

Q&A series

Coronavirus (COVID-19) Questions and Answers for Individuals Affected by Rare Neuroimmune Disorders

Part III with Dr. Carlos Pardo



Dr. Carlos Pardo, Associate Professor of Neurology & Pathology and Director of the Johns Hopkins Myelitis and Myelopathy Center at the Johns Hopkins University School of Medicine, answers some of our community's most frequently asked questions surrounding the COVID-19 pandemic in the context of rare neuroimmune disorders.

If someone is diagnosed with a rare neuroimmune disorder, does this mean that they are immunocompromised or more susceptible to infection, or what does that mean in terms of their immune system? And does that differ based on the rare neuroimmune diagnosis?

It's a very important question. There is a lot of variability in the term immunocompromised and a lot of variability in the meaning of that situation in patients with rare immunological disorders. For example, there are patients with a diagnosis of monophasic myelitis, meaning that patient had experience only one episode of myelitis and after that, they never experience any episode or any flare up of myelitis again, or the myelitis basically remains just as a one-time episode for life. Those patients have a tendency to have a better immune system compared with other patients who have tendency to have a relapsing or remitting pattern.

For example, patients with neuromyelitis optica, in which there is a pattern of recurrence or flare ups, those patients may be more susceptible to a challenge to the immune system like infections by coronaviruses. Patients that have other autoimmune disorders, let's say NMDA or the encephalitis associated with NMDA. Those patients, again, may have some susceptibility based on the fact that there was some sort of pre-disarrangement of the immune system, and there is more damage of structures in the brain that may expose them to be more susceptible to secondary symptoms or problems that present in coronavirus infections. So those patients for

example, if they experience fever or they experience a decrease in oxygen content in the blood, may have secondary effects from the infection.

So the summary is, rare neuroimmunological disorders are frequently associated with some disarrangement of the immune system response. And the susceptibility is not necessarily defined because the presence of that rare neuroimmunological disorder but is defined by the medical disarrangement that that patient may have in their immune system and particularly if they are exposed to immunosuppressive regimens or immunosuppressive treatment.

Someone was diagnosed with transverse myelitis seven years ago and was told that they have a low immune system. Is that necessarily something that happens with transverse myelitis? Is this usually just a one-time thing where the immune system malfunctions and then things get better? Or is this an indication of a problematic immune system? And how can someone tell if that might be the case or not?

Yes, I'm just coming back to my statement from the last question and answer. A patient that has experienced only one episode of myelitis in life, at this moment, if that happened for example seven years ago or ten years ago, I don't believe that those patients are going to be the high risk. Our theory, because if these is no pattern of recurrence or flare ups, that means that immune system at this moment may be stable and may be in good condition.



The problem is, what was the reason those patients presented with myelitis several years ago. And again, myelitis shows up and is associated with different factors. There are patients that have monophasic or one-time myelitis because they were exposed some time ago with one virus that produced a post-infectious reaction in the spinal cord and subsequently there was a myelitis. Those patients likely are going to be at higher risk at this moment, even if the trigger for the myelitis was viral infections in the past. What we know about this virus is, this virus is eventually going to infect a large population in the world and the immune system is going to react with a lot of variations. There are patients that are going to react strongly and will be able to control their viral transcription, their vital proliferation and replication, and eventually are going to have a more successful control of the infection. There are other patients unfortunately in which the immune system is unable to produce enough immunity to protect against the replication of the virus, and the virus may spread and produce more damage in different organs like lungs and heart and produce more problems.

So a summary of the answer is having only one-time episode of myelitis in previous years is not necessarily going to enhance the possibility that the coronavirus is going to produce a more aggressive or less aggressive disease. Eventually patients will be in contact with the virus, and the immune system will decide what will be the magnitude of response against that virus.

Is everyone with an autoimmune disorder at greater risk of a severe case or death than those without an autoimmune disorder?

The autoimmune disorder, per se, is unfortunately a risk factor for further complications associated with an infection by a virus. And that doesn't happen only and exclusively with coronaviruses. That happens also with flu. If patients with autoimmune disorders get infected with flu, actually the consequences are also going to be not necessarily very good consequences. That's the reason we always advise patients with autoimmune disorders to get vaccinated for flu, because we like to avoid as much as we can contamination and infection by flu. So autoimmune disorders, per se, increases the risk of severity of coronavirus infections.

Unfortunately, many of the patients with autoimmune disorders are also exposed to immunosuppressive regimens, like medications that decrease the likelihood for autoimmune attacks. Unfortunately, those medications also will decrease the immune system reactivity against viral infections. So that

is one of the reasons we are emphasizing to patients that they need to practice extreme precautions if they have autoimmune disorders, or rare neuroimmunological disorders, and they are simultaneously receiving immunosuppressive regimens. And the reason is because the immune system at this moment in those patients is unable to produce a very efficient neutralizing response to minimize the infectivity by coronaviruses. So that is one of the reasons we emphasize extreme caution and the patients to take extreme precautions to avoid contamination.

