Understanding Pediatric ADEM, AFM, MOGAD, NMOSD, ON, and TM

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[00:00:00] **Lydia Dubose:** Welcome to this session, Understanding Pediatric ADEM, AFM, MOGAD, NMOSD, ON and TM. We'll get started shortly. We encourage you to submit any questions that you have in the Q and A section. That's on the right-hand side next to the chat. Please note that there are closed-captions available in English and Spanish. You'll find that in the CC, or closed-captions, section also on the right-hand part of your screen. If you have any general questions, you can let us know in the chat. And again, feel free to use that Q and A section to submit any questions for our speaker. So, we'll give everybody just a moment to join. And okay, we can go ahead and get started.

[00:00:59] We're pleased to be joined today by Dr. Sarah Hopkins. Dr. Hopkins is section head of MS and neuroinflammatory disorders at Children's Hospital of Philadelphia and is also Assistant Professor of Clinical Neurology at Penn and the co-director of the Penn/CHOP MS and Neuroinflammatory Disorders Fellowship. Thank you for joining us, Dr. Hopkins.

[00:01:28] **Dr. Sarah Hopkins:** Thanks so much, Lydia. It's so great to be here. I always love being here, and I can't wait until we can do it in person again. I guess this is the second year for virtual presentations, so, all right. So, I've got the very small topic of understanding pediatric ADEM, AFM, MOGAD, NMO Spectrum Disorder, optic neuritis, and transverse myelitis. So, this is going to be a little bit of a whirlwind tour. So happy to talk about this. And please, I set my alarm, so we should end right at, between 11:50 and 11:55, so please feel free to ask any questions at all as well. Just a couple of disclosures so you know where my support comes from, I do receive salaried support from the CDC for activities related to AFM surveillance, and I am involved with two studies, one of AFM through the NIH and one of the International Pediatric Opsoclonus Myoclonus Registry, another rare disorder that we won't be talking about today.

[00:02:37] And just to let you know, I will be discussing the off-label use of medicines. Unfortunately for these disorders, there really aren't clinical trials in kids with the exception of NMO where there's a little bit of data, so most of these medicines are used off-label in these conditions for pediatric patients. So, basically, the first thing we're going to do is we're going to just briefly talk about how neurologists think about the problem and finding what the problem is. We're going to talk a little bit about imaging and the tests that you can expect if your child presents to the hospital with concerns for one of these disorders, and then we're going to talk

about the disorders themselves, imaging findings, pediatric-specific things about these disorders, and then we'll talk a little about treatment and things to know about for long-term. So, how do we find the problem, or as neurologists like to talk about, how do we localize the lesion? So, the very first thing we do is a history and physical exam. You will, you know, as anyone who's been in the hospital with a child with new presentation of neurologic symptoms knows, you will probably get asked about the history so many times you'll get tired of talking about it. But, you know, that's how we make sure we're not missing anything. And then in terms of localizing where in the central nervous system the problem is, we'd like to talk about the two nerves that are involved in any problem. We talk about the first nerve cell, so that's the nerve cell that goes from the brain to the spinal cord, and that's called the upper motor neuron. And then there's the second cell which starts in the spinal cord in a place called the anterior horn and goes out to the other, to the arms and legs and your muscles and other parts of the body.

[00:04:35] So, for upper motor neuron weakness, so when you have a problem with that first nerve, your muscles are weak, but they're usually tight. Your reflexes are increased, and also, when we run our thumb or something sharp along the bottom of the foot, your toes go up. And then we also talk about lower motor neuron weakness, so in these cases, the muscles are weak, but they tend to be floppy, and reflexes are decreased. Of course, the other thing that's important for us to think about is the pattern of findings, so if for instance, you have a right face, arm, and leg weakness, then the problem is probably in the brain on the left side. But if you have just arm weakness, either one side or both sides, then that may be in your cervical or upper thoracic spinal cord.

