ROUGHLY EDITED COPY

EHDI – Florence

Massachusetts Eye and Ear Pediatric Case Studies of Congenital Cytomegalovirus (cCMV)

Casey Judd

March 5, 2019

3:45 – 4:15 pm

CART/CAPTIONING PROVIDED BY:

ALTERNATIVE COMMUNICATION SERVICES, LLC

[WWW.CAPTIONFAMILY.COM](http://WWW.CAPTIONFAMILY.COM)

"This text is being provided in a rough draft format. Communication Access Realtime Translation (CART) is provided in order to facilitate communication accessibility and may not be a totally verbatim record of the proceedings."

>> Okay... looks like we can get started. Good afternoon, everyone. We've got a minute if you want to finish ‑‑ it's okay. It's snack time, I get it.   
[laughter]

All right... good afternoon, thank you so much for coming. After one of the last talks of the conference, we really appreciate it. My name is Dr. Cheryl Glovsky. I'm an audiologist at Mass Eye and Ear Infirmary. I'm the Program Director of the universal and newborn hearing screening program. For Mass Eye and Ear. We have three hospitals we work with. I'll be presenting with my colleague, Dr. Heidi Leonard who is the Pediatric specialist at Mass Eye and Ear.

For the past nine months ‑‑ Dr. Leonard and I have been working together on putting together initial case studies from Mass Eye and Ear and we spent time understanding and learning Congenital CMV. I'm an audiologist and thought I knew a lot about Congenital CMV, but turns out, I didn't. We'll give a brief overview ‑‑ if this is repetitive ‑‑ I'm sorry. I don't know exactly who my audience is today, but I wanted to briefly review things I recently learned as well.

CMV, cytomegalovirus is the most‑common infectious cause of birth defects in the United States. According to the CDC, one in 200 infants is born with Congenital CMV infection.

Of these, about 10 to 15% have symptomatic Congenital CMV. 85 to 90% of them have asymptomatic Congenital CMV.

Isolated hearing loss is considered asymptomatic. So... as an audiologist, that was really confusing to me, but it was considered, maybe, just hearing loss. Another statistic, studies have shown that about 15% of asymptomatic Congenital CMV ‑‑ so... no symptoms develop late onset hearing loss.

So... of these babies that do have symptoms... there are several that you can see here, of course, hearing loss, petechiae, jaundice, microcephaly, intrauterine growth restriction, seizures, retinitis, these are symptoms we see.

This is a slide from the national CMV foundation. Every hour, according to the National CMV Foundation, one child is permanently disabled by CMV. It's the leading nongenetic cause of childhood hearing loss... and... 90% of babies born appear healthy at birth.

When we talk about the symptoms ‑‑ some of the conditions we see... can vary from severe to very mild. Of course, at the severe end, we see cerebral palsy, seizures, failure to thrive, hearing loss, vision loss... and you know... in the middle, you're also going to see all of these cognitive ‑‑ cognitive delays, learning issues, feeding and sleeping issues ‑‑ vision loss, hearing loss... all the way to no symptoms whatsoever.

As I started to learn about this condition... and understand ‑‑ again... surprised that I did not know a lot of this, and... finding out that there are a lot of people out there that don't know anything about this condition.

Most people don't realize they have been infected with CMV. One of the highest risk groups are pregnant women who have not contracted CMV prior to pregnancy.

And... what we're finding, studies have shown, and estimate that as many as 70% of healthy children between ages 1 to 3 are infected with CMV. So... of course, it's very common in home and daycare centers. So... daycare providers are, are particularly susceptible. We did learn recently that in Germany, that a pregnant daycare provider is not allowed to go into work until she's given birth to prevent the primary infection of CMV.

This is just another slide to illustrate how little is known about this condition. So... as you can see on one end... the number of children that are born in the U.S. with Congenital CMV, versus the percentage of how many people are aware of this condition, 14%.

So... if we can do anything, it's really to spread the word and to make sure everyone is aware of this condition.

Some of the recommendations, for pregnant women... this is very difficult. You shouldn't, you know... share a toothbrush or kiss your toddler on the mouth or put the pacifier in your mouth. Things that moms do every day, try not to share food or drinks. Wash your hands all the time. Clean toys, countertops, those things ‑‑ they're saying, you know, can help prevent this primary infection.

