

What is Acute Flaccid Myelitis (AFM)?

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Dr. Michael Sweeney: [00:00:00] My name is Mike Sweeney. I am at the University of Louisville and the Norton Children's Hospital. And I'm going to be talking, in 15 minutes or less, about acute flaccid myelitis. So what is AFM? So acute in neurology refers to rapid onset of symptoms, typically within 24 hours from onset to peak severity of symptoms. Things like stroke often reach the peak nadir within four hours, and more inflammatory processes take a little bit longer. In AFM, we can see a rapid onset of symptoms that happened within hours, but some cases people take several days to reach their peak weakness.

[00:00:47] So, in AFM, the flaccid refers to loss of muscle tone or loss of reflexes. This happens in AFM because of damage to the motor neurons in the anterior horn cells in the spinal cord. So why are we talking about AFM now? Adding to the alphabet soup of the SRNA. In 2014, a cluster of cases became reported and, out in the Western United States. And since then, every two years there's been a rise in the number of cases, typically occurring in the late summer months.

[00:01:26] So in 2014, this is a map from the CDC showing the distribution of cases. You can see that the majority of cases were out west, with Colorado and California having the majority and some sporadic cases throughout the rest of the country. In 2016, cases maybe more understood and more reported, came from all across the country. And then in 2018, pretty much throughout the entire United States. So far in 2020, we have, as far as I know, 16 cases reported this year and majority of cases, being reported out of Texas. But still not a sharp rise in cases reported thus far.

[00:02:17] So what causes AFM? So historically, enteroviruses like polio virus, have been known to cause AFM, with some other neurotropic viruses or viruses that like to infect nerve cells like West Nile virus or herpes viruses, adeno viruses, and these have also been reported. But what about this unique rise in cases every two years? What's causing this? So there's mounting evidence that suggests a specific strain of enterovirus, enterovirus D68, may be the culprit. So typically, enterovirus D68 causes a respiratory illness. It was circulating around the time, in 2014 and 2016 when we started to see these cases. And, you know, some strains isolated from these years appear to have acquired neurotropism, meaning that something changed about this virus that allowed them to start infecting nerve cells.

[00:03:23] When they looked at samples of the virus taken from people who had AFM and infected this virus into mice, some of these mice became paralyzed similar to how patients become paralyzed with AFM. And if they took the antibodies that those mice developed and gave them to other mice and then infected them with enterovirus, those antibodies were protective. And then when they gave those same mice steroids, it seemed to worsen their symptoms. And some more evidence that would suggest enterovirus D68 is the agent, when we look at CSF from people who had AFM, enterovirus peptides or proteins were the most commonly identified. And there was also an increased number of enterovirus-specific antibodies found in patients with AFM.

[00:04:22] So how does AFM present? I'm going to use this case from a child that I saw in 2018 to illustrate, and then we'll go through some of the more detailed clinical criteria. So, I saw this boy, who's a three-year-old guy who had a history of some mild asthma. And he presented with, to the hospital, with respiratory distress. He was actually admitted to the hospital for what was thought to be an asthma exacerbation.

[00:04:50] And then, the night he was admitted, his respiratory symptoms just kept getting worse despite treatment for his asthma and, really, over the next day, he started to not be moving around as much. And an astute nurse noticed that his right arm wasn't moving at all. And so the neurology team was consulted, and we went and saw him. He was having some weak movements on the left and not moving his right arm at all.

[00:05:23] He initially had very brisk reflexes and upgoing toes. And, by the time we got him into the scanner, he had no reflexes, and this is what we saw. So in the MRI, we found that he has this very long, abnormal signal in his spinal cord. You can see on the left picture, that bright signal in the middle of his cord extending all the way up from his brainstem down into his cervical spine. You can appreciate that there's some spinal cord swelling. The second sequence, the T1 sequence, you can see that the cord is a little bit dark. And when we do the cross section of the spinal cord, you can appreciate that there are some abnormal signal predominantly in the gray matter of his spinal cord. When we gave him contrast there was no evidence of contrast enhancement.

[00:06:18] We did some investigating and his spinal fluid was abnormal, showing 76 white blood cells in his spinal fluid. And on a nasal swab he had, there's a test called a respiratory pathogen panel that detected rhino/enterovirus with PCR. So he was treated with plasmapheresis and steroids. He was intubated at the time of diagnosis because of his severe respiratory weakness. And he also developed, what we thought was neurogenic pulmonary edema because it was not consistent with his asthma diagnosis and this improved with steroids.

[00:07:02] Ultimately, he ended up getting a tracheostomy or breathing tube. He got a G-tube or feeding tube and spent several months in our inpatient rehab and had a very slow, limited recovery. I just saw him recently at a two-year follow-up and he's requiring a ventilator only at nighttime. During the daytime he's sitting up, he's able to support his head. He can move his right arm again. He can kick his legs. And he's a very happy guy.

[00:07:31] So, if anyone has ever been diagnosed with AFM or if this has come up, sometimes there's a lot of ambiguity around the diagnosis itself because there's a lot of overlap between other myelitis causes. And so, the CDC AFM case definition says that someone has to have acute flaccid weakness and a lesion that involves at least some part of the gray matter. We can then further differentiate this into a confirmed case, or a probable case, or a suspect case depending on the other clinical features.

