

Respiratory complications of Acute Flaccid Myelitis

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[00:00:05] **Dr. Benjamin Greenberg:** As we've been going through the different management issues, whether it's pain, spasticity and the like, everyone in the room has a who's been affected by one of these conditions, has a different pattern of symptoms they suffer from and for a lot of our community, when inflammation occurs in certain parts of the nervous system, breathing can be affected. And this is something we saw with really painful details during the outbreaks of acute flaccid myelitis going on in 2014 and 2016 and '18. And what we're watching for right now and seeing a little peek of it occurring as we speak around the nation. At the forefront of work in AFM, was Dr. Keith Van Haren, who's joining us from Stanford University, who in collaboration with Carol Glaser, even before the 2014 outbreak was seeing and identifying patients for what we would now classify as acute flaccid myelitis. And we're thrilled that Keith could join us today to talk about the respiratory complications of acute flaccid myelitis and what his experience has been. So, Keith, it's all yours.

[00:01:06] **Dr. Keith Van Haren:** Hi. Yeah, thanks for inviting, delighted to be here. I'm a child neurologist and pediatric immunologist at Stanford. And I'll be talking about respiratory complications. I don't have any real financial disclosures to make. My biggest disclosure is that I'm not a respiratory specialist. So, I'm speaking from the perspective of neurologist looking through the lens of neurologic disease on respiratory complications and I'm going to be discussing some things that we just have a little bit of introductory data for us. So, I'll caveat that as we get to it. So, to provide a little bit of background on AFM since we haven't covered it too much quite yet, this is the general experience for individuals who experience AFM, is they typically have a respiratory or infectious prodrome followed by a period of recovery and then followed then thereafter by a period of neurologic weakness. Weakness is unique in that it's flaccid weakness most of this syndrome that we see in neurology that involve injury or to the central nervous system cause spasticity as mentioned in the two prior talks. This causes flaccidity, which means just kind of floppiness.

[00:02:39] And that's what characterizes this syndrome in part. So, along with this weakness to the arms and legs and sometimes the face can also include respiratory weakness. So, the weakness of the breathing muscles specifically of the diaphragm. And this can get really dangerous. It's one of the reasons we treat acute flaccid myelitis as a neurologic emergency, as opposed to some of the other syndromes, we see where we consider it urgent, but we don't have to move patients right to the ICU for monitoring. Here, this gets dangerous and in a meaningful number of patients. So, that period from most patients passes and they recover from the acute respiratory ailment and that's what the part I would say we all know best as a

neurology community in an intensive care community, but as I allude to at the end here, we don't know the kind of long-term area quite as well, or we haven't described it quite as well.

[00:03:43] I think there's probably more for us to learn. So, in patients with acute flaccid myelitis, there's a characteristic injury of the central gray matter of the spinal cord and this is specifically affecting the neurons in the spine that control the muscles is right at the level of the muscles. And this is just a slide from the California Cohort of patients between 2012-2015. But what I'm pointing out here, is this kind of inverted bar graph here shows that where most of the lesions in our patient group were occurring. And I've highlighted the C3, 4, 5 at cervical level 3, 4, 5. Those are the nerve roots coming out of those areas of the spinal cord. Those innervate the phrenic nerve, and the phrenic nerve is what drives the diaphragm.

[00:04:49] So, if you injure those nerves famously you can impair breathing and this is a very common and dangerous complication. For some individuals, it's very severe injury to these nerves, for others, it's mild and can recover. But this is again what makes acute flaccid myelitis a neurologic emergency. So, respiratory support during hospitalization, this is what we know the most about. And from several cohorts we have today to say, "Well, it's common." So, we have California cohort where about 30% were intubated requiring mechanical ventilation. And then the National US cohort in 2014, similar numbers in 2015 to 2017, we have like about 30%. Again, in the 2018 National Cohort we had about a quarter of patients. So, we're talking about a large group of patients here who are experiencing this and Carlos who is around here at the meeting this week did a wonderful job of putting together and with team Owen Murphy and group of others putting together some guidelines for acute flaccid myelitis. And they included care of respiratory complications.

[00:06:21] And so in the acute setting, the most important thing to know up front is you need to stabilize patients for triage and stabilize patients for the possibility of respiratory failure. And there's some pretty detailed guidelines here on acute management. Those include just monitoring for respiratory function on a frequent basis, maintaining specific thresholds for intubation and ventilation. I'll say that typically we expect patients to move through this and if they need respiratory support, it is more often temporary and many recover afterward, but for a subset of patients, it is not. It requires longer term respiratory support. And I would say that the post hospitalization period is the part we really need more information on. We don't have great follow up guidelines quite yet. And so, I will-- There was a case that brought this to the forefront for me.

