Acute Flaccid Myelitis (AFM)

You can view this presentation at: youtu.be/vWe0yPujjx4

Dr. Carlos A. Pardo: [00:00:05] Good morning, good afternoon, good evening, everybody around the United States and the world. Thank you so much for inviting me to talk about acute flaccid myelitis. My name is Carlos Pardo, I am a neurologist at the Johns Hopkins Myelitis & Myelopathy Center. I'm part of the Acute Flaccid Myelitis Working Group and it's a great honor to be in this SRNA symposium to discuss aspects and different issues related with acute flaccid myelitis. What I'd like to accomplish in the next few minutes is number one is to update you about preparedness for AFM outbreaks, particularly focusing on diagnosis and management. And second to open the door to all of the different efforts from public health and research that we are doing for acute flaccid myelitis and discuss future on management. I need to acknowledge that my research support comes from the National Institute of Health, and I don't have any commercial disclosure, but I am very grateful with the Bart McLean Fund for neuroimmunology research as well as SRNA for all the support that has been provided for us in the past several years for the Johns Hopkins Myelopathy & Myelitis Center and the research focus on myelitis.

[00:01:48] What is acute flaccid myelitis? An acute flaccid myelitis is a new problem that we have seen in the past 10 years. Acute flaccid myelitis is a disorder that affects predominately children from ages one to 12 but acute flaccid myelitis may happen in children, even older than 12 and even in young adults. It affects both male, females and there is no sex predilection and importantly, acute flaccid myelitis is an illness that appears to be associated with viral infection that have some pattern of seasonality, meaning that it shows mostly in periods of the summer and the fall, particularly in the United States. However, acute flaccid myelitis may happen in many areas of the world in Europe, Africa, South America and Central America, Asia, where they may have a different seasonality as well. The most important aspect of acute flaccid myelitis is disease that affects several members of the family, is a disease that affects children and adults, but inter virus is the suspected virus that is associated with respiratory disease. Many family members may be affected by the respiratory problem and only few children are affected by acute flaccid myelitis meaning that despite the magnitude of viral infection that may occur in communities, only few children fortunately are affected by these neurological problems.

[00:03:41] What is acute flaccid myelitis and what is the link with viral infections? The suspect number one in acute flaccid myelitis as a potential triggering factor is an enterovirus that is called enterovirus D68. Enterovirus is a respiratory virus, is an illness that affects children predominately producing respiratory symptomatology

that is leading to systemic illness including fever and respiratory symptoms, but eventually in a small subset of children, this enterovirus that is classified as enterovirus D68 have the capability to produce immunological responses that not only affects the lungs and upper respiratory airway, but also may have capability to affect the spinal cord and produce a polio like syndrome in the patients that are affected.

[00:04:45] What we know about acute flaccid myelitis is that it was for the first time noted in 2012, when cluster of cases of acute flaccid myelitis were described in California and Colorado. But after 2012, we became more aware about this Illness and the seasonality. And in the past several years, we have observed outbreaks of acute flaccid myelitis in 2012, 2014, 2016, 2018, and in 2018 we have the major outbreak of this illness around the United States. What is going on right now after COVID-19? Well, the public health measures that were implemented for the outbreak of COVID-19, very likely knocked down the circulation of enterovirus D68. And the face mask measures, and the lockdown measures dramatically decreased the circulation of enterovirus around the United States and many areas of the world. And that's the reason we believe that in 2020, there was one of the suspected outbreaks, there was no areas of such outbreak because basically, many countries were in lockdown and the extensive measures, public health measures that were implemented for COVID-19, decreased the circulation of the virus. And subsequently there was a decrease in the number of cases of AFM and you can see this decrease in the epidemiological graphic that is published by CDC on a monthly basis.

[00:06:36] What is going on right now in 2020 to this moment, we have a very few cases of acute flaccid myelitis described the United States, particularly in the West Coast, in California and some in Nevada. But also, we have cluster of some cases described in the southeast of the United States as well as the northern part of the United States. So, there are still cases of AFM being recorded as we speak. And if you compare it in 2018, where the majority of the states of the United States were affected in 2022 only a few states have reported cases of AFM. However, it is still very early to describe that acute flaccid myelitis is not showing up in 2022 and it's very likely that in the next couple of months in September, October and later in November, we may see cases of acute flaccid myelitis.

