Identifying Relapses vs. Temporary Worsening of Symptoms

You can view this presentation at: youtu.be/m3sCxLwCmtQ

[00:00:00] **Roberta Pesce:** From acute treatments, we are now moving on to our next talk, which will focus on worsening of symptoms and relapses. And I'm joined today by our next speaker, Dr. Barreras, who is a neurologist at Johns Hopkins Medicine. Dr. Barreras, hello. Welcome, and over to you.

[00:00:26] **Dr. Paula Barreras:** Thank you, Roberta, for the introduction. So, like Roberta mentioned, I am going to talk about how to identify relapses and differentiating those from temporary worsening of symptoms. So, I'll start by mentioning that some but not all neuroinflammatory disorders, or people that have experienced attacks of optic neuritis, myelitis, ADEM, will go on and have relapses. But some do, and for those people that have a risk of relapse, early identification of those relapses is important to start the management early and prevent disability. This can be a little bit tricky sometimes because not all neurological symptoms that patients experience indicate actual relapse.

[00:01:14] Let's go over the terminology a little bit. What do doctors mean by relapse? So, a relapse is a new event, a new neurological event or a new attack of neurological injury caused by new inflammation in the brain or the spinal cord. And usually, it's associated with a new lesion in the MRI that explains those symptoms. Classically, or usually, these are new symptoms that the person has never experienced before, or a significant worsening in old symptoms. The symptoms of a relapse usually progress over hours to several days and usually last for longer than 24 hours, as opposed to just transient, short, fluctuating symptoms.

[00:02:00] And the symptoms of a relapse are usually attributable to a specific part of the nervous system. And this is what neurologists called that the symptoms localize. And what we mean by this is, for example, somebody who has weakness in one arm. That can be explained from a problem in the spinal cord or the brain in a very specific area. But if somebody has generalized weakness or just worsening fatigue, it wouldn't be expected just by a single lesion in a part of the nervous system, and therefore, it's less likely to [[be connected]] to the relapse. Relapses usually require additional treatments to prevent disability, like we saw in a prior talk. And these treatments may vary, including steroids, plasma exchange, and in some cases, other treatments.

[00:02:50] So what to do if there is a suspicion that you're having a relapse. So, the first thing is to let your doctor know, but if symptoms are rapidly progressing and severe, then the emergency room would be the way to go. It's always useful to time the progression of symptoms and write down at what time of the day

everything started and how new symptoms are developing because that's ultimately what neurologists and doctors use in the emergency room to decide if the symptoms are due to a relapse or not. In the emergency room setting or sometimes in the outpatient setting, evaluation of relapses requires an MRI. And I say usually because sometimes if the symptoms are very typical, we may just decide that it's consistent with a relapse and not do the MRI. But in most cases, the MRI would follow to demonstrate the lesion and just see the extent of the inflammation that is happening at that time.

[00:03:50] And like we said, usually treatment will follow and if this is a relapse that is occurring in the setting of a treatment, beside to prevent relapses from happening, then a relapse may indicate treatment failure and may lead to a change in therapy. And that's key because this implies that labeling something correctly as a relapse is very important because it has implications for the overall disease management for the future.
[00:04:22] Now let's talk about pseudo-relapses. And the terminology here varies a little bit. So other terms that are used to describe this are recrudescence, pseudo-exacerbations, or pseudo-flares. Another term that I don't like but you may have heard is fake relapse. And I don't like it because fake may imply that the person is faking the symptoms, and the symptoms are very much real. We just mean that it's not a true, new inflammatory attack on the brain or the spinal cord. The symptoms of pseudo-relapses are usually temporary worsening of old symptoms. These are not caused by new inflammation in the brain or the spinal cord, usually lasts less than 24 hours, usually fluctuate a bit during the day, and they fluctuate in parallel with stressors in the body. And we'll talk a little bit more about that in a second.

[00:05:22] These symptoms are reversible and not associated with new lesions and MRI. And, they do not affect the course of the disease. They are not, by themselves, harmful, and so they feel and look a little bit scarier than they actually are. So, what's happening when somebody's having a pseudo-relapse? What happens is that after there's an injury to the nervous system, the body compensates to try to maintain function. So other areas of the brain are sort of working a little bit harder than usual to maintain function. And when there's a stressor, that can break the balance of the system and cause a decompensation. So, the focus here is to determine what is the stressor that is breaking this balance and bringing out the old symptoms.

[00:06:20] What are some common causes of pseudo-relapses? Fever is one of the main ones, and for some patients, particularly with demyelinating disease like multiple sclerosis, overheating even in absence of fever can bring out old symptoms. Infections can definitely be a stressor on the body, even if in the absence of fever. And for patients that have experienced myelitis, urinary dysfunction, bladder dysfunction is very common. And with it, urinary tract infections are also common. And one of the things to keep in mind is that bladder sensation may be affected, so people can have urinary tract infections and don't feel the classic burning or pain that urinary tract infections cause. So, you can have one of these infections and not know, and that may be the underlying cause of the worsening of the neurological symptoms.

