Recently discovered ReNU Syndrome diagnosis provides 'renewed' purpose and hope

Jessica (ReNU Syndrome Mom)

My son is thirteen now and as I look back to the beginning, it's been quite a roller coaster ride. Excited to bring the first baby boy into my family, I remember going in for the ultrasound. I was told he had clubfoot but was reassured that it was relatively common. Later in the pregnancy, I learned that his head size was measuring on the smaller side. All of the genetic test results came back normal, and I was again hopeful that everything would be fine.

We welcomed my little guy via c-section due to his frank breech position. He was a cute and cuddly little baby, but as the days passed, we started having concerns. He struggled to gain weight and was so floppy that he couldn't hold his head up. The doctor treating his foot told us he also had hip dysplasia. He kept looking in an upward direction and we noticed that he had nystagmus, where his eyes constantly move side to side. Brain abnormalities showed up on his MRI, and as time went on, we really started panicking about the missed milestones, poor vision, low muscle tone, easily broken bones, and lack of speech. We began traveling to many specialists to figure out what was going on. It was scary to not know what had happened in the past that might have caused this, or what we had in store for the future.

I would stay up all night googling his symptoms and emailing his doctors, but none of the diagnoses I could find tied it all together. I couldn't believe that in this day and age, there could be no medical explanation, and that my son was the only one in the world to have this combination of issues. As the years went by, more medical problems arose for my sweet boy to overcome, and there were still no answers.

Eventually, a geneticist informed us about an Undiagnosed Disease Network program. I submitted the lengthy application, and five years ago we piled in the car to travel for a week-long extensive testing session at the NIH in Maryland. We also participated in another Undiagnosed Disease program through the Broad Institute of MIT/Harvard. I had almost resigned that this would remain a great mystery when, to my complete surprise, I received the life-changing call this past April.

"You won't believe it, but we finally have an answer for you" I was told. I learned that most known genetic disorders are caused by protein-coding genes. However, there are many genes that don't code proteins that scientists had not previously explored. Remarkably, a small insertion in a non-coding gene called RNU4-2 had caused all of my son's symptoms. What's more is that this variant is actually quite prevalent. RNU4-2, or ReNU syndrome, has now been identified as one of the most common monogenic neurodevelopmental disorders and is thought to possibly affect over one hundred thousand people!

I was put in touch with the families diagnosed right before and right after mine and was shocked that these children not only had familiar medical challenges, but actually looked and acted just like my son. From loving water, music, and motion, to having affectionate personalities and similar mannerisms – it was mind-blowing! As there were no papers or articles published yet at that time, I set up the Facebook group RNU4-2/ReNU Syndrome Family Connect so that our families could discuss our experiences and post new information as it became available. Amazingly, parents from all over the world including the United States, Canada, Europe, Australia, and beyond rapidly followed. All of us had been on our own parallel odysseys, searching for answers for our children their whole lives. No longer feeling lost and alone, the members of our growing group have forged a connected family. We began sharing ideas and tips, supporting each other, and building a united global community.

I've had the incredible opportunity to meet with some of the talented researchers who have discovered this syndrome, wonderful organizations like Unique, and award-winning scientists and clinicians. These great allies have inspired creating the RNU4-2/ReNU Syndrome Facebook Page as a collaborative space for families to interact with clinicians, researchers, pharma, and others to further advance impactful research. The website **www.renusyndrome.org** has also been launched as a repository for emerging content and will certainly evolve over time.

I never expected to be involved in one of the most significant genetic discoveries, but this experience has undoubtedly provided me with new perspective and purpose. Even the name 'ReNU' syndrome is so meaningful; it was created as a collaboration between the researchers and the families and symbolizes that finally having answers after all of this time truly 'renews' hope for a brighter future for those affected. On this roller coaster, there have been highs and lows, but now the fear of the unknown has been replaced by excitement for what's to come.

www.rarechromo.org