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Recognizing the Early and Subtle Signs and Symptoms of Rett Syndrome

Announcer:
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Dr. Neul:
Hello, my name is Jeff Neul, and today I'm going to talk about Recognizing the Early and Subtle Signs and Symptoms of Rett Syndrome.

So first, what is Rett syndrome? Rett syndrome is a severe neurodevelopmental disorder and is characterized by a characteristic disease pattern, where you have a normal initial apparently development, with some delay, with some failure to meet milestones, and then a regression, specifically loss of acquired hand skills and spoken language.

After this, there's also a characteristic feature such as gait abnormalities, and stereotypic hand movements classically wringing or washing. This regression is time limited; it doesn't go on continually. Then you have stabilization, which is called the plateau phase, and you start having evolution of clinical issues and changes in motor function.

The majority of cases of Rett syndrome are caused by mutations in the X-linked gene, methyl-CpG binding protein 2, or MECP2. However, there are people who have clinical issues that are like Rett, but do not have mutations in MECP2. It's mostly, but not exclusively found in girls and women in about 1 in 10,000 live female births.

There are challenges in the diagnosis. The regression typically occurs between 18 to 30 months of life, but the average age of diagnosis is 2.7 years. This diagnosis is much less likely to be made by a pediatrician than a specialist. There are some features such as marked delay in acquisition of basic motor skills that can lead to an earlier diagnosis. And there's a later diagnosis with normal head circumference.

One of the issues is that the developmental delay may be mild, the family may be raising concerns that a child's not meeting milestones at a rate of siblings, but still within the accepted norm. There's also a misconception that their regression of skills is rapid. This loss of skills may occur quickly in some cases, but often occur over many months. And the loss of spoken language enhanced skills may occur at different times, which can lead to confusion and challenges in the diagnosis.

There's also some confusion about the degree of regression; it doesn't require that there's a quick complete acquisition of hand skills or spoken language. And it doesn't require a complete loss of skills. It just can be a loss of, say, having spoken multiple words, now only speaking one or speaking a word, now only babbling.

There's also a misconception about microcephaly. Not all people with Rett syndrome have absolute microcephaly, meaning they've gone below the 2nd percentile. But the change in the rate of head growth is a very important feature even if it is not objectively microcephalic. And we may see falling off these growth curves even as early as 1 to 2 months of life.

There are boys who have Rett syndrome. And one example is a family once told me if we had let his hair grow out long and put it in

braids, we would have made - had the diagnosis much earlier. This can happen when you have Klinefelter's such as you have XXY and a mutation in MECP2 gene, or somatic mosaicism mutation in the MECP2 gene in boys.

Now we need to develop ways to identify people earlier with Rett syndrome. So there are some things that have been noted. So oftentimes families will describe them as being too good of infants with evidence of hypotonia and reflux early in life. So basically, they would sleep a lot and didn't really interact that much early in life. There are also subtle sensitive and specific developmental abnormalities that have been reported by different groups with careful analysis of videos before regression. The MECP2 mutations with well-known relationship with Rett syndrome, if we found those early too, that might help. And then physical clinical features such as the careful early head growth assessment that I mentioned.

So in closing, I want to emphasize that Rett syndrome is a clinical diagnosis. Most of the people who are affected are female and have mutations in MECP2, but there are boys and people who do not have mutations in MECP2 who have Rett syndrome. The developmental delay may be subtle and within a broad range of normal development. Regression with a loss of spoken language and hand skills define the disorder. But this regression may occur over many, many months or very rapidly. And the timing of skill loss may occur at different times for specific domains. Abnormalities in head growth rate, even without becoming microcephalic. And unusual vocalizations and hand use prior to regression might allow early identification of people with Rett syndrome.

So thank you for watching, and thanks to all my friends with Rett syndrome.

Announcer:
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