[00:07:22] Surgeries are also common causes of pseudo-relapses. High blood sugar in diabetes is a very common one, and electrolyte abnormalities as well, and specifically low sodium levels. Intoxication with drugs or alcohol can also decompensate the system. And one that we don't talk about as much but is very important is psychological stress, emotional stress and depression can worsen old symptoms, particularly symptoms of pain and cognitive dysfunction. There's actually something called pseudo-dementia, where people lose cognitive function. They are labeled sometimes erroneously as having dementia, and if you look deep enough, it's depression. You cure the depression, and the cognition gets better.

[00:08:17] And sometimes new medications. So certain medications for pain or for seizures or muscle relaxants can have potential side effects like dizziness, gait problems, some can be sedating and cause fatigue and that may be interpreted as worsening weakness. So, it's always important when you're experiencing one of these symptoms to try to see if any of these factors may be playing a role.

[00:08:47] So what symptoms are more suggestive of a true relapse? So, symptoms that are completely new, that the person has never experienced before, like we said previously. A relapse can be from old symptoms, but usually this is a marked and sustained worsening of old symptoms, not just mild fluctuations in the old symptoms. For optic neuritis, the symptoms that we're looking for are decreased visual acuity or loss of vision in one eye, and usually this comes with pain with the eye movements and abnormal color vision, where the vision through that eye is grayed out or pale compared to the other eye. Symptoms just like flashing lights or floaters that are transient and went away are less likely.

[00:09:45] When weakness occurs in both legs at the same time, usually paired with numbness in both sides with bowel or bladder dysfunction, this is concerning for a myelitis episode and ascending symptoms. And I believe at the end of the last talk, there was also mention of in NMO in hiccups and vomiting that seems unexplained but is persistent is also a symptom that can suggest a true relapse.

[00:10:18] Now, what are some symptoms that are less likely to be a relapse? Isolated increase in pain or spasticity. Isolated increased urinary frequency, and what I mean by isolated is in absence of other things that indicate spinal cord problems. If there is increasing pain or spasticity but the strength is the same, the sensation is the same, there's no new areas of numbness, there's no new urinary incontinency, is less worrisome for a relapse. Isolated increased urinary frequency, we're typically thinking about evaluating for urinary tract infections. And, the reason for this is that in the spinal cord, all the structures are very close together. So, it's very hard to have a lesion that causes one of these things in isolation without affecting the rest. Worsening fatigue or generalized weakness, usually not a relapse.

[00:11:19] Tingling or pins and needles without other symptoms, and here, I want to mention that in areas that are numb, where when somebody's lost sensation before in the recovery process sometimes is very common as the nerves sort of start regrowing to experience tingling. And that feels abnormal, but it's part of the healing process and can be expected and a good thing as long as it doesn't come with deficits that are new or rapidly worsening. Brain fog, headache without vision changes, symptoms like we've talked about that fluctuate rapidly and symptoms that, like we said before, don't localize. And this is an assessment, really, that your doctor will do when you call and report these symptoms.

[00:12:14] So why is this important? Recognizing pseudo-relapses prevents unnecessary testing and treatment. Like we said before, when something gets labeled a relapse, it may result in escalating of treatment or saying that your maintenance treatment, if you failed that treatment, that you require a stronger immunosuppressants, and that's a big deal. And so, we don't want to get it wrong here. But also, understanding that some things as pseudo-relapse is important to search for the underlying cause. It may lead to identification of infections or other medical problems that also require attention and management.

[00:12:57] So what are symptoms that are suggestive of a pseudo-relapse? So, what to do? One thing that is very useful is to keep track of the old attacks and the old symptoms during those attacks in a journal or a Google Docs document that you can refer to quickly, so you know if you've had that particular symptom before. And that can be very reassuring if you've had the exact same thing before, to show your doctor that can clarify the situation very quickly. To time the symptoms in the same way that we're interested for true relapses, to see the progression and evolution of symptoms, here as well. Because it's this tracking of the intensity of the symptoms over time that will suggest the relapse versus a pseudo-relapse, or that we want to know if the intensity is fluctuating or not, and if we're crossing those 24 hours. This is often referred to as the 24-hour rule, where we don't send people to the hospital unless symptoms have lasted beyond 24 hours.

[00:14:10] Check your temperature, because like we discussed, overheating and infections are a common cause of pseudo-relapses. And, try to identify if there is any obvious stressor that may be impacting your

overall situation at that time, like heat, but also sleep deprivation, a particularly stressful situation, a new medication that was started that day. And, evaluate if it's possible that you have a urinary tract infection and not know, by checking if your urine looks cloudy or has a strong smell.