So does that mean that if someone has one of these diagnoses, it puts them in the high-risk category? And if so, what does that mean?

Yes, so there is a high risk for infection. And the severity of the disease may be higher because the immune system will be unable to have a very good neutralizing reaction against the viral infection. And subsequently, the involvement of organs like lungs and blood vessels and heart for example may be more severe and subsequently, the severity of the disease may be higher. It's difficult to predict at this moment which patient populations, which autoimmune disorders, or which immunosuppressive treatments are going to be exposing the patients to a higher and higher risk.

We have, for example, some concerns that one of the reactions that the virus may produce in patients is aggressive immunological reactions that are called cytokine storms in which immune mediators or chemical mediators from the immune system that are called cytokines, are going to basically be over-enhanced in patients with coronavirus infections, and damage lungs and damage other organs of the body.

Interestingly, some of the clinical trials that are being used at this moment for coronavirus involves some of those medications that we have been using for controlling the immune system. For example, there are some rheumatological medications, some medications that have been used for rheumatological disorders, that have some degree of immuno-depression or immunosuppression, actually are being used in patients with severe immunological reactions associated with coronaviruses. That doesn't mean that everybody who is taking immunosuppressive medication may have somewhat protection. That means that unfortunately, in a subset of patients, the immunosuppressive treatment is going to be bad because we'll open the door to the infection, but we don't know exactly what is going to be the consequence of that.



If someone becomes infected with this coronavirus, could this trigger a relapse? And does this risk differ based on the disorder? So whether they have a monophasic disorder or a more relapsing disorder? And just for a real-world example of this, one patient's physician told them that their attack of optic neuritis could have been caused by a respiratory infection and their body attacked themselves in error. Could getting sick with this coronavirus cause another attack to occur?

I don't believe there is a right answer to that question. The right answer is we don't know. And there are many efforts going on right now by different groups in the United States and the world to have a better understanding of that, of the answer for that question. And there are already registries that been in place for tracking down patients with rare neuroimmunological disorders - myelitis, neuromyelitis optica - other disorders like multiple sclerosis, neurosarcoidosis. We'd like to understand that situation, if getting infected with a virus is going to modify the natural history of the disease or is going to increase the amount of relapses or flareups. The answer is we don't know. And until we have a very objective description and follow-up of patients with rare neuroimmunological disorders, we are not able to know that answer.

But, I'd like to come back to a basic principle that we already know from many years of experience. Any type of infection, regardless if it's coronavirus, flu, or a regular cold, may produce exacerbation of neurological symptoms in patients with preceding neuroimmune disorders. In other words, if a patient with myelitis that happened three or four years ago experiences coronavirus infections, some of the symptoms associated with that myelitis or residual myelitis or residual symptoms, some of those symptoms actually may get worse, transitorily. And that is not because of specifically coronavirus infection, it's that because the infection that they are experiencing at that moment. And if you remember when you come to our visit in clinics, we always emphasize "pay attention to infections." Because the infections are frequently major triggering factors for what we call false flareups of the disease, or pseudo flares.

And we are going to see this with coronavirus infections. That patient with a previous history of optic neuritis, if they get coronavirus, transitorily they are going to have worsening of visual blurriness. Or if the patient had a previous episode of myelitis, very likely patients are going to experience transitory worsening of sensory problems or bladder dysfunction problems or motor dysfunction. Is that meaning that patients are basically get worse by coronavirus, or coronavirus is basically triggering

another flareup? Not necessarily. It means that the immune challenge produced by the infection is triggering and reactivating those areas that were symptomatic before, like in the spinal cord or in the optic nerve.

Do you think that we'll see new cases of rare neuroimmune disorders being triggered by this virus like we see with potentially other viruses?

This is a very good question. Thank you for asking that. So, one thing that we know based on the experience observed in China, in Italy, in Europe, and right now in the United States is coronavirus, this novel coronavirus is not a neurotropic virus or neurovirulent virus. What is the meaning of that? Neurotropic means a virus that is going to target specifically the brain, the spinal cord, or a structure of the nervous system. This [corona] virus is behaving in a different way. This virus is not neurotropic. This virus is not neurovirulent. In other words, this virus is not producing a major impact in the central nervous system because the virus is invading the central nervous system or spinal cord or optic nerve or brain. This virus doesn't have that property. It may happen readily, extremely readily, but those are very different situations and circumstances, particularly because the patient is extremely immunosuppressed and may have neurological consequences after that.