[00:05:26] And then leg weakness, again, depending on the other parts of the pattern, may be really at any level of the spinal cord depending on what else is involved. Sensory changes, of course, can also help us to localize the problem, and then certain areas are more or less likely to have bowel or bladder problems as well. So, once we know where we suspect the problem is, most patients will have an MRI just to orientate what normal MRIs look like, these are T2-weighted images which means that water is bright. So, the spinal fluid is bright in these images, and any area with swelling or edema is also going to be bright when we look at the images that have problems later. So, just for orientation purposes on this left image, this is what we call an axial image. It's like you are, your child is lying on the bed, and you are looking up through their head.

[00:06:24] So, the right side is over here. I'm hoping that you can see my cursor. The left side is here, and then front, back, and you see the bright spaces here in the middle are the normal fluid spaces or the ventricles. The second image is just a side image of the spinal cord. And then this third image, another axial image, is through the level of the optic nerve, so you can see the optic nerves going to both of the eyes here, and these are all normal images. And then also important as we talk about clinical presentations and pictures to know that when we talk about the spinal cord, we've got the grey matter, which is here in the middle, looks like a butterfly or an H sometimes depending on the picture, and that's where the first part of the lower motor neuron sits. And then you've got the white matter which is where you have the second part of the upper motor neurons.

[00:07:35] So, once we've done imaging and we know for sure where the problem is in the central nervous system and what the imaging looks like and whether or not that suggests any specific diagnoses, then we also do blood work. This looks for evidence of inflammation, and some specific neuroimmune conditions like MOG and NMO we can find evidence of this way as well. We also typically will check an ANA because lupus is something that can be associated with these disorders. And then we look for infections and vitamin deficiencies. Vitamin deficiencies are especially important when you have a spinal cord problem. And sometimes we also look for trouble with the way that your body uses energy.

[00:08:23] We will also often do a lumbar puncture that lets us look for evidence of infection and inflammation. We look for things like white blood cells, increased protein levels and something called oligoclonal bands.

When we see oligoclonal bands, those are antibodies that are produced primarily around the brain and the spinal cord rather than in the blood, so that tells us that there's a process going on that's producing antibodies within the central nervous system itself. And then ideally if we remember to think ahead, we collect these, and we put in an order that says, "Please save this specimen in a way that we can use it later," so that we're not having to go back to ask your child to repeat tests they've already done or to give us additional specimens that we'd already like to have. One second. All right.

[00:09:20] Then when we talk about these disorders themselves, one way that we like to think about them is whether this is a disorder that's likely to be a one-time thing or whether this might be something that's multiphasic. So, things that we think of that are usually one and done are idiopathic disorders, some people would say. Some would say it just means that the doctors are idiots and can't figure out what's going on. But so, disorders without a clear-cut cause that are typically one-time things, so those are things like ADEM, acute disseminated encephalomyelitis, and idiopathic transverse myelitis, or optic neuritis. Also included in this are some of the clinically isolated syndromes that might be suspicious for multiple sclerosis, but we're not going to go into those right now.

[00:10:17] Interestingly, MOG, so myelin oligodendrocyte glycoprotein associated disorders can be either monophasic or multiphasic. So, they may or may not reoccur, more often monophasic in kids, but again, that's something we'll talk about later. Then the multiphasic disorders are really, tend to be the MOG or aquaporin-4 associated disorders, although you can have recurrent optic neuritis or transverse myelitis in certain situations. It's pretty rare. So, I wanted to talk first about optic neuritis. So, optic neuritis means that there's inflammation of one or both of the optic nerves. These patients typically present as having pain with eye movement, or blurry vision. They also have a decreased ability to see colors and, interesting because the severity of the vision loss can really be anything from my vision is usually 20/20, and now it's 20/50, to really can't see anything, maybe just able to see the difference between light and dark.

[00:11:36] This MRI on the right side of the image is a really nice image of one of my patients with optic neuritis, and you can see right here in the middle, we're just right near an area called the optic chiasm where the brain is sending the projections that are going to form the optic nerve, and then they meet, and then they cross and go back out as the optic nerves, and you see both of the optic nerves here. And this patient had optic nerve involvement bilaterally, but you see especially in this, nerve, it's brighter, and it's thicker. So, this is what optic neuritis looks like on an MRI. The other thing is that if we give contrasts in these cases, then because of the inflammation, we expect that optic nerve to get bright with the contrast.

