Significance of Brain Lesions in Pediatric MOGAD

You can watch the video of this podcast at: youtu.be/bG92qcmHuKA

[00:00:02] **Announcer:** "ABCs of MOGAD" is an education podcast series to share knowledge about MOG antibody disease, or MOGAD, a rare neuroimmune disorder that preferentially causes inflammation in the optic nerves and spinal cord. "ABCs of MOGAD" is hosted by SRNA, the Siegel Rare Neuroimmune Association.

[00:00:26] SRNA is a non-profit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our web site at wearesrna.org. This episode is made possible in part by the generous support of Amgen; Alexion, AstraZeneca Rare Disease; Genentech; and UCB.

[00:00:59] **Krissy Dilger:** Hello and welcome. My name is Krissy Dilger, and I moderated this episode titled, "Significance of Brain Lesions in Pediatric MOGAD." For today's podcast, I am pleased to be joined by Dr. Vivien Xie. Dr. Xie is a pediatric neurologist and neuroimmunology fellow at Children's National Hospital and MedStar Georgetown University Hospital. You can view her full bio in the podcast description.

[00:01:28] Thank you so much for joining me today, Dr. Xie. Can you start off by providing a brief explanation of what MOG antibody disease is?

[00:01:39] **Dr. Vivien Xie:** Sure. Thank you so much for having me. MOG antibody disease is an autoimmune condition of the central nervous system, of the brain and spinal cord, and it's an antibody mediated disease where your immune system, which generally generates antibodies to fight infections becomes a little bit confused and misdirected and will attack the brain and the spinal cord and results in a condition called MOG antibody disease or MOGAD. It can happen in people of all ages, but it is commonly seen in young children and adolescents, and it can present with a variety of symptoms. But we find that a lot of patients get lumped into certain buckets.

[00:02:23] And one big bucket is that of optic neuritis, where there's inflammation of the nerve that connects from the brain to the eyeball called the optic nerve. And that is the basis of what we studied through this paper.

[00:02:39] **Krissy Dilger:** Great. Thank you. You mentioned your paper. I'm interested to know how you started or how you became interested in researching MOGAD.

[00:02:52] **Dr. Vivien Xie:** MOGAD is definitely one of those up-and-coming conditions in that we only started testing for it in the 2010s. So, I think part of the interest in studying that is because it's a fairly new condition. There's still lots to be discovered about how it affects patients, what are the most effective treatments, and also prognosis where we still don't have a perfect formula of knowing how people will do, how well they'll recover.

[00:03:18] I think all of those factors were very appealing for me in that I wanted to be able to really contribute to medicine and be able to discover something that directly affects my patients.

[00:03:29] **Krissy Dilger:** That's awesome. And we're so grateful that you did decide to research MOGAD because it affects many in our community and research is what gives us hope for the future. So, thank you. Can you talk about the background of this study and what led to the development of this particular research study?

[00:03:51] **Dr. Vivien Xie:** Yes, absolutely. The background of the study came about just through our observations. We see a lot of children with MOGAD optic neuritis in the hospital and our clinic.

[00:04:04] And we started to see a pattern in that a lot of children who have optic neuritis or inflammation of the optic nerve, when we do their MRIs, we find that they have a lot of lesions in their brain. Sometimes those lesions also had symptoms and a lot of those lesions didn't have any symptoms.

[00:04:24] And we saw this pattern of optic neuritis and brain lesions over and over again, to the point we started to wonder, "Do these brain lesions have any meaning to these patients? Did it have any impact on whether they responded to treatment, how well they recovered?" It was just such an overwhelming number that my team and my mentor, Dr. Kornbluh, thought it was appropriate to really study it as a research question since it affected such a large number of our patients.

[00:04:54] **Krissy Dilger:** So, what is the broad research question this study was attempting to answer?

