Educational & Developmental Intervention Services (EDIS) Personnel Development

KIT

Keeping In Touch

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Resource Article

At the Pediatrics Neurologic Clinic in Mashhad, Iran, an 8 year old boy was diagnosed with Angelman syndrome (AS). His diagnosis took more than 6 years to make. While this may sound like a long time, properly diagnosing rare disorders is a difficult challenge for the best of doctors. Going through this process is especially taxing on families as they communicate their ongoing and sometimes changing concerns about their child with doctor after doctor. In their article, Angelman Syndrome: A case report, Ashrafzadeh, et al., (2016) describe the process of diagnosing a child with AS.

The National Institutes of Health describe AS as a genetic disorder affecting between 1 in 12,000 to 20,000 live births. Children with AS typically demonstrate jerky, ataxic movements, developmental delay, significant speech and language delays, recurrent seizures and small head size. Another distinguishing characteristic is their happy disposition with frequent smiling, laughing and hand-flapping. Facial features are often affected and scoliosis may develop. Attention problems (hyperactivity), sleep problems, needing less sleep than typical children and fascination with water are also listed as common characteristics. As children get older their excitability diminishes as their sleep time increases. But cognitive and communication delays persist into adulthood. Lifespan does not appear negatively impacted. AS is caused by a mutation in the maternal copy of the UBE3A gene on chromosome 15 and most cases of AS are not inherited. Prader-Willi syndrome is closely related as it is also caused by a malfunction of the genes on chromosome 15.

In the case of our 8-year-old boy, he was born to healthy parents. His vaginal delivery was unremarkable with the exception of jaundice for which he received phototherapy. APGAR scores were within normal limits. At age 2 years, his parents noticed he was falling behind developmentally and he had an overly happy face. He began having tonic-colonic (formerly known as grand mal) seizures. He was also diagnosed with hypothyroidism and took

Resource Article (continued)

medication to address it. Motor milestones were delayed and he did not start walking independently until he was 4 years old.

Two years later, at 6 years of age, he was referred to Children Neurology Department in Mashhad due to attentional concerns (hyperactivity). The preliminary work-up suggested normal muscle tone, reflexes and range of motion. However, his gait was unsteady and he was unable to run. He presented with significant speech-language delay and mental retardation. As the work-up continued, laboratory results suggested nothing unusual except for his previously diagnosed hypothyroidism. Brain Magnetic Resonance Imaging (MRI) and complete blood count test (CBC) were also normal. As expected, electroencephalogram (EEG) findings showed abnormal electrical activity, but this was not surprising as his seizures had persisted since the age of 2 years and were difficult to control with medications. He received the diagnosis of AS after genetic testing showed malformation of genes on chromosome 15.

While this little boy initially presented with some symptoms consistent with AS (e.g., delayed walking, talking, seizures), his doctors pointed out additional characteristics, which were not of initial concerns to the parents, but which were consistent with a diagnosis of AS: jerky movements, wide mouth with unusual laughing and lip positioning.

The authors suggest, "…all physicians should consider rare syndromes such as AS in children or adults with neurodevelopment delay. Noting clinical presentation is very important, because clinical suspicions play a crucial role to choose the required laboratory tests" (p. 88). And yet, many of the behaviors parents note as concerns are not observed at 15 minute Well-Baby visits (and perhaps not even during longer developmental pediatric evaluations).

As early intervention providers, we certainly do not diagnose disorders. However, we help families understand typical development and as a team recognize the presence of any atypical behaviors. It is through the delivery of respectful support that early intervention providers can empower families to document, video and/or otherwise communicate unusual or concerning behaviors to the doctors whom their children see.

Ashrafzadeh, F., Sadrnabavi, A., Akhondian, J., Beiraghi Toosi, M., Mohammadi, M., and Hassanpour, K. (2016). Angelman Syndrome: A case report. Iranian Journal of Child Neurology, 10 (2), 86-89.

What do the data say?

What are challenges associated with achieving an accurate diagnoses of rare diagnoses?