[00:12:36] So, optic neuritis, again, may be idiopathic, or it can be associated with multiple sclerosis, ADEM, NMO or MOG, but it can also be associated with infections including Lyme disease and bartonella and some viruses. Optic neuritis is typically treated with high-dose steroids. One important thing to know is that high-dose steroids help people with optic neuritis get better faster. We don't think that in most cases they actually help them get better than they were going to get anyway. Optic neuritis does typically get better but gets better over a very long period of time. Fortunately for many children, the prognosis is actually quite good. 60 to 97 percent of children have full recovery of high-contrast visual acuity, so that's what we're testing when we test with the routine Snellen chart that you do in eye clinic or screening for vision at your pediatrician. 13 to 36 percent of these children are eventually diagnosed with multiple sclerosis, but that's really exclusively kids that have white matter lesions that are suspicious for multiple sclerosis.

[00:13:58] If there are none of those white matter lesions, then the risk of going on to have MS is very low so 2 percent or less. Interestingly, even though the high-contrast visual acuity often returns to normal, there is often some subjective residual vision difficulty, and I think that may be related to what we call low-contrast visual acuity. So, when you've got black on white, it's fairly easy to see things. But if you've got different

shades of grey, then that might be more difficult to see on a white background. So, that may not recover as well. There will be less vision recovery in a patient with a diagnosis of neuromyelitis optica, and additional treatment may be needed. As we'll talk about down the road, sometimes patients with neuromyelitis optica don't really get better with steroids or just time and need plasma exchange.

[00:14:57] Thinking about transverse myelitis, so transverse myelitis is a inflammation of the spinal cord. And when we talk about how we prove that there's inflammation of the spinal cord, we do that with MRI and enhancement on the MRI or looking for white blood cells in the spinal fluid. So, transverse myelitis typically presents with weakness, changes to sensation and bowel or bladder dysfunction. It typically develops over hours to days, and that's one thing that helps us differentiate it from a spinal cord stroke which typically, typically presents very quickly. And then other things that affect the spinal cord like vitamin deficiency or a tumor tend to occur over a longer period of time even then transverse myelitis.

[00:15:50] Patients with transverse myelitis, because there's a lot of involvement of that white matter in the spinal cord, typically tend to have upper motor neuron signs. So, their legs are more spastic. Their reflexes are fast, and they tend to have more bowel and bladder dysfunction. In order to be given a diagnosis of transverse myelitis, there has to be no evidence of a compressive lesion, and that's one of the reasons that if you present with signs referable to the spinal cord to an emergency room, you will typically get imaging quite quickly because there is always this concern that, "What if there is spinal cord compression, and is an emergency surgical procedure needed?"

[00:16:34] So, the patient on the right-hand side here is a 6-month-old with a presentation of bilateral lower extremity weakness and basically just a refusal to walk. And there's this longitudinally extensive lesion in the spinal cord that you see, so the spinal cord should typically look darker, like you see here or down here, but you see this line of brightness running through the spinal cord, and that's an abnormality. And then on this axial view of the spinal cord, you see all of this brightness in the central part of the spinal cord with just a little rim here of white matter that looks a little bit more normal, and that's a typical appearance of transverse myelitis in a pediatric patient. Transverse myelitis may be idiopathic, or it may be associated with MS or ADEM or NMO or MOG. So, again, this is one of the reasons why it's often very hard for us to say the first or second hospital admission, this is it, and it's a one-time thing, or this is exactly what we were expecting, which can be frustrating.

[00:18:02] Transverse myelitis is typically treated with steroids, but if there's no response because of the chance that this could be neuromyelitis optica, we will often rapidly go to plasma exchange. And in plasma exchange, if you don't know what goes on there, basically we put in large IVs so that the blood can be removed, washed of the antibodies and other molecules called cytokines and things that cause inflammation. And then once the blood is washed, it's put back in. So, that's an option particularly when we're concerned about a neuromyelitis spectrum disorder, but we also know that for severe transverse myelitis, early plasma exchange may also help with the outcome. And then cases that are really severe that haven't responded to anything else, we will occasionally give a dose of cyclophosphamide which is a chemotherapy that's a more significant immunosuppressant.