[00:05:03] **Dr. Vivien Xie:** Right. Since we saw that there was this pattern of people with optic neuritis and brain lesions, the best way to understand the impact of these brain lesions was to compare it to children with MOGAD optic neuritis that didn't have brain lesions. By seeing if there were any differences between these groups, we could then extrapolate whether or not those differences were due to the brain lesions themselves and whether or not that meant something to patients long-term.

[00:05:31] **Krissy Dilger:** Interesting. How was the study set up? Was it retrospective? About how many cases or participants did you include? What was the criteria, et cetera?

[00:05:45] **Dr. Vivien Xie:** Yes, absolutely. We were fortunate to be able to collaborate with Johns Hopkins Hospital on this project. So, this ended up being a multicenter cohort study that was retrospective, meaning that we obtained all the information through past data we collected from these patients within our electronic medical record.

[00:06:05] We had a fairly big group of patients for a rare disease like MOGAD. We ended up having 35 cases of optic neuritis. In the 35 cases, we studied one group that only had optic neuritis, which was 20 cases, and then the other half, the 15, had optic neuritis and brain lesions.

[00:06:29] We essentially did a cohort study, meaning we just looked at the clinical characteristics, the MRI data, and the lab data of these two groups and descriptively compare them together to see if we could identify any patterns.

[00:06:42] **Krissy Dilger:** I guess the big question is what were your findings from the study?

[00:06:48] **Dr. Vivien Xie:** It was really interesting. Broadly speaking, we found that essentially the two groups weren't that different. To start off, we looked at the symptoms that the patients had. And besides the symptoms of optic neuritis in both groups, which included vision loss, pain with eye movements, or evidence of inflammation on the MRI of the optic nerve, we found that most of the patients didn't have any other symptoms.

[00:07:14] Whether you had brain lesions or not, most patients didn't have additional things like seizures, neurologic deficits, such as weakness, numbness, tingling. So, that was our first sign that these groups really weren't that different and that the brain lesions were essentially asymptomatic or didn't confer any sort of neurologic symptoms or disability.

[00:07:36] We then looked at the brain lesions themselves. We looked at MRIs of all these patients, both during their attack of optic neuritis. And then if we had an MRI later on, we compared that to the original attack. We found that the brain lesions themselves mostly were small, mostly were what we call discreet in that they had clear borders, they didn't look fuzzy, or they didn't blend into the surrounding background, and that they could be in all parts of the brain.

[00:08:10] One interesting finding is that it sometimes didn't matter how big the brain lesions were. Even the biggest brain lesions didn't mean that patient was going to have symptoms. So, that part was really good to note because sometimes MRIs can look a lot scarier than the patient actually looks.

[00:08:26] That was a good finding for us to support that. Then we looked at how these patients did long-term, meaning did they still have any signs of neurologic disability, three, six, twelve months out? We found that those with brain lesions did have some more evidence of disability in the first several months out as they were recovering, especially if they had symptoms during their initial attack.

[00:08:53] But by month three, pretty much everybody had very limited neurologic disability. We use something called the modified ranking scale, which is a way to judge how well a person is functional in their day-to-day life. And by month three, whether or not you had brain lesions, everybody had a score of zero to two, which essentially was considered a good outcome.

[00:09:15] To really summarize, our major findings were that there weren't dramatic differences between optic neuritis with brain lesions and optic neuritis without brain lesions. What this tells us is that we don't know if there are more subtle things that the brain lesions cause that we maybe have just not picked up on the testing or the evaluations we did but it is reassuring that those with brain lesions don't substantially do worse which gives us a little bit of counseling to give when a patient comes with this exact presentation.

[00:09:49] That's really interesting and I'm curious to see what more can come out of your research because that is good to know and it's good to, like you said, it gives you a positive outlook for patients who do have that scarier looking MRI, that it's not as scary as maybe it looks. What implications do your findings have moving forward with pediatric MOGAD patients?