[00:07:29] It was often the case, it's a patient and a family who tell us what really needs to be done. And this is a young man who had, had a reasonably typical course except perhaps for how well he recovered. He had almost complete flaccid paralysis of all four extremities with respiratory failure. And he recovered unusually well over a two-month period. At the time we sent him to rehab, he was needing BiPap only at night. And then I think at the time, sometime during rehab, apparently he was taken off the nighttime BiPap and sent home and then time passed, he was followed up in various clinics and then one day came to see me and dad was, I think reasonably upset and the young man had gone away to college and had a heavy night of drinking and his roommates had found him breathing very irregularly and taken to the emergency room where he was. I should specify, he was incredible athlete, had recovered very well in almost every aspect. And so, I was just functionally doing great and physically and intellectually in college.

[00:08:51] So, they were somewhat surprised to find out that he had really severe sleep apnea, so he was evaluated at his local university medical center, and they diagnosed really severe sleep apnea. He was put on a BiPap machine and was doing very well thereafter had much less fatigue and drowsiness thereafter and the father came in and said, "Listen, why wasn't this caught, how was my son sent home with this? Has this been going on for longer?" And I said, "Probably has." And this was the first patient I've seen like this, and I ask around if any other colleagues have seen this and it wasn't something that was recurring commonly, but there was another patient I saw thereafter and I said, "Okay, there's not quite as severe as this one." But I

said, "There's something to this, we should look a little further." So, I had a wonderful medical student at the time, this is Razina, she's now at MGH, by the way, Michael, and Anastasia, she's in child neurology there, she's terrific. I highly recommend trying to recruit her into your clinics. But she and I put together a nice case series with some of our team and we our goal was to describe the acute and post hospitalization course of acute flaccid myelitis. And we had a fairly small cohort of only about 20 patients, but half of them had respiratory complications as defined by needing supplementary oxygen intubation or similar features. And then the part I want to draw your attention to in this long table is the post hospitalization care.

[00:10:39] And specifically I want to point out that several of the patients did get sleep studies after their acute care and a meaningful number of them had central and obstructive sleep apnea. So, what we're calling here central hyperventilation. So, one of our patients was this one who was a sentinel case and then a follow up that I've seen and when I didn't even quite recognize at the time, but I also want to point out that several patients who were not in the respiratory complication group had post hospitalization, respiratory complications, mostly asthma attacks. And there's a high coincidence of asthma in the children with AFM already that's just it seems to be one of the risk factors for developing acute flaccid myelitis. I think the larger point here was there's more probably of a respiratory story to good quality care for these kids, are mostly kids. And I think this is a good place for us to circle back and take a closer look at.

[00:11:50] So, I think we're probably not offering enough referrals for these children and screening them as well as we could. And I think this is a good place for us to think further. So, these are the three kids that I saw with the central hyperventilation syndrome. I'm pointing this one out specifically because it's one that I wasn't really tuned into. I'm not a sleep specialist, I'm not a respiratory specialist, but these three kids had meaningful complications. None of them, I should say had long term intubation. One of them does still have a tracheostomy, and two of the three still require ongoing support. And I will just a few words on sleep apnea, so how is it diagnosed? Well, you need a sleep study to diagnose it. And the sleep study involves you going into a hospital, outpatient unit and you get all kinds of electrodes taped to you and they measure your breathing and your electrol activity and how much oxygen and carbon dioxide are going in and out. And they diagnose sleep apnea if your blood oxygen levels fall below certain threshold for a certain amount of time and your carbon dioxide levels rise too far. And there are really two major kinds of sleep apnea.

[00:13:15] One is called central sleep apnea when the problem originates from the brain or the nervous system somewhere. The other is the much more common form, which is called obstructive sleep apnea, which is the kind that most of us will be familiar with where we're snoring at night and not breathing regularly. And they're both treatable. Let's see. I think I've got one. Yeah, so they're both treatable. One is treatable with CPAP, typically that's the obstructive sleep apnea. But the central sleep apnea that we're thinking about here is treatable with-- It's a very similar machine. It just has a few other settings called BiPap. We'll just add here that for those wondering what is central sleep apnea and why is it happening to these patients with AFM, and I would say it's probably just a general complication of neuromuscular weakness. There may be more to the anatomical association here. I thought there might be, we didn't find one in our study, but it is common among neuromuscular disorders, and it was reported as uncommon complication of poliomyelitis in the historic literature. And I suspect we're probably missing some number of kids who might have this, who've had AFM, but I don't expect it to be common, but I think it's one of these things that's important and can impact children's lives because it can affect their nighttime oxygenation and their sleep level, and their fatigue and it can potentially be dangerous. So, I do think we should look for it. I would say to kind of circle back on kind of larger story here.

[00:14:57] So, outpatient management of respiratory recommendation complications, any of them, we don't really have guidelines for this yet. I would say we can say they're still in development. I think need to consider more pulmonologist outpatient evaluation, so that's a respiratory specialist. I would say we should consider

this probably in most maybe all patients with a high cervical cord lesion and certainly anyone who have been intubated and then for those who may have experienced or maybe wondering about sleep disordered breathing or funny sleep sounds or just curious in general, I think it's worth talking to your local neurologist and pulmonologist about this. To truly diagnose it, you need a sleep study but that may be appropriate.