[00:19:19] When we look at outcomes for transverse myelitis in pediatrics, the data shows that rehabilitation is really, really an essential part of recovery for these patients. Even if recovery is less than we want with the medicine sometimes, patients still typically do have significant functional improvements with rehab. Historically, we talk about the rule of thirds in transverse myelitis. This is what I learned in medical school. So, a third of patients don't get any better. A third of patients get some better, and a third of patients recover completely. However, there are some newer studies from 2015 on, I'm sorry, I don't know how to go back, from 2015 on that demonstrate that recovery is actually somewhat better in kids, that recovery to a good

or near baseline status actually occurs in as many as 70 to 80 percent of kids with transverse myelitis. And again, as I mentioned, you can have continued recovery, even improvement in things like bladder function that you wouldn't have thought you would get just with rehab even a year out so important not to give up on that rehab.

[00:20:45] So, then I wanted to talk a little bit about acute flaccid myelitis which some people would consider a variant of transverse myelitis. So, acute flaccid myelitis is something that we didn't really hear much about until 2012 when there were increases in cases in Colorado and California. And then in 2014, we saw more nationwide spikes and since then has set up, well, seem to be setting up as an every other year kind of a disorder. Although when COVID started in 2020, we think that the masking and the hygiene and the social distancing may have changed that epidemiology a bit. So, we'll see what happens as society gets back to more normal. But acute flaccid myelitis is inflammation of the spinal cord that is thought to be related, that is related to a viral infection.

[00:21:46] Specifically when we're talking about these outbreaks of AFM, we're talking about infections that are associated with enteroviruses, enterovirus called enterovirus D68. These patients present with the acute onset of flaccid weakness, so they're floppy, and it's lower motor neuron of one or more extremities usually in the setting of a febrile illness. This weakness is usually asymmetric, so it's most often one side or one extremity that is the worst, but sometimes it's an arm and the opposite leg. The pattern can vary a bit. But it almost is always asymmetric, and typically because of the levels of the spinal cord that is involved, it's almost, it's usually proximal, so shoulders and hips more than distal, so more than hands and feet. So, kids have trouble with things like putting their hands over their head or stooping down to the floor and standing back up, can have associated stiff neck, pain in the limb as well as cranial nerve problems.

[00:22:51] And what we see in imaging for patients with AFM is, again, there's this longitudinally extensive lesion of the spinal cord. You can see in this patient this lesion goes all the way from the cervical spine, all the way down to the very end of the spine at the lower thoracic, upper lumbar region. And then when we look at the cross-sections, we see this distinct butterfly in the axial grey matter, and that longitudinally extensive involvement of the grey matter is important to making the diagnosis. Interestingly, if we scan these kids over time, what we find is that this abnormality in the grey matter tends to settle more in just the anterior horn which of course is where the main cell part of that second motor neuron lives, and that's why these patients get so floppy in their muscles.

[00:23:46] Unfortunately for AFM right now, there is no proven treatment. IVIG is often used, and other therapies may be used if there is extensive swelling of the spinal cord. There are some treatments, specifically an enterovirus-D68- specific antibody that are in development, so that's encouraging. Onset may be hyperacute, can take several days to reach maximal weakness. One problematic part about AFM is that the diagnosis can be challenging and can be missed if a child is subtly weak. So, if the physician in the urgent care or ER doesn't have the child lift their hands over their head or do a high five, it could be missed. And we know that patients particularly with lesions in their cervical spine can have rapid progression to breathing trouble, so that's always my biggest concern around AFM season, that somebody is going to have breathing trouble and not get the help they need.

[00:24:44] In terms of outcomes, there's really a wide range. I have patients that just have some subtle weakness and are back to almost everything that they could do before, but then we also have patients who are quadriplegic and on ventilators. Completely normal outcome is less common. We have found that really early involvement of PM&R, PT, OT and speech is essential to getting the best outcomes. And then early consideration of nerve transfer surgeries, so if there's an anterior horn problem at a specific level and it's affecting a specific pattern of muscles, sometimes they can harvest a nerve that has kind of redundant

function that's doing something that another nerve can also do and kind of hook it back up to the spinal cord at another level so you can get some innervation to those muscles. All right. Moving on, it looks like we've got about 20 minutes left. So, just a brief word about ADEM, so ADEM is acute disseminated encephalomyelitis. It is typically a pediatric disorder, most often affects school-age kids, so 5 to 8.

