COVID-19 and Rare Neuroimmune Disorders

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Dr. Benjamin Greenberg: [00:00:00] I'm Dr. Benjamin Greenberg from the University of Texas Southwestern in Dallas. I'm happy to be with you today for this symposium and talking to you about a very timely topic that we've been getting a lot of questions about, specifically the intersection of COVID-19 and the rare conditions that we treat.

[00:00:21] I'm going to preface this talk by saying, while this has raised a lot of concerns, we are actually still in the early days of ensuring that we get accurate data about COVID-19 and neurologic complications. And as we've all experienced under these very surreal and unusual times, the data can change. And so I encourage everybody to keep in touch, stay abreast of information, check back at the Siegel Rare Neuroimmune Association website on a regular basis. Because if the information about our understanding of COVID-19 and neuroimmunologic additions changes, we will be sure to update it there. But with that in mind, I thought I would go through as a backdrop, the questions that we're asking. And as you're all very aware, there is an intersection in our world between the immune system and the conditions that we treat. Normally, the immune system is meant to defend our bodies against viruses.

[00:01:22] And it was Sir William Osler who noted that. Of the three great enemies that humanity had, fever, famine, and war, fever was the most terrible. And indeed infectious diseases have caused, more loss of life, in the world over the history of humankind than probably anything else. And it is actually not unusual in history for us to see episodes of dramatic and severe infectious diseases, going through the world and causing the type of calamities that we've seen with COVID-19 and even worse. When we put this in the context of what's been happening in the world around us, everybody I'm sure is aware of the history that we've had with COVID-19 where the first cases in December of 2019 being identified in Wuhan, China, but quickly spreading from there all the way to, just in the last couple days, the data for worldwide daily new confirmed COVID-19 cases with Brazil, the United States, India, leading the world in terms of having greater than 50,000 cases per day of new confirmations of COVID-19. And we are indeed still dealing with what is a global pandemic that changes month to month in terms of where hot spots are, but is still very much a part of our daily life. And it has obviously caused dramatic changes in our day to day existence, our family life, our school life, and our work life. But in the backdrop of all of that, for the populations we serve, there have been questions about unique safety issues that may relate to our constituency. And so with that, I wanted to list the five top questions we've been receiving relative to COVID-19 in our community. So the first question that I've received is whether or not a COVID infection can actually cause any of the conditions that the SRNA advocates for and supports. Can it cause transverse myelitis? Can it cause acute flaccid myelitis? Can it cause neuromyelitis optica spectrum disorder? Can it cause ADEM? Can it cause optic neuritis? Et cetera. And so that is probably one of the top causes, top questions we get in our clinics. The next question should we get is whether or not a preexisting diagnosis of one of those disorders will put somebody in a high-risk category relative to a

COVID infection. Meaning if you were to get infected with COVID-19, would you be in the categories that we hear about that have a higher rate of morbidity or mortality when an infection occurs? The third question we get is, does my medication that I take make it more likely to have a complication?

[00:04:14] So if you're on immunosuppression or not, does it change your risk category? The fourth question we get is whether or not the COVID infection can cause a relapse of my condition? So I've, I've already had it once. If I get infected with COVID, could I have a new transverse myelitis, or could I have a new attack of neuromyelitis optica? And then finally, the fifth question we receive is, when a COVID vaccine becomes available, will it be safe for me to take given my history or given the medication I'm on? So what I would like to do with, just a few minutes of time is go through our understanding of the answers to each of these five questions.

[00:04:54] So the first was whether or not COVID infections cause any of the conditions that the association supports? And the answer is, in general no, with recognition that there have been case reports of individuals who had had a COVID-19 infection who developed transverse myelitis or acute flaccid myelitis or even anti-MOG antibody-associated optic neuritis.

[00:05:21] And finally, probably the most common, even though it's still extremely rare, but the most common of the conditions we see, ADEM, acute disseminated encephalomyelitis, have all been described in the setting of COVID-19 or after COVID-19. There doesn't seem to be a specific pattern. There doesn't seem to be a high prevalence of these conditions.