[00:15:51] Okay, so to summarize, respiratory complications are common in AFM. They typically occur with lesions in the highest cervical cord. It's what makes it a neurologic emergency and why we take such care to triage it. During outpatient hospitalizations, I think we should consider pulmonary follow ups for more patients than not. And I think abnormal breathing during sleep can persist even when other respiratory symptoms have resolved. So, we can have young people who look very healthy in every other respect, and they may have sleep disordered breathing that's going on unrecognized as is the case with one of our patients. And I think asking about this is maybe something we can consider more of and considering when asleep referral is necessary. So, even among our patients without respiratory complications in the inpatient setting, we may have more in the outpatient setting. So, another good reason for pulmonology referral. And that's it. I want to thank the Siegel Rare Neuroimmune Association. It's been a great meeting. I've really enjoyed it. So, thanks for hosting. Thanks for inviting. It's been really a delight to hear people's stories and the discussion, so I'm happy to take questions here. This is kind of an obscure topic. But yeah, thank you. Go ahead.

[00:17:26] **Audience Member 1:** So, was one of the major, let me rephrase this, "Fatigue is something that I see with my child that has AFM. And she spoke yesterday, and she seems to be doing really well." Is this something that you think we should look at or? And obviously--

[00:17:52] **Dr. Keith Van Haren:** Well, yeah, I'll start by practicing that fatigue is one of the complications that we as a medical community have the hardest time assessing and treating and it can have many different causes. And it is one of the things that I find-- I'll say to patients, I consider it foundational, if you're tired, you can't do anything else or if you're in pain you can't do anything. It's one of these really foundational if you have it, it disrupts every other part of life. Fatigue is really important. Assessing it is tough. I do think as a neurologist, especially in kids. In adults we think about obstructive sleep apnea much more frequently. In kids we don't because typically obstructive sleep apnea comes from other kinds of adult complications and kids are less common.

[00:18:49] So, could it be relevant to your daughter's case? It certainly could be. I think the questions to ask your daughter, is she more tired in the morning, does she wake up feeling tired? And I think discussing that with the neurologist is a possibility is certainly good one if-- I don't recall of him, I'm sorry if she was intubated as a patient. And so, it might put her at high risk for sleep disturbance as well. So, it could be and to really figure that out, you need a sleep study to solve that.

[00:19:33] **Audience Member 1:** Is there any particular sleep study that's different than another? I've been through one and they sent me home with this little thing and I put it on and yeah, I got a CPAP, out of the deal. But are these children or is this in hospital setting? Do you prefer that as opposed to the take home kit or?

[00:19:55] **Dr. Keith Van Haren:** Yeah, that's a good question. I think they're pretty standardized. They may have the ability to do them in different settings. A home setting or kind of a hospital setting. And typically, the children's hospitals have their own special setup because kids aren't used to sleeping all by themselves in a room and they might need a little bit of parent company. But if you got a referral to a pediatric sleep specialist, or for teenagers, an adult sleep specialist may suffice to, but they would set the person up for the right device. As far as I know, the sleep studies that are done are all very similar. What differs maybe the interpretation.

[00:20:42] **Audience Member 2:** A question that came in online. Dr. Van Haren. Are there any cases where the patient did not have respiratory symptoms at the time of hospitalization, but some respiratory complications came up years down the line.

[00:20:55] **Dr. Keith Van Haren:** Yeah, I'll caveat that by saying they were more asthma related and occasional like pneumonia related. So, whether they were true, they may not have been related to the acute flaccid myelitis event directly. But just to identify or flag individuals with acute flaccid myelitis. Just being at risk in general for respiratory complications and needed to connect with a pulmonologist is being a good probably standard of care that is put out there. We didn't have any patients in our very small cohort who had sleep disordered breathing that was not present probably during the initial hospitalization. All of them I think had sleep disordered breathing during their hospitalization. Some of it was triage better than others. But yeah, a good thought for fatigue. If fatigue is present, I think worth considering. Well, thanks very much.

[00:22:05] **Dr. Benjamin Greenberg:** All right, thank you Keith and thanks everyone for the great discussions this morning. So, let me just before everyone runs out to lunch, let me just tell you how things are gonna work from here. So, lunch is across the hall in the Los Angeles room. And if you look at your schedules after lunch, our breakout sessions. So, if you look at the schedules, there are three tracks. Each track has two different talks. You can go from one track to the other. So, if you want to do the first talk in track one and the second talk in track two, you can move throughout. Track one which includes transitioning from hospital to home and then later early rehabilitation strategies is gonna be here in this room. The track focused on pediatrics, starting with pediatric mental health, and then going to transitioning from childhood to adolescence to adulthood is happening in Century A. And the track on building a health care team, followed by therapy for retaining function is happening in Century B. So, what's listed as track one is here. What's listed as Track two is Century B and track three is Century A. Those are all gonna start promptly at 1:30 because there are online portions to this. So, you have a solid hour plus 9 minutes, thank you guys, to have lunch, connect, walk around, stretch. But we're gonna ask all the tracks to start right at 1:30. Alright, enjoy lunch, everybody.