[00:26:05] These are patients who present with altered mental status, so these kids should, to have a diagnosis of ADEM, you should always be lethargic or sleepy or sometimes even unresponsive. It's pretty widely variable. And then also have symptoms that are multifocal so referable to several different parts of the central nervous system, and because of that, these patients typically have many, many lesions. And when we think about the brain imaging for ADEM, like this patient on the right, what you typically see are these great big kind of fluffy-looking almost lesions. ADEM, we think of as something that can be idiopathic or postinfectious, but lately, we are finding that more and more of our cases seem to be associated with MOG antibodies. ADEM is typically treated with steroids. That's one nice thing about ADEM. Typically, we start steroids, and the patients recover pretty quickly. They do very well for the most part but may have some attention and focus cognitive difficulties or mild motor issues after the presentation.

[00:27:22] The other thing to note about ADEM is while the vast majority of our patients do well, there are also some more severe subtypes that can be associated with severe and rapid brain swelling and sometimes even bleeding. There's one form called acute hemorrhagic leukoencephalopathy where you actually can have bleeding into the lesions, so those can be more difficult to treat, require more therapies and also put the patient more at risk because you can have rapid brain swelling with those. One thing that is fascinating to me, I was an epidemiologist before I went to medical school, so I love the epidemiology part of it, is that talking to some of more senior colleagues who are in their 70s now, one of them said to me a couple a weeks ago, "We used to see ADEM all the time. You'd walk into the hospital, and there was ADEM everywhere, and now we hardly ever see it at all."

[00:28:22] So, I thought I'd look into the epidemiology here since it was so common in the past, and ADEM was so associated with measles, it was actually called rubella encephalopathy, and one in 1,000 patients with measles would have this. And then the measles vaccine was introduced in 1963, and the incidence of ADEM now is 0.25 to 0.4 in 100,000 children. So, if you figure that there is 73 million children in the US, at a rate of 0.4 per 100,000, there are about 292 cases per year in the US. And then prior to the vaccine for measles in the '60s, about 3 million, 3 to 4 million, I went with the lower number, kids per year got measles. So, at one case per 1,000 measles cases of ADEM, that gives you about 3,000 cases per year just from ADEM alone. So, by my calculation, that would put us at somewhat less than 10 percent. So, I think my colleagues are right. We do seem to see it a lot less now. Moving onto neuromyelitis optica, I've got more slides for NMO and MOG, so I'll pick up the pace a little bit.

[00:29:43] NMO is rare. Originally known as Devic's disease, first described in 1864, there is a known autoantibody. That's aquaporin-4. It's an antibody to water channels in astrocytes, and that does predispose certain areas of the brain and the spinal cord and the optic nerve to involvement here. Basically, these patients present with recurring episodes of optic neuritis and transverse myelitis. They may also have findings referable to the brain stem. This is one case when, or this is one the reasons why when a patient has vomiting without symptoms of a GI illness, we want to get a good picture of their brain because we want to make sure their brain stem looks normal. And then also intractable hiccups is a known presentation because of the brain stem involvement. You can also have involvement of the areas of the brain called the thalamus which is a big factor in being able to maintain awareness and staying awake, and those patients can present with narcolepsy because of these lesions.

[00:30:51] Important with NMO is that these episodes often have severe sequelae, so when we think that a patient is presenting with symptoms that could be consistent with NMO, we're very aggressive about treating those, and steroids are often relatively ineffective, so we go to plasma exchange very quickly. Because when we have a patient with NMO with positive aquaporin-4 antibodies, we know that the risk of relapse is so high and almost guaranteed, these patients after a first event will always be put on long-term immunosuppression. There are diagnostic criteria for NMO spectrum disorder that were developed in 2015. There are core clinical characteristics. We just reviewed some of them, and then you can be positive or negative for the antibody. You can meet criteria for NMO spectrum disorder if you're negative for the antibody, and many of our patients with MOGAD actually do meet NMO spectrum disorder criteria.