[00:07:36] Now the emergence of acute flaccid myelitis changed dramatically the epidemiology of myelitis in the pediatric population. As you can see in this graphic, this is our experience at the Johns Hopkins Myelitis & Myelopathy Center, between 2010 and 2018. Many of the cases actually of myelopathies were associated without immune disorders like neuromyelitis optica isolated. I'm going to face the cases of myelitis or even myelin oligodendrocyte like a protein antibody associated disease, MOGAD, that were part of the spectrum of inflammatory myelopathies or even some other type of myelopathy, like strokes and vascular myelopathy. However, as you can see here in 2010 and 2018, many of the cases that actually happened and cases of myelitis that happened in the pediatric population, almost a third of that patient population in our experience were associated with acute flaccid myelitis. So, the epidemiology of acute flaccid myelitis changed dramatically the epidemiology of myelopathies in the pediatric population. And that's the reason we need to be aware about the presence of this myelopathy in the children, particularly below age 12.

[00:08:58] As you can see in this graphic, that again represent our experience. You can see that the majority of patients that we saw between 2010 and 2018 with acute myelitis in the pediatric population, a third of them were clustered in ages 0-10 and they were basically an important cause of myelitis in this pediatric group. So, it's important to remember that also, other myelopathies may happen in children, monophasic myelitis associated with MOGAD, or myelitis associated with [inaudible] during this age population. Now, what is the clinical profile of acute flaccid myelitis? And I'd like to summarize this profile in the graphic that is showing here, that reflects the characteristic and the profile of cases that presented in the outbreak of 2018. And this is based on the statistics derived from the Centers for Disease Prevention and Control, the CDC in Atlanta that put out a very good and extensive profile of cases that presented during that outbreak. This is

extremely important for all clinicians, family members to understand is the majority of patients with acute flaccid myelitis show up with a preceding illness that is frequently fever and upper respiratory symptoms. The majority of patients, almost 94% of the patient actually have present systemic illness, fever, and all of the respiratory problems that I mentioned before.

[00:10:48] Few days after is when patients experience a very acute and hyper acute neurological syndrome that is characterized mostly by weakness that progress rapidly and, in some cases, involved the respiratory system and produce catastrophic situations like ventilatory respiratory failure that leads to the hospitalization of some of these children in intensive care units. This is a disease that progressed very rapidly between hours to 48 hours. Many patients are admitted in during the acute phase and many of these patients actually require intensive care unit setting and care because the magnitude of neurological problems and respiratory problems. Almost 56% of the patients that were admitted and diagnosed in 2018 actually require intensive care units setting because they had significant neurological problems including quadriplegia and severe respiratory problems. Almost 96% of the patient requires other hospitalization setting and 41% require admission to the hospital for evaluation and management of the neurological and respiratory problems. A very small percentage of patients have really what is called a mild case of acute flaccid myelitis in which only mild weakness is noted.

[00:12:27] But the most important aspect of acute flaccid myelitis it is the fact that it behaves as a polio like syndrome and leave almost a quarter of the patients, 25, 26% of the patients with important problems of motor disability, including quadriplegia and almost 43% of the patients have a very important involvement of the upper extremity function with decreased mobility and paralysis. So, this is unfortunately, the main problem that we are dealing with in acute flaccid myelitis is the severity of the disease and the fact that many patients are left with neurological disability, weakness in upper and lower extremities and some of them with ventilatory respiratory problems that require chronic ventilatory support. So, this is extremely important for the clinician to understand that these patients may go to have a mild illness at the beginning, that may end up with significant disability, including a requirement for continuous ventilatory support and continual mechanical support and continuous support for mobility. So, this is a disease that have the possibility to produce devastating problems in the patients that have been affected.