However, that is very well known, at least up to now, is that this is not a neurotropic virus. So that means that the neurological consequences of the coronavirus infection at this moment are mostly secondary. So in other words, the damage of the lungs, the damage of the blood vessels, the damage of the heart, eventually may produce secondary neurological effects. The complications associated with coronavirus and the brain or the spinal cord or the peripheral nervous system are mostly associated with secondary complications.

For example, there has been an increase in the effect of strokes. In other words, patients who are susceptible to strokes get coronavirus infection, those patients actually increase the risk of strokes because the cardiovascular situation, the pulmonary situations. It has been noted, for example, that patients with coronavirus infections develop more brain dysfunction, secondary to the lack of oxygenation. So that is mostly a secondary effect, but that doesn't mean that the virus is damaging directly the brain, the spinal cord or peripheral nerves. There are very few case reports, mostly anecdotal reports, of some very rare neurological complications like Guillain-Barré syndrome that is a neurological disorder in which there is an autoimmune damage



of the peripheral nerves that eventually may lead to paralysis. There is only one report up to now of a patient suspected to have that situation. But again, in millions of people that have been exposed to coronavirus already in the world, there are extremely, extremely rare descriptions of neurological complications.

From the experience in China or Italy, is there any information about patients infected with coronavirus who have neurological diseases or rare neuroimmune disorders in general? Do we have any experience from them that might indicate how things might go here? Or is that stuff we're still learning about?

There are already in the literature coming from China in January through April, early April, as well as from Italy and some European countries, and some of the Asian countries, that the description of the complication that I mentioned before in the previous questions. And again, the majority of these complications that are neurological complications are derived not from the direct damage by the virus but rather by complications like strokes, or lack of oxygenation in the brain, or other type of immunological reactions that eventually produce some secondary effects in the nervous system function.

It's very frequent for example that elderly patients that are affected by coronavirus develop very high, high temperatures and develop a very important pulmonary dysfunction that leads to lack of oxygenation of the brain. Those patients actually exhibit a lot of mental status abnormalities. The patients go into a coma very quickly because the lack of a good oxygen supply and in some patients, strokes for the lack of blood supply to the brain because of damage of blood vessels.

We did have some questions that people were worried about potentially being denied care because of their disability or their pre-existing diagnosis. Is there any talk about that potentially happening if ICUs get overstretched, or that sort of issue?

The ethical situation at this moment has been discussed at many different levels, and my understanding and our belief as physicians and human beings is we have the social responsibility to take care of everybody regardless of diagnosis or secondary conditions. I don't believe that that is a discussion in our country. I don't believe that's the discussion in any of the hospitals where we take care of patients. I think that we have the social responsibility and medical responsibility as healthcare providers to provide attention regardless of age, secondary problems, race, and other situations, even immigration status, if you'd like to go to the social side of many areas in our country.

So, we need to take responsibility as physicians for everybody who is affected by this infectious disorder.

We've talked a lot about the immune system, but if someone has one of these disorders and they maybe have weakness or paralysis or residual effects after one of these diagnoses, how would they know if their respiratory function is impaired by their diagnosis?

The patient is the first one in getting the alarm sign, the shortness of breath, right? So patients with any rare neuroimmunological disorder that are infected with coronavirus should report his or her situation right away to their care team, primary care physician and neurologist. Any symptom of fever, chills, sore throat, in a patient with a rare neuroimmunological disorder, immediately trigger, or need to trigger a call to the care team. And it's extremely important that patients understand that any sign of all of these infection symptoms, associated with shortness of breath, need to prompt urgent care.

So, in other words, any sign of shortness of breath, that means that there is some respiratory difficulties, and this needs to be taken seriously. Patients and families need to take serious care of that situation and notify that primary care provider and neurologist about that situation.

Is there anything else that you think we should cover?

I think that the most important aspect of this difficult situation in the world for patients with neurological disorders and rare neuroimmunological disorders and families is to be alert. I think that following all recommendations that have been explained, following recommendations of isolations, and families need to take extreme care when they have some member of the household affected by rare immunological disorders. Because any misstep, any potential exposure to those patients with the rare neuroimmunological disorders may have difficult consequences.

There has been a lot of talk about how to prevent, how to be proactive in the prevention of this, and unfortunately, the only thing that we know is just the public health measures, like isolation and extreme care to avoid contamination are the only ways to minimize those potential infections. There has been a lot of talk about medications that may be prophylactic, medications that may avoid potential infections, but the reality is there is no proof that those medications are really helpful. There is no proof at all that you can take tons of vitamins, tons



of Plaquenil or hydroxychloroquine to prevent this disease. Unfortunately, the answer is, at this moment, there is no proof that these approaches are going to work. And the only thing that is important at this moment is to follow the precautions, the isolation, the quarantine recommendations, and extreme care to protect family members that are exposed to higher risk because they have rare neuroimmunological disorders.

Visit wearesrna.org/covid-19 for the latest information on COVID-19 and rare neuroimmune disorders.