[00:31:55] When we're talking about neuromyelitis optica, aquaporin-4 neuromyelitis optica in particular, the worldwide prevalence ranges from 0.5 to 4.4 cases per 100,000. Most cases are really in middle-aged people, and only 3 to 5 percent of all NMO spectrum disorders are in pediatrics. It's more common in women, more common in East Asian populations and generally a sporadic disease, meaning there doesn't seem to be a major genetic predisposition. There are poorer outcomes for NMO spectrum disorder when we compare to MS and MOG, higher disability scores within 2 years of disease onset. Within 5 years of disease onset, more than 50 percent of patients are blind in one or both eyes or require assistance with walking. Predictors of the worst prognosis are a very severe first attack, the number of relapses in the first 2 years and having additional autoimmune disorders. Aquaporin-4 NMO can be associated with lupus or Sjogren's disease, and those can be associated with a more severe course.

[00:33:14] We do think that kids with NMO typically have more favorable outcomes than in adults. They tend to have a lower relapse rate, longer time to reach significant disability and lower mortality rates compared to the adults. Most patients do have relapses as we discussed. Median time to first relapse is 5 to 12 months. But we talk with multiple sclerosis about something called secondary progressive MS where patients get progressively worse even in the absence of discrete flares, and we don't really see that in NMO. All right. So, moving on from NMO to MOGAD. So, myelin oligodendrocyte associated demyelination, so MOG is a protein that's expressed in the central nervous system, and these antibodies to it in some cases cause disease.

[00:34:20] It is unclear whether MOG antibodies are always pathological. We know for instance that in some other disorders like leukodystrophies and maybe even stroke, MOG antibodies are a little bit elevated, but really marked elevation does suggest an autoimmune process and an antibody-mediated process as the cause of this neuroinflammatory disorder. I just included two MRIs here. The one on the left is actually not a T2-weighted image. I tried to show you mostly T2-weighted image, but this is a postcontrast image, and you can see here on this side, the left side of the brain, the right side of your screen we see some bright signal here in the sulci so in the folds of the cortex, and that's contrast enhancement. Most of these disorders don't have this kind of contrast enhancement which is contrast enhancement of the meninges so the coating around the brain which we're more likely to see in a meningitis. We would see it in an enterovirus meningitis or bacterial meningitis, but interestingly we also see it in MOGAD.

[00:35:36] And then this is a little patient of mine who presented with ADEM, so just to underscore that ADEM can be associated with MOG antibodies as well. So, classic phenotypes, we talked a little bit about already can present with ADEM, optic neuritis or transverse myelitis. And then has also multiple other presentations including meningitis, encephalitis, cerebellitis which is inflammation of just the cerebellum at the back of the brain. These patients may present with fevers as well. They don't typically have other autoimmune disorders. The majority of pediatric patients tend to demonstrate a monophasic disease course. It seems like adult patients may relapse a bit more. Persistent MOG positivity though does not necessarily mean that a patient

will relapse. So, we are still figuring out what persistently positive MOG antibodies mean to our patients. So, in the pediatric population, MOG antibodies are present in a third of all children with acquired demyelinating syndromes. The majority of those are kids less than 10. MOG antibodies are found in more children with NMO spectrum disorder than adults, and also as we already talked about, aquaporin-4 antibodies are less commonly found in children. In the adults, prevalence of MOG antibodies is less, maybe more like 2 to 4 percent of acquired demyelinating syndrome patients. For both MOG typically affects more male patients than we see with MS or NMO. Coexisting autoimmunity is rare, so we know that patients with MOGAD don't typically have lupus or Sjogren's or associated disorders, and MOG appears to be predominately in Caucasians. I am not going to go through this whole slide, but we will just go with the take-home points.