[00:14:43] Even if you think that this is a pseudo-relapse, I think it's a good idea to let your doctor know. And the reason is that there may be diagnostic testing that is indicated specifically if there is no obvious trigger to the pseudo-relapse. An infectious workup should be done, and this usually includes blood work to check blood cell count, basic electrolytes, glucose, urinary analysis, and depending on the situation, sometimes we do chest x-rays as well to look for pulmonary infections.

[00:15:22] So there's, like with everything, the exception to the rule. So, we've said that usually true relapses are symptoms that the person has never experienced before. Now, it's possible, in some diseases, to have repeat attacks in the same are, specifically in NMO, this can happen. In sarcoidosis, this can happen, where the same area gets inflamed again. And in that case, the old symptoms would reemerge, and this would be a true relapse. The difference here is that in that scenario, usually the symptoms progress rapidly. They're more severe and they stay. They don't fluctuate. They just progressively worsen until you get proper treatment.

[00:16:12] The other thing is about waiting 24 hours, is that if there is a symptom that is rapidly worsening and is severe, then I would seek immediate medical care at that time, even if it's less than 24 hours. And to that point, I want to talk about stroke a little. So, people with neuroimmunological disorders can have, like everybody else, cardiovascular risk factors, such as hypertension, diabetes, obesity, high cholesterol. And if that's the case, then like everybody else with these risk factors, there is a risk of stroke at any time. So, it's useful to try to see how relapse from myelitis looks different from a stroke, and if there is concern for stroke, then don't wait 24 hours. Just go right away to the hospital because treatments for stroke work better in the first few hours.

[00:17:15] So usually symptoms of stroke are unilateral, so one side of the body, face, arm, or leg is weak or numb. There's sometimes difficulty communicating, understanding language. But the key is the tempo. So, with stroke, all symptoms come at the same time, and they are maximal when they start and stay, as opposed to symptoms of neuroinflammation that gradually build up slowly or more slow over several hours to days.

[00:17:50] So in conclusion, patients with neuroimmunological disorders can experience symptoms due to relapses, pseudo-relapses, or other neurological conditions, like stroke. And differentiating between those is very important to avoid misdiagnosis, overtreatment, and guide the next steps in management. And the key to differentiate these things is the type of symptom that is being experienced, the tempo or evolution of those symptoms, whether they are crossing those 24 hours or not, and whether they are new symptoms or not. And that is the key to make the right diagnosis. Then, if it's not a relapsing, good news. But then we still need to do some workup to make sure that there's nothing else that needs attention. Okay. That's it. Any questions?

[00:18:43] **Roberta Pesce:** Thank you so much, Dr. Barreras, for this. We did receive quite some questions from the community. The first one is how to judge if the patient is experiencing a relapse versus a functional neurological disorder if old symptoms return and stay for over a month. Can there be an overlap of the relapse and FND?

[00:19:03] **Dr. Paula Barreras:** So, function neurological disorders, because I don't know if that everybody in the audience is familiar with the term, are neurological symptoms that are real that the person experiences, that are not associated with lesions in MRI and they're not coming from inflammation. Then usually they are coming as a manifestation of psychological stress sometimes because the body manifests stress in different ways. And it can be tricky to differentiate. But in this situation, if the functional symptom, if the functional

impairment looks similar to what a symptom of myelitis, let's say, or optic neuritis or ADEM would look like, the MRI is really the way to differentiate which one is it. Because in a true relapse, let's say, you would see a new lesion there. Roberta, I'm not hearing you.

[00:20:07] **Roberta Pesce:** There's a slight echo. Could you mute yourself while I'm talking, please?

[00:20:12] **Dr. Paula Barreras:** Yes.

[00:20:14] **Roberta Pesce:** Perfect. Sorry, I was saying that we got quite some questions, Dr. Barreras, so I don't think we can catch them all. I'll ask this one here, but if you want to, you can go in the events chat and reach out to the participants. They asked some really good questions that we can reach out about that later. But there's another question that says, "I have NMOSD, and I've had numerous MRIs after worsening of my condition, but the results don't show any new damage to the spinal cord. What should I ask my neurologist in this instance?"

[00:20:45] **Dr. Paula Barreras:** So, it depends a little bit on the temperament profile of that worsening. The first thing is that could this be a pseudo-relapse, and should we look for other things that are decompensating your situation? So, I think there's workup to be done. Not everything is that a patient with NMO experience is due to NMO. So, it's truly, there is no new inflammatory activity, but you're taking, for example, NMO suppressant medication, we want to make sure that you don't have a hidden infection that you don't know about, that your electrolytes are all good, that there's no new medication that may be worsening your symptoms. So, I think ask the neurologist if that workup has been completed and if other causes have been excluded.

[00:21:28] **Roberta Pesce:** Yup, perfect. Thank you so much, Dr. Barreras, for your talk. We really appreciate your time here with us today. And I think we're going to move onto our next speaker. So, thank you, Dr. Barreras.