[00:13:56] Now back in 2020 many of us became part of the Acute Flaccid Myelitis Working Group and discussed the criteria for diagnosing this disease. And this has been published already in Lancet in 2021. And what we pay attention as a criterion for establishing a definite diagnosis is number one is the presence of acute answer of weakness in any of the four limbs leading to flaccid paralysis, and most of the cases in general are preceded by prodromal fever or systemic illness. But one of the critical elements for establishing the diagnosis is the physical examination, neurological exam, that you have a good documentation of weakness in either upper or lower extremities or lower cranial nerves as well as decreased muscle tone, that in other words is equivalent to the flaccid tone that patient with acute flaccid myelitis present. In many of these patients, there is absence of reflexes, and the MRI is perhaps the most useful tool for establishing a diagnosis of this disease, along with the cerebrospinal fluid analysis that should demonstrate presence of inflammatory changes, including pleocytosis and increasing protein.

[00:15:26] So, as I mentioned before, the most susceptible areas of involvement in acute flaccid myelitis are the brain stem in which the MRI may demonstrate signal abnormalities, particularly in lower portion of the brain stem and regions of periventricular region, and the most important areas of involvement are the cervical spinal cord as well as the thoracic and lumbar spinal cord. And this MRIs demonstrate clearly the extensive involvement that may happen in acute flaccid myelitis in which the gray matter of the spinal cord is affected prominently, producing obviously a very characteristic picture of extensive and longitudinal extensive inflammation and abnormalities in MRI. Now during the acute phase, the most critical aspect of

management focus on evaluation of the respiratory situation because this patient may go from having a normal pattern of breathing to have a very severe respiratory failure that requires admission to the intensive care unit. So that's the reason many patients need to be evaluated carefully avoiding too much sedation and obviously treating the discomfort and pain very early to avoid more difficulties with future management.

[00:16:50] And many of these patients require early intervention with rehabilitation measures including a physical therapy and occupational speech pathology therapy. Later on, when patients go to chronic phase there is need for more aggressive intervention including nerve and neuron and tendon transfer, and obviously long-term medical management is required particularly when the severity of the disease is an important element of disability. Now, unfortunately what we know is that many of the non-measure for management of myelitis fail in an acute flaccid myelitis and we already know that unfortunately many of those measures like the steroid use, plasma exchange, IVIG or even medications like fluoxetine are not necessarily useful in the management of the acute phase. And there is ongoing studies trying to characterize better ways to mitigate the progression of the disease and limit the extensive neuronal damage that is happening in these patients. But unfortunately, situation is that at this moment we are at the mercy of rehabilitation efforts and surgical efforts like nerve transferring for improving the quality of life of many of these patients.

[00:18:19] Now, what is in the future? And the future is development of new antiviral medications that may decrease, the likelihood that enterovirus or the virus associated with the disease produced extensive damage of the motoneurons. In the future is the development of a specific antibodies that will limit the damage produced by enterovirus D68 and eventually development of vaccines that will prevent the magnitude of infection and problems associated with this disease. And obviously, in nerve and tendon transfer are ways to mitigate the progression of disability in these patients. This is one of the possible future treatments. This is from studies from a group that developed human antibiotics that neutralized enterovirus D68 and in that way may protect the infection and paralytic disease. This is an important piece of work that was produced by Dr. Matthew Vogt who is right now UNC University of North Carolina, and this work was developed while he was a postdoctoral fellow in Dr. Cross laboratory in Tennessee.

[00:19:48] But the other thing that is very important is that we need to expand our research on this disease, particularly understanding the role of the new system, understanding the role of the virus in the progression of the disease, and particularly bringing more avenues and treatment options for the management of this horrible disease. And this is important because we need to improve the quality of life for the patient and improve obviously the quality of life for the families that are struggling in the management of patients with acute flaccid myelitis. And I'd like to bring the topic that the Acute Flaccid Myelitis Working Group have centers around the country that are able to help with acute flaccid myelitis and the Natural History Study supported by NIH and led by the University of Alabama in Birmingham are part of a research effort in which many centers around the country are teaming up to investigate in detail what is the natural history of this disease.

[00:20:55] Again, thank you very much to SRNA for the invitation to talk about acute flaccid myelitis and I invite you to google about our group, the Acute Flaccid Myelitis Working Group and see our website where there is extensive information about acute flaccid myelitis and all the aspects of management and treatment. Thank you very much.