[00:37:56] So, the majority of MOG patients especially in pediatrics have a monophasic disease course. That's 70 to 80 percent. If we check your MOG at the beginning and then we check it 6 months later, it may or may not be negative when we check it again. Just because it stays positive does not necessarily mean you'll have relapses, but patients who are persistently positive are more likely to relapse than patients who have switched to negative. But because at this time we're not great about predicting who's going to go on to relapse and who's not, we do not recommend long-term immunomodulatory treatment at the time of presentation. Outcome is typically favorable, more favorable in kids. Complete recovery is more the norm with MOGAD. Patients, it may be that patients who initially present with optic neuritis are a bit more likely to have relapses, but again, we're still learning about the factors that go into this, and particularly with adults, there can be some permanent disability if there are multiple relapses.

[00:39:15] So, going back from the individual conditions to talk about treatments, in most situations and this is true for the antibody-associated disorders, as for idiopathic TM, optic neuritis, ADEM, we typically start with IV steroids, IV methylprednisolone for 3 to 5 days, and then if that doesn't work, go onto IVIG which basically is just giving good antibodies to try to counteract the ones that are causing the problems or plasma exchange if the methylprednisolone doesn't work. Exceptions here are that, like we talked about, if NMO spectrum disorder is suspected, a patient may receive more rapid plasma exchange. If AFM is suspected, it may be starting with IVIG and doing the methylprednisolone or plasma exchange in only certain situations.

[00:40:14] And then chronic treatment for relapsing disorders is another area where things are slightly different in pediatrics than in adults just because we don't have as much data, so we use the things that have been used in other pediatric disorders like rituximab which has great data in some of the pediatric rheumatologic conditions. So, most of our NMO patients are treated with rituximab right now in spite of the fact that there's really good data about things like eculizumab in adults, and then we'll reserve those things typically for very difficult-to-treat cases or older patients. With MOG, there's good evidence that monthly IVIG actually seems to work really well, and right now our current protocol at CHOP is that we'll do monthly IVIG for about 2 years and then reassess.

[00:41:10] Also, just as important as medical treatment is psychosocial support, so it is really tough to be a child who is totally functioning typically and then has the sudden onset of weakness or mental status change or any of these disorders, so really important to involve the child life teams who help kids to understand what's going on as well as behavioral medicine early on in the process just because this is very hard. And also, involvement of rehab services, PT, OT, speech, medicine and rehabilitation early on to be sure that we're planning even at the beginning for how things are going to go later and also keeping in mind that a significant amount of the improvement we see over time comes from rehab services.

[00:42:04] Thinking about returning to school, it is important to maintain close contact with the school. If there is any concern about mental status changes or thinking changes, we recommend neuropsychological testing, considering a walk-through with PT, OT at a quiet time to identify challenges and then developing 504

plans. Good follow-up is also important because we want to know if there are any new problems that come up that need to be addressed, so we do like to see our patients typically every 3 months at the beginning at least for the first year, and then we'll stretch it after that. Alright. Well, I think we barely made time.

[00:42:48] **Lydia Dubose:** All right. Thank you. Yeah, thank you, Dr. Hopkins. We do have just a couple minutes before we'll head back to the stage for our next session. But I did see a couple questions come through the Q and A. I know that you kind of had addressed rehab and other kind of supports, but somebody was asking about long-term care or specialists to help prevent or combat other health issues after AFM, and they named bone density loss, scoliosis, leg discrepancy, and things like that.

[00:43:23] **Dr. Sarah Hopkins:** Yep, so, that's super important. I didn't go into much of that because of the limited time, and also, I know Dr. Benson is going to be talking about AFM in one of the sessions later, but super, super important. And bone density is actually something that's really important for all of our patients, as is scoliosis. Any time you have trunk weakness and things like that, it's certainly an issue. So, we have a bone density clinic here. We will do, I do order DEXA scans not infrequently, typically after the first year or so, but we also do have a bone density clinic that follows those kids and then close orthopedic follow-up for the scoliosis and leg length discrepancies as well.

[00:44:13] **Lydia Dubose:** Okay. Wonderful. Well, thank you so much. You had a lot to cover in a short amount of time. We appreciate you. And now everybody can head to the stage where you'll be learning more about SRNA. Thank you again.

[00:44:32] **Dr. Sarah Hopkins:** Have a good day.

[00:44:33] **Lydia Dubose:** Alright. Bye.