[00:05:43] They seem to be exceedingly rare at the case report or case series level. And recognizing the fact that we have literally millions of people who have been infected in the United States, and we are only seeing single digit numbers of these types of conditions means, if there is an association, it is an extraordinarily rare association between COVID-19 and these types of conditions.

[00:06:08] The second question that was asked was whether or not, if you have transverse myelitis or neuromyelitis optica or any of these conditions and you develop COVID-19, are you more likely to have a complication? And the short answer is no, we have not found evidence that a preexisting diagnosis of transverse myelitis or acute flaccid myelitis, neuromyelitis optica, optic neuritis, or ADEM puts an individual at risk, if they are infected with COVID-19. But, and this is the key, if you have had pulmonary complications - if you still use a ventilator, if you have restricted lung function as a long-term sequelae of your acute flaccid myelitis or transverse myelitis or ADEM, then your pulmonary issues may put you in a different risk profile, but it's not because of your neurologic diagnosis.

[00:07:01] So for anyone who has had lung issues after their neurologic condition, we do encourage you to talk with your primary care physician or your pulmonologist relative to whether or not that would change what risk reduction precautions you need to take in your day to day life. Third question: does the medication you take make you more likely to have a complication?

[00:07:24] So for some of you who have anti-MOG associated disease or neuromyelitis optica spectrum disorder, you may be on an immunosuppressant. It may be a steroid. It could be Rituximab. It could be CellCept, known as mycophenolate, or one of the newer drugs for neuromyelitis optica. And all of those medications suppress the immune system.

[00:07:45] So if you were to get infected with COVID-19, would there be a higher rate of a complication? So far, the data we have is extremely limited relative to the impact of immunosuppression on COVID risks, but we do have concerns. These are theoretical. We have had some patients on immunosuppression get COVID-19. The rates of infection appear to be similar to the general population. But when we look at the rates of individuals needing to be in an ICU or be on a ventilator, there is some concern that the rates might be slightly higher than the general population. At least on my read of the data, it doesn't seem to be as big an issue as if you have diabetes or preexisting lung or heart disease or obesity. Those tend to be a bigger risk factor, but immunosuppression is probably changing the risk of some individuals.

[00:08:39] So for those of you who are on one of these medications, at least in my clinic, we do have a conversation about how that should impact decisions around return to school, return to work, and a lot of that depends on what's happening in your community relative to transmission rates. What we do in one community may be very different than what we do in another community.

[00:09:00] Fourth question: does an infection with COVID-19 change the risk of a relapse of your condition. And most often I hear about this question from individuals who have neuromyelitis optica or anti-MOG antibody-associated disorder and whether or not a coronavirus infection could trigger the relapse.

[00:09:18] And the short answer is, we don't think so. We are not seeing any data in our patient populations who have been infected with COVID-19 that the infection triggers a relapse. And if we extrapolate from our cousin condition, multiple sclerosis, an example of an autoimmune disease that relapses over time affecting the brain and spinal cord, but it has a much bigger population of patients.

[00:09:43] When we look at the MS literature, we are not seeing evidence that COVID-19 infection in multiple sclerosis triggers any relapses. So we are comfortable for the most part that if you were to get infected with COVID-19, there wouldn't be an additional concern that it would change your risk of having a relapse and we wouldn't change your prevention regimen because of that infection. The last question and the one I wanted to take the most time with, because it's going to be an evolving question and one that has obviously excitement and potentially concern for lots of people in the world.

[00:10:29] And that is the development of a vaccine for the SARS-CoV-2 virus, the virus responsible for COVID. And the question we get in our clinics is, when the vaccine gets released, will it be safe for me to take? And we are all aware of the large controversies in the world and concerns in the world relative to vaccinations.

[00:10:54] And I wanted to start off my response to this by reminding all of you that the literature overwhelmingly supports the safety of vaccination in our community. So, we do not see recurrences of transverse myelitis or acute flaccid myelitis or ADEM. We do not see outbreaks of relapses in our patient populations in the setting of getting approved vaccines, including the flu vaccine, tetanus vaccine, hepatitis vaccine, et cetera. And so, you will read a lot online. It is a controversial issue that, really in my mind shouldn't be controversial, about the relative risks of vaccination. In this season,

more than any other season in history, I cannot stress enough how important it will be for everybody to get their flu vaccine.