I mean, I have to say, I'm learning about all this ‑‑ my, my sister‑in‑law is pregnant with her third child and I'm telling my brother, you need to let her know about this. I don't want her to be nervous ‑‑ I don't want her to be scared. Please... you know, it's much scarier to contract ‑‑ for her baby to contract this condition, so... it is, it is just something that we all need to spread the word about.

So... much like how universal newborn hearing screenings started. Everybody's working towards universal CMV and we're so not there yet.

What is starting to happen is a targeted CMV screen, so... any refer on a hearing screening at birth, will trigger a screen for CMV. And of the other risk factors, such as ones that were mentioned before, the testing needs to be done within three weeks... otherwise ‑‑ you can't separate out a congenital infection, versus an acquired infection ‑‑ the testing can be performed by urine or saliva or blood spot testing.

We have been talking with Massachusetts General Hospital, they are now doing targeted screening there and the cheek swab is used at that hospital and has a 98% sensitivity. Uh‑oh. Frozen.

>> We need some IT over here.

>> Okay... so... Mass Eye and Ear and Mass General Hospital have come together ‑‑ it was frozen, but... now it's not ‑‑  
 >> Is it working now?   
 >> Sometimes if you accidentally click up here ‑‑ you just have to click below it. And it may work ‑‑  
 >> Got it. So... Mass General and a few other areas in Boston plus a few across state are implementing the targeted referrals. At Mass General ‑‑ if a baby comes back positive, they immediately see infectious disease and we've had babies like five days old go to the infectious disease people and then come get a hearing test, the last baby was nine days old, that we tested.

Infectious diseases prescribe the antivirals. All babies with symptomatic CMV, the really involved babies with cerebral palsy and the ‑‑ all of the other, much more involved symptoms automatically receive these antivirals because it's thought that it, it helps with the neutral transmission, so... any advantage that that baby can get through the antivirals, it's no question that they just receive it.

Babies that are testing positive for CMV are referred to ophthalmology, audiology, autology, and early intervention.

So... the treatment is Valganciclovir, which is antiviral. Babies receive automatic treatment for six months because of that neural transmission improvement. Asymptomatic CMV or isolated hearing loss ‑‑ it's really up to the parents if they want to pursue that or not.

We're kind of in our Boston bubble, I thought that this was offered to all babies ‑‑ and... it's not ‑‑ so... we're actually in a pretty woke environment in Boston, so... the infectious disease people at these hospitals will lay it out for the parents and it's really a parental decision.

They start with a six‑week course. They have to do blood draws every couple weeks to make sure the white blood cell count is doing okay. If they're okay at six weeks, then they will continue on for six months.

So... no consensus on how to treat asymptomatic CMV. What the infectious disease folks are doing at Mass General, they're actually following the symptomatic CMV protocol and offering it to the parents as an option. There is a clinical trial starting out, that Mass Eye and Ear is involved in. They picked about 15 sites across the country and they're randomizing positive CMV babies that have hearing loss into half get the antivirals and half don't ‑‑ they're seeing ‑‑ it's actually trying to nail down what a good protocol would be, so that we have that.

So... again... during the study, there's six months of the study drug, there's blood draws, they do phone surveys, because the ultimate goal is to make sure that hearing is adequate for speech and language development for as long as possible.

The audiological side of it is that they are tested by ABR test ing pretty quickly, within two or three weeks of age and tested at 12 months and 24 months to see how and if the hearing changes.

Case studies, we chose four case studies. The first two I'll present are actually patients that are teenagers or just entering college. This is something that ‑‑ this is how we approach CMV, 15, 17 years ago. So... the first patient had a left ear refer on her newborn hearing screening. Didn't receive antiviral treatment, because we weren't doing it back then.

At five months, she came to us for a second opinion. We don't have actual data from when she was a newborn, but via ABR, her right here was normal and left ear had a moderate to severe hearing loss.