[00:10:23] Absolutely. I think this study contributes to a growing understanding of phenotypes or classifications of pediatric MOGAD. There're some very well-established phenotypes like the optic neuritis. There's spinal cord inflammation, which we call transverse myelitis.

[00:10:42] We're wondering if this optic neuritis and brain lesions will be another identified phenotype that as we study more about it, we'll be able to see if it marks a distinct flavor of this condition that we can use to help people understand what their long-term prognosis is or whether or not they'll respond better to certain treatments.

[00:11:02] I think this study also encourages people to continue to study all the possibilities of MOGAD phenotypes. It's been pretty well established in several big landmark papers about the classic things to look out for, but I think as we get more and more patients, we start to better understand the large spectrum that

MOGAD can come in and the better we classify it and identify MOGAD, I think patients with atypical or unique presentations might get care sooner. So, that is the foundation that our paper is on.

[00:11:37] **Krissy Dilger:** That's amazing. I think that's so important. And like you said, MOGAD is relatively new in the medical world having only been researched in the last 10 or 15 years, or so. The fact that you're making strides in understanding it better and also helping to break it down so that it's not missed when it's not the classical presentation is so important. So that's great.

[00:12:14] **Dr. Vivien Xie:** Yeah. We're studying the rare presentations of an already rare condition.

[00:12:20] **Krissy Dilger:** Exactly. My final question is, do you anticipate future iterations of this study will develop?

[00:12:29] **Dr. Vivien Xie:** I do think so. In our group we're trying to study some more nuanced outcomes of patients with pediatric MOGAD, which can include neuropsychologic testing where we have them do essentially comprehensive cognitive memory focused, that type of testing, with one of our neuropsychologists, because then we can actually identify if there's any difference in their cognitive outcomes and not just in their neurologic outcomes of how well they can move their body, speak, walk, et cetera.

[00:12:59] We also think that in the future it's possible that we can dive a little bit deeper into their MRIs. For the purpose of this study, we really just looked at the lesion location in the brain, whether it's in a certain lobe, or certain side, and how well demarcated the lesion was. For example, did it appear fluffy and blended in, or if it had nice sharp edges?

[00:13:21] We want to hopefully look at the actual size of the lesion. Maybe the percentage that the lesion falls under in terms of the total brain volume and some other MRI features that might be able to help us distinguish those sort of MRI patterns with their outcomes or with their initial presentation.

[00:13:38] I think there's a lot of different directions that this type of study can go. I think right now people are looking into those subtle, more nuanced radiologic and outcome measures because we have a pretty good understanding of MOGAD and we have some good counseling, but there are a lot of atypical cases and people who don't really fit the mold. There's a lot of drive to, again, fill in the gaps and be able to give everyone the best understanding of their condition and their care going forward.

[00:14:09] **Krissy Dilger:** That's awesome. Thank you so much for joining me today on this very special episode of the "ABCs of MOGAD" podcast. We are so appreciative of clinicians like you and researchers like yourself who do this work and are dedicated to bettering the lives and outcomes of our community.

[00:14:32] Thank you to Children's National as well, who is one of our newest Centers of Excellence in Rare Neuroimmune Disorders and we're so happy to have that partnership.

[00:14:44] **Dr. Vivien Xie:** Thank you so much for inviting me. Being able to share our research has been really special. I hope we can have some future discussions.

[00:19:10] **Announcer:** Thank you to our "ABCs of MOGAD" sponsors, Amgen; Alexion, AstraZeneca Rare Disease; Genentech; and UCB. Amgen is focused on the discovery, development, and commercialization of medicines that address critical needs for people impacted by rare, autoimmune, and severe inflammatory diseases. They apply scientific expertise and courage to bring clinically meaningful therapies to patients. Amgen believes science and compassion must work together to transform lives.

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[00:20:40] UCB innovates and delivers solutions that make real improvements for people living with severe diseases. They partner with and listen to patients, caregivers, and stakeholders across the healthcare system to identify promising innovations that create valuable health solutions.