[00:11:45] There are significant concerns relative to a flu season that has both circulating coronavirus and circulating flu at the exact same time. And it is extremely important to prevent the flu in yourself and to prevent the spread of the flu in the community through vaccination. And so from the outset, I encourage everybody, the moment flu vaccine is available in your community, please, please, please get vaccinated because this season has the potential to be very different than other seasons because of the ongoing COVID pandemic. But with that as a backdrop, it's worth turning our attention to the COVID vaccines. And this is going to be an interesting era in vaccination because of the uniqueness of some of the vaccines that are being developed.

[00:12:37] And so, it's a good opportunity for us to remind ourselves that not all vaccines are the same. And there are lots of different types of vaccines that have been generated over time. But the three most common that we use today are the middle three columns of this chart. The first is what's called a live attenuated virus.

[00:13:04] So, this means you take the actual virus that's responsible for a disease and you weaken it so that it can't replicate in the same way in the human body, but it can replicate some, it just won't cause an illness or cause damage to any organs. And you inject this live attenuated vaccine, for the virus can replicate in the human, and it stimulates a very robust immune response, but you don't get the serious illness.

[00:13:31] And that way, when your body gets exposed to the measles or to the mumps or chickenpox, you already have an immune response to it. You don't get sick. There's also what's called an inactivated vaccine. So this is when you take a virus and you kill it, you inactivate it so that it cannot replicate. And in this situation, the inactivated, virus, particles, will stimulate an immune response to protect you against things like polio.

[00:14:02] And then finally there are what are called subunit vaccines, where instead of putting in a whole virus, whether it be live or killed, you only put in certain proteins from the virus. And these proteins are typically the critical proteins on the surface of the virus that allow them to attach to cells and infect cells.

[00:14:21] So as you develop an immune response to those specific proteins, that immune response can block viruses from entering the human body or entering cells within the human body and causing damage. So those three types of vaccines are technologies that we have used literally for many decades, over a hundred years, to try and develop and successfully develop vaccinations.

[00:14:46] And all three of those strategies are being used in the development of COVID-19 vaccines by different groups, different countries, different pharmaceutical companies. But with COVID-19, there are two other technologies that are being used to try and induce an immune response to the virus. And these are ones that are not commonly used in humans, one of which has not been used in humans before. And that's the DNA and RNA vaccine. So in a DNA and RNA vaccine, instead of injecting a virus, instead of injecting protein into the human body, it's actual DNA or RNA that codes for the proteins of the virus. And when this DNA or RNA is injected into your arm or into cells within

the human body, you can actually make some of the viral proteins, not the whole virus, just some of those subunit proteins. And those proteins can be presented to the immune system by your own cells and trigger an immune response. This has not been done before. This has not been used in any licensed vaccines, but is being pursued relative to COVID-19. The company that's been in the news the most, Moderna, is pursuing an RNA vaccine; Inovio is pursuing a DNA vaccine.

[00:16:15] And this would be a first for us in terms of a wide scale vaccination using DNA or RNA. The fifth type of vaccine is called a viral vector vaccine. And this is where we take certain proteins and certain genes from the virus that you want to elicit an immune response, but you place them in a harmless virus.

[00:16:40] So you have a live virus, but it's a hybrid. The shell of the virus for the majority is perfectly harmless, the DNA is harmless, and you could, like a live attenuated virus, it can get in, replicate, but won't cause any problems. But on its surface, it will express one of the proteins from what would be a harmful virus.

[00:17:01] And it basically attracts an immune response, and when responding to that harmless virus, you also get protection. You get antibodies against that protein that's part of COVID-19 in this example. This has been done as part of the Ebola virus vaccine that's been in testing. So while this has been used in testing, it has never been used in widespread use for widespread human vaccination.

