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ReachMD

www.reachmd.com

info@reachmd.com

(866) 423-7849

Diagnosing Rett Syndrome: A Lifespan Approach to Clinical Recognition

Announcer:

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Dr. Gu:

This is CE on ReachMD, and I'm Dr. Payal Gu. Here with me today is Dr. Edward Dabrowski. Welcome to this case-based discussion on Rett syndrome, a complex neurodevelopmental disorder in which early recognition remains critical.

In this episode, we'll review the hallmark clinical features, as well as atypical signs that can obscure diagnosis and delay care. Our goal is to strengthen diagnostic suspicion and improve timely identification in clinical practice.

So let's begin with the case. We have a 20-month-old girl who was brought in by her parents with concerns regarding developmental regression. She previously had normal development. She sat independently by 7 months, was babbling by 8 months, and using "mama" and "dada" by 12 months. She was able to grasp toys, self-feed, and engage socially. But over the past 2 to 3 months the parents have observed that she is babbling less and is no longer demonstrating use of the words that she had started to use purposefully. She has also stopped reaching for toys and trying to feed herself. In addition to that, her parents mentioned that they've started to observe an odd behavior where she's rubbing her hands together repetitively without a clear purpose, and at the same time they're also observing that she's less socially engaged, doesn't want to make eye contact, and at times they've noticed that she will have bouts of just laughing without a clear purpose.

Dr. Dabrowski, given the pattern of normal early developmental progress followed by this abrupt regression associated with loss of purposeful hand use and emergence of these odd characteristic hand movements, how do you begin to differentiate Rett syndrome from other conditions like autism, hearing impairment, or other genetic conditions?

Dr. Dabrowski:

Well, that's a great question. And the first thing that I do in a situation like this is I take a step back, and I think about what are the criteria of classic Rett syndrome. And they include a partial or a complete loss of acquired purposeful hand movements, a substitution, if you will, of hand movements, whether it's handwashing, hand-wringing, scrubbing, or rubbing, etc., a loss of spoken language, and of course a gait disturbance, if the child was further along and that they had been walking or started to walk, and then they've had a regression.

And so that's the very first thing that comes to mind as a possibility. And then the question is, what is the differential, and you're absolutely correct. Many times, children with hearing loss don't respond, they're delayed in their language, or they may stop for a short period of time, etc. But it's not the same thing. And you can classically give them a hearing test and make it very, very simple to differentiate.

Autistic kids never really connect with you. They never have this developmental, like, mommy and daddy are mine. It's more interested

in external objects and that sort of thing. So those are the things that you can start thinking about as being different from what the 4 criteria are.

And on top of that, you have, did a person have a head injury? Did the person having a neurologic infection that may have intervened in this child's development? And most certainly you start thinking about more serious disorders, which are degenerative disorders, which involve metabolic problems, inclusive of Batten's disease and Niemann-Pick disease, or other lysosomal disorders.

So those are the things that you really take a peek at and to give you a sense of should Rett's be on your radar.

Dr. Gu:

Wonderful, thank you for covering that.

Now, I have some other questions for you. Rett syndrome does not always present in a classic way, so how do you approach identifying atypical versus variant forms of Rett syndrome?

Dr. Dabrowski:

And that, again, goes back to if you don't fit into the typical or classic Rett's category with the 4 items that I've mentioned, you take a look and look for at least 2 of the 4 main characteristics to fit this atypical Rett's-like presentation.

And so then you also look for 5 of the 11 other supportive criteria that are out and available, including breathing disturbances, and that can either be, for example, hyperventilation, breath holding, etc.; bruxism, or grinding of the teeth while you're awake; an impaired sleep pattern; a growth retardation, particularly, for example, small head; small, cold hands and feet; diminished responses to pain; scoliosis; kyphosis. In addition, tone may be different. They may either be a little stiff, or they may more likely be a little bit more hypotonic or low tone. And they may be getting vasomotor disturbances where you start seeing changes in color in their limbs, particularly their feet. They turn very blue. Some may actually turn bright red. It all depends on the kid.

Dr. Gu:

Great, thank you for going over that. Really quite interesting how different these variations can be.

What role do you think does genetic testing play in confirming or clarifying a Rett syndrome diagnosis? And how do you interpret these results in clinical practice?

Dr. Dabrowski:

Yeah, again, I think the genetics is what's going to give you a diagnosis, for the most part, realizing that Rett's is a clinical diagnosis, and sometimes we don't find the classic gene changes that we would expect.

But typically, if you take a look at the MECP2 sequencing, looking at exons 1 through 4, which is your first line, you find that 80% to 90% of the classic Rett's cases are detected. If you take a look at atypical, it's 50% to 70%.

Now, if it's positive for the MECP2 gene, you are diagnosis confirmed; you're in good shape in that respect. If it's a negative, then you can move on to deletion and duplication analysis of the MECP2 gene, which will pick up another 10% or so of the cases.

And then finally you may want to do broader genetic testing, like whole genome, or what have you. You may be able to find CDKL5 or FOXP1 or other similar genetic disorders.

Dr. Gu:

Well, this has been a great bite-sized discussion. Our time is up. Thank you all for listening.

Dr. Dabrowski:

Thank you.

Announcer:

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