At 17 months, her hearing had gone to this. She had a mild hearing loss on the right side, stable on the left. We put a hearing aid on that right ear... at 27 months, this is what her hearing was at that time. Moderate hearing loss on the right and profound on the left.

And 2.5 years, she was profound bilaterally. 3 years had a cochlear implant for the right here. 7 years, got one for the other side. The reason they kept on top of the hearing ‑‑ she had a lot of speech and language delays that were related to this hearing loss and currently, she receives excellent benefit from her implants. She does incredibly well.

The next one... actually past their newborn hearing screening in both ears, we know the mother tested positive for CMV at eight weeks gestation. Parents didn't want the baby tested for whatever reason, but... it's kind of obvious that it's a CMV.

They were enrolled in early intervention because there was delayed speech and language and they referred for a hearing test... and we saw her first at two and a half years of age ‑‑ so... the left ear was normal, the right ear did have a hearing loss ‑‑ she did pass her newborn hearing screening.

>> Sorry... hold on... continue...

>> So... with this particular kiddo, did they test because he was referred to early intervention for language delays?   
 >> Early intervention ‑‑  
 >> Did they test his hearing?   
 >> They referred him to us ‑‑  
 >> Okay.

>> Any speech and language is so common for a hearing test to rule it out. That's when she was first identified.

>> Okay... what we've found is that routinely, hearing screenings are not done or referred from early intervention. So... I was just curious.

>> Not Massachusetts. Almost always ‑‑  
 >> Yeah... that's on the checkoff list. They were referred.

>> Yep.

>> Three years of age, the left ear progressed, as did the right. And four years ‑‑ they are now both severe.

So... five years of age, cochlear implant for the right ear. The left ear, word recognition was 2%. The left ear was implanted as well. She is either entering college or is a freshman right now and doing beautifully. So... another success story.

All right... case number three... these are kiddos that are more recent to our clinic and... so... the first case, this kid is about five years old now... she referred on the left ear only in the newborn hearing screening. Might be seeing a trend. Many of these kids refer on one or both ears.

I'm sorry ‑‑ actually, pass one or both ears. This kid was isolated hearing loss... so considered asymptomatic and she was treated with antivirals. This was the first test ‑‑ this is test at two weeks... and... we see slight to moderate hearing loss in the right ear. Moderate hearing loss in the left ear. She was tested at two weeks and was treated at that time.

She had a behavioral hearing test, at eight months ‑‑ she was tested in between this time. But... this was the first behavioral hearing test we got and... her hearing is improved on the left ear, considerably and... she does still have some residual, high frequency hearing loss on the right side, but hearing did improve considerably on the left.

Since that time... we did five audiograms, from ages 14 months to 28 months... and very stable, left ear normal, high frequency hearing loss on the right side. You can see a big difference. These more‑recent kids are tested every three months or as needed in our clinic now.

This happened at three years. There was a decrease that happened very suddenly ‑‑ it went from normal to moderate hearing loss and... right ear stayed stable and this kid did get a second round of anti‑bio treatment. We're seeing mild moderate right, continued severe on the left. We tested every three months, 14 audiograms, things stayed pretty stable ‑‑ she had good recognition on the right side... very poor on the left and then, again, she was referred ‑‑ you know, she didn't even really need to be referred, because we tested her so often. But... she kept telling mom that her hearing aid was broken on her good side, on her right side. It was broken, mom, something's broken and teachers were complaining about, she was very distracted and something was concerning.

In three months she went from understanding about 78% of the words on the testing we gave her to 2%. So... her hearing did plummet on that side.

So... she was implanted three months later with cochlear implant in the left ear. At this point... given the regular maintenance, monitoring schedule, and very closely followed, early intervention, speech language evaluations, she still has speech language development that is normal and meeting milestones and at this point, she has ‑‑ or she does receive very good benefit from her left cochlear implant and we've been recommending a right cochlear implant.

Case four, also very recent. Right ear refer ‑‑ left ear pass ‑‑ and... he was seen in nine days ‑‑ this was hearing loss at the first test ‑‑ which was mild, moderate, left, severe profound right. And... treated again, antivirals. That left ear did come up ‑‑ both ears did come up a bit.

