMO? I think about it in kind of two different ways. The first is what do we do right at the onset of disease? And the second is how do we prevent further attacks? And so for acute therapies, IV steroids in these diseases are the main stay in treatment. More recently, we found the plasmapheresis, also known as PLEX or PEX sometimes, done early on in the disease presentation has a lot of benefit. And so at our institution, we have kind of adopted the idea that as soon as patients come in and we've found a diagnosis for NMO, we're treating them aggressively upfront, both with plasmapheresis and steroids together. IVIG, especially in the acute period, doesn't seem to have as much benefit. Although it's certainly something in patients with severe disability that we can think about with the caveat that we always will give IVIG after PLEX because PLEX will pull off all the IVIG if we give that first.

[00:11:09] Long-term immunotherapy. So patients will generally stay on immune therapy for life, as you can relapse really at any point in the disease. Like we talked about, if we can avoid relapse, we can usually avoid a significant progression of disability. And when we make the transition from acute treatment over to long-term therapy, oftentimes we'll need oral steroids to kind of bridge that, to prevent any relapse. Now, until recently, most of the immunotherapies we'll talk about were being used off label. They had decent data for efficacy, but we just didn't have any FDA approvements. A lot of that has changed within the past year, which we'll briefly talk about. So, many different medications have been studied. And some of the medications that you may be on or have heard about include azathioprine, mycophenolate and, methotrexate, which all have some degree of benefit. Although I will tell you, at our institution, our kind of go to at least... you know, up to now has been rituximab, which is a very targeted therapy that targets what are called CD20 positive B cells, and it wipes them out. And the idea behind that is it's wiping out an arm of the immune system that is contributing to the disease.

[00:12:33] A lot of studies have shown benefit with this. That being said it was never really FDA-approved for use in NMO. You'll see Tocilizumab which targets something different, interleukin, which is a inflammatory molecule, which has shown good efficacy and can be used in refractory cases.

[00:12:55] And I think it's really important to note here, you know, when we're teaching our trainees or when we're having discussions with patients, we really, really have to do a good job deciding between, is this multiple sclerosis or is this neuromyelitis optica? Because there are certain therapies that we use in multiple sclerosis that may actually worsen NMO.

[00:13:17] And so it's a very important thing for us to distinguish. And so if we gave this speech, this talk, you know, a year and a half, two years ago, we'd be done. However, uh, we've had a really big boom in the treatment of neuromyelitis optica over the past year or so. With new drugs coming out, including eculizumab, inebilizumab, and satralizumab, all which target a little bit different areas of the immune system between them. But they're all are FDA approved for aquaporin-4 positive patients. So this is a really big step in the right direction. We're going to learn a little bit more about this later this afternoon. So the factor behind as well. We'll kind of skip through this, but it's a really exciting time for both, us as providers, but also for our patients.

[00:14:15] With that said we'll wrap up my presentation. This, dabbing unicorn is a kind of shout out to all my CCK kids who have taught me to dab among doing other ridiculous dances over the past couple of years. And my buddy Ryland who probably would insist that I do a dab today on camera, but I'm probably going to let him down and not. And so with all of that said, we're going to head to the sessions area and do a question and answer a session about the last several talks.