[00:17:23] But it is another technology that's being pursued for COVID-19 vaccination. So back to our question: when a vaccine becomes available, will it be safe for me, an individual with transverse myelitis, acute flaccid myelitis, ADEM, neuromyelitis optica, anti-MOG mediated disorder, optic neuritis, et cetera?

[00:17:43] Will it be safe for me to take the vaccine? The answer I'm going to give is probably yes, and here's the caveat. For the live attenuated vaccines, the inactivated vaccines, and the subunit vaccines, we have a long-standing history of success and safety relative to using these to elicit an immune response.

[00:18:04] The phase three trials that usually occur with any of these types of vaccines include tens of thousands of human beings. And if there was to be a significant risk of inducing some sort of immune response to the brain, I would expect to see it in the phase three trials. And so if the first vaccine that comes out is live attenuated, inactivated or subunit, in general, I will suggest that it will be safe, assuming the data looks good. For live attenuated vaccines or viral vector vaccines, if you are on an immunosuppressant, you will need to speak to your healthcare provider to decide whether or not you would get a live attenuated or viral vector vaccine. But the inactivated and subunit should be safe. The DNA and RNA vaccines, however, are going to be harder for me to comment on at this time. While I hope and I trust that they will have a robust safety profile, we need to finish the trials, and we need to finish the trials completely before we can answer the question on relative risk and safety. The reason we do controlled trials is to determine not just if something is efficacious, but whether or not it's safe. And so while I have every reason to believe and hope that these vaccines will be safe, we do want to see the data from the trials. So what I encourage

everybody to do is to pay attention, stay engaged with the Siegel Rare Neuroimmune Association, watch the updates to the webpage.

[00:19:32] And as these vaccines become available, you can bet we will be doing reviews of the data, posting reviews of the data, and then encouraging a conversation around thoughts on relative safety for any of the patients and families we serve. I am hopeful we'll get there. It just can't come soon enough.

[00:19:52] I'm sure for all of us, we are ready to have a successful and safe vaccine on the world market so we can get past what's been a pretty dark time for us in the setting of the pandemic. So with that, what else can we do? You'll notice at least one of these recommendations is something that we've been saying for a long time in the setting of acute flaccid myelitis: wash your hands.

[00:20:20] It really does make a difference on cutting down the spread of viruses. Social distancing, wearing a mask, especially indoors around people, is the right thing to do. I remind everybody, if you or your child is sick, you shouldn't go to work or school. We really can stop the spread of this virus if we all change the way we interact with the world for a period of time. Without a susceptible human being moving around and spreading and receiving the virus from somebody who's spreading it, the virus disappears, and we've seen that worldwide with the data. So we are not powerless against COVID-19. There's a lot we can do to end this, and I encourage everybody to follow the recommendations that have come out around social distancing and wearing a mask, so that we can finally get rid of this and go back to work and go back to school and do all the things we want to do.

[00:21:17] So with that, before I introduce the next speaker, I'm happy to take any questions in the chat. And I'm looking at some of these, which I think we addressed. So in terms of, does having several autoimmune disorders increase the likelihood of an autoimmune reaction to COVID? It's a good question.

[00:21:49] So far, we haven't seen that be the case. So in the individuals where we've had case reports, some sort of inflammatory event in the setting of COVID-19, these were not in individuals who had preexisting autoimmune diseases. And likewise, we're not seeing reports of people with multiple autoimmune diseases having different reactions to COVID.

[00:22:14] So, so far, my read of the data says there's not a unique association. The question about live vaccines being more risky for individuals with neuroimmune disorders: they are not. But if you're on immunosuppression, then you do need to talk to your healthcare provider. So with that, I am going to turn things over to a colleague, a friend, and an outstanding speaker, Dr. Cristina Sadowsky. We're going from the B team to the A team. We're moving up in the world. Dr. Sadowsky is the Clinical Director of the International Center for Spinal Cord Injury at the Kennedy Krieger Institute. She's an Associate Professor in the Department of Physical Medicine and Rehabilitation at the Johns Hopkins School of Medicine.

[00:23:02] And I am very much looking forward to her talk on updates and rehabilitation in rare neuroimmune disorders. Cristina, take it away.