He stayed stable at nine months and... so... left ear, some high frequency residual hearing loss, and then... continued severe on the right. Had some otitis media that caused a little trouble, pushed things down a little bit, but relatively stable. And we saw him recently, a couple weeks ago, things are decreasing a little bit on that left side. We're going to follow him very closely. He's using a hearing aid on the right and on the left as needed.

At this point, we recommended did a cochlear implant for the right ear and amplification for the left ear is needed. He was immediately enrolled in early intervention and at this point, his speech and language development is meeting milestones and has been relatively normal.

So... the discussion, prior to antiviral treatment, we saw more rapid progression of hearing loss on the small number of cases that we looked at so far. Those two ‑‑ there's several of them we've seen. Severe to profound by age three. And we had much less vigorous monitoring schedule. And... less timely intervention, because we just didn't understand the progression of this condition.

What we're seeing after antiviral is that there's longer time periods of normal hearing in at least one ear and that this allows access to speech, sounds during very critical speech/language learning period... and it increasing the probability of meeting milestones.

So... again, we recommend frequent monitoring and our conclusions...

>> The main goal is that CMV testing should be incorporated into the Universal Newborn Hearing Screening Program. Even because those babies that pass their screening, we've seen the hearing loss come up at age 2. There's a delayed onset that kind of happens. So... having a universal screen would be amazing.

The antiviral treatments can certainly improve hearing ‑‑ we're trying to preserve normal hearing through the critical period for speech and language acquisition. Although... that hearing improvement may not be permanent. It usually seems to trend downwards at some point.

We changed on how we approach this type of patient ‑‑ we test them much more often and really, we'll do a threshold ABR probably within the first two weeks and then do one at two months and four months and then... as soon as they're ready to go into the booth. It's like every two months at this point.

We're also more aggressively intervening with cochlear implants at this point. I mean, a few, few years ago, it was unheard of to implant unilaterally when the other ear was okay... but... the trend seems to be that the other ear will be compromised at some point, so... get the implant in and the child used to it before everything starts to change.

And... again, the kids that we have in cochlear implants are doing amazing with them. They get really, really good benefit. So... it seems to be a good option.

And we have one and a half minutes. Any questions?

>> I'm wondering, did you see any patterns in configuration? It looked like they were all over the place. Was there a point where they all plummeted to profound or age, I guess?   
 >> We certainly saw asymmetry, with a lot of the kids we were looking at, we actually are going to open this up and try to look at all of our cases, but that is one thing we were seeing, the asymmetry, some of the earlier cases seem to go out by age 3 and we're still seeing that progression.

Another interesting thing ‑‑ when I started working at Mass Eye and Ear, I was told by the more‑experienced audiologists, if it's unilateral, it can't be CMV, it's always a bilateral hearing loss and we only see unilaterals, at this point, so... wrong.

>> I've been working with CMV babies for a long time. I can tell you from experience, there's no typical pattern. It can be unilateral, asymmetrical, progressive, stair step, fluctuating, there's no way to diagnosis it based upon the audio metric pattern.

In hospitals across the country, we are really good about testing mom for HIV, we're really bad for testing for CMV. Part is because of the cost of the test. Universal CMV is the desired outcome and... as this movement to bring CMV to the forefront gains momentum, one of the things that needs to be done is to develop a screening test that's going to be much less expensive than what it is now.

Once we get that, and then, the, the results come back with appropriate specificity and sensitivity, then we can start thinking about incorporating that as universal and making that an adjunct to the universal newborn hearing screening.

The challenge is, the baby who is asymptomatic at birth. The child who first, first trimester, CMV is going to be very obvious that this child is affected. But... late trimester or contracting the virus in the birth canal ‑‑ the child might show [indiscernible], but that's transitory, and then the majority will be asymptomatic, completely and that's going to be the challenge to track them and find them.

>> Great, thank you.

>> We're out of time for more questions, but if you guys wanted to if not asking questions, the conversation, more than welcome to in the hallway, thank you.

[Presentation concluded at 5:11:00 p.m. ET].

"This text is being provided in a rough draft format. Communication Access Realtime Translation (CART) is provided in order to facilitate communication accessibility and may not be a totally verbatim record of the proceedings."