[00:08:08] So people with AFM typically present with acute onset of flaccid weakness. They have low tone, low reflexes, and then they also... This happens in the setting of a recent infection, in most cases. Sometimes it happens during the acute infection. We tend to see people having weakness more proximally in their upper arms or upper legs, compared to their distal muscles. And in some

people, we find some maybe more atypical presentations would involve neck stiffness, meningismus, headaches, pain in the limbs that are affected. There's been some reports of cranial nerve involvement. So the nerves that involve the face swallowing, and then numbness is a very uncommon presentation.

[00:08:57] So this single center group published their data from the 2014 and 2016 cases. And in this group, 57% of their patients had fever at the onset of symptoms. 64% of their children had multiple limbs involved and 85% of those kids had white blood cells elevated in their spinal fluid.

[00:09:25] So what do we see on the imaging? The, so just like in our patient, we tend to see a central gray matter involvement, long segments, meaning that the abnormal signal extends for several vertebral body lengths. And this is contrasted to the, on the right here, the idiopathic transverse myelitis, or just transverse myelitis, where we see a lot, there's more heterogeneous patterns. So we have some people who have predominantly a dorsal column or posterior white matter tract involvement, or we can have a more global involvement, so much wider spectrum, I would say.

[00:10:09] In AFM, the abnormal signal tends to affect the upper cervical cord and the lower thoracic cord predominantly. Although we've seen cases that can affect anywhere in the spinal cord. And the brain is not exempt from involvement. So in this group, abnormal signal in the brain was identified in half of patients. This tends to be kind of extension of the involvement of the spinal cord, kind of extending up into the brainstem and lower brain.

[00:10:45] So what do we do when we have a patient who has, suspected to have AFM? So what we do is we get urgent imaging. These patients get MRI of the whole neuro axis, from the brain all the way down to their spinal cord, perform lumbar puncture to look at their spinal fluid and look for signs of active infection. And we sent blood work to look for other causes of myelitis or myelopathy.

[00:11:13] So the CDC has recommended some diagnostic testing to consider. So, in the spinal fluid, we're looking for other infections that can cause a flaccid myelitis. We're looking for other signs of inflammation, so other inflammatory diseases like neuromyelitis optica, that can cause an extensive myelitis. In the blood, we're looking for evidence of autoimmune diseases and other infections like Bartonella, HIV, and syphilis. We look for vitamin deficiencies, even though they tend not to present so acutely. We still want to be pretty comprehensive. And then when we are looking specifically for enterovirus D68, we know that we hardly ever isolate that virus from the spinal fluid itself. So we look in the nasopharyngeal area. We look at urine and stool samples and in the blood.

[00:12:15] So there are no... as of now, there are no universal treatment guidelines for patients who have AFM. We are trying to avoid steroid use, given the concern for acute infection. That being said, there's probably some role of significant spinal cord swelling for steroids. Plasmapheresis may be avoided if there is concern for a vascular etiology. So a spinal cord stroke could present very similarly to acute flaccid myelitis. IVIG is probably the most utilized treatment as of now and it may offer some humoral immunity.

[00:12:54] They, at the time, so fluoxetine was studied in 2016. It was a, it's an already established medication, FDA approved, for depression and it has anti-enterovirus properties. So a, a group

studied that in 2016, but didn't find any benefit in outcomes. So we focus on treat- on symptom management, making sure that we support the child when they have a weakness. We look for autonomic instabilities with swings in heart rates and blood pressures, look at bowel and bladder function. These can all be affected. And we look at their respiratory function. We have to monitor these patients very closely because they can decompensate pretty quickly and end up in respiratory failure.

[00:13:43] So, thus far the vast majority of improvement happens with time and rehab. So patients get traditional physical therapy and occupational therapy. Electrical stimulation is appropriate for many patients. Aqua therapy is often helpful. Assistive devices like the Amadeo where you can have kind of repetitive movements of limbs if you have focal weaknesses. And nerve transfer surgery is also being used in some patients over time. Really that could be a whole talk in and of itself, but these are kind of the sorts of things that patients go through after they are diagnosed with acute flaccid myelitis.

[00:14:36] So this year there is an NIH funded AFM natural history study that is going to be enrolling patients. And this is the pathway. So, if you have a patient who you suspect has AFM, you want to report your symptoms to the state health department and submit samples through their collection system.

[00:15:00] They will collect CSF serum, stool, and nasopharyngeal swabs. And they coordinate getting that data to the CDC where the testing is performed. And then a panel of neurologists that are working with the CDC adjudicator look at the, the case information and say whether or not this meets criteria for AFM. We're using that data to try to understand better kind of the spectrum of disease that we're dealing with. And use that data to look at, you know, medications or interventions in the future for things that might make an impact.

[00:15:37] All right. So I made it on time, and I think we're going to take questions later in the questions session. So with that, I am going to introduce Dr. Mateo Paz Soldán. He is a faculty at the University of Utah and was integral in my training there. He's a great guy to work with, and he is going to be talking about acute disseminated encephalomyelitis or ADEM.