There is no doubt that rare diseases present particular medical challenges. Among these challenges is the relatively small number of patients affected. This contributes to the unfortunate reality of little market incentive to fund the essential research needed to understand different rare diseases. Also impeded is the ability to fully understand the nature and outcomes of various rare conditions, which complicates a doctor's ability to make an accurate and timely diagnosis. According to a survey conducted on behalf of Global Genes, patients visit an average of 7.3 (range, 1-300) physicians before receiving an accurate diagnosis and the mean length of time from symptom onset to accurate diagnosis was 4.8 years (range of 0 to 20 years) (Engel, Bagal, Broback, & Boice, 2013). Other challenges include identifying appropriate treatment and medication options and optimally finding cures.

In an article by Shaikh-Lesko (2014), Dr. Francis Collins, famous for leading the Human Genome Project, remarked, "*The doctors and scientists hunting for new cures and treatments work in a constant state of tension. They operate in a tremendously high-stakes environment, pouring years of their lives into research as the people who inspire them continue to suffer and even die. Drug hunters face failure after failure, almost never followed by success. Decades of work flame out. Promising ideas turn into dead ends*" (p. 1). While the bleakness of this statement easily pulls at one's heartstrings, the drive and interest of doctors and scientists to do the work is promising. In fact, the Global Genes survey reported that most physicians (60% of primary care physicians and 80% of specialists) said they welcome the challenge that rare diseases bring and want to be part of finding a diagnosis (Engel, et al., 2013).

The difficulties associated with accurate and timely diagnoses present challenges for patients and physicians. When it comes to conducting the necessary workups for a rare diagnosis time is a recognized barrier. According to health care providers (N=367) responding to the Global Genes survey, 40% of primary care providers and just under 25% of specialists either "strongly agreed" or "agreed" to the statement *"I am not allowed sufficient time with a patient to do a workup for a rare disease even if I suspect one."* (Engel, et al., 2013). The upside to this is that specialists are often involved in the diagnostic process. In fact, 64.6% of primary care providers reported that when they suspect something is wrong they refer the patient to a specialist to make the diagnosis (Engel, et al., 2013).

From the patient perspective, the patient, parents of patient, and spouse respondents included in the Global Genes survey, rated their physician's knowledge of rare diseases more positively for the physician who made the diagnosis, yet less positive for the physician first seen at symptom onset. Regarding the diagnosing physician, 62.3% of patient respondents reported satisfaction with the physician's training. Yet, they also perceived that all physicians need more training in rare diagnoses.

Considering the possible outcomes of delayed and or mistaken diagnoses accurate and timely diagnosis is critical. As early intervention providers supporting families and helping them navigate the diagnosis process it is important to consider the myriad of challenges associated with the diagnosis process.

Shaikh-Lesko, R. (11 December 2014). Finding cures for the most challenging diseases. SCOPE, Stanford Medicine. Accessed from: http://scopeblog.stanford.edu/2014/12/11/finding-cures-for-the-most-challenging-diseases/

Engel, P. A., Bagal, S., Broback, M., & Boice, N. (2013). Physician and patient perceptions regarding physician training in rare diseases: The need for stronger educational initiatives for physicians. The Journal of Rare Disorders, 1(2). Accessed from http://www.journalofraredisorders.com/pub/IssuePDFs/Engel.pdf

Consultation Corner

From September through December 2016 we are excited to have **Dr. Deborah A. Bruns** as our Consultation Corner expert. This series will explore *Supporting Families Through the Diagnosis Process and Looking Closer at Rare Conditions.* This month we briefly explore two questions and review some helpful resources.

What is the range of outcomes for a child with rare chromosomal disorders?

The diagnostic process can be a difficult one (see September 2016 article). An additional facet is when determining a rare diagnosis, one with limited information about prognosis and necessary services (developmental and medical). Parents need information as well as support to navigate into, for many, the unknown landscape of a rare diagnosis.

For children diagnosed with trisomy 21 (Down syndrome), for example, much is known of physical characteristics, medical needs and developmental status. Making it somewhat easier for possibilities to be considered and decisions to be made. However, for children with rare conditions such as trisomy 18 (Edwards syndrome) and encephalocele (group of neural tube defects affecting brain development), it is not as well defined. Both include a number of distinct physical characteristics but long-term outcomes are less clear. Research articles primarily highlight limited mortality and reluctance to medical interventions such as surgery to correct, for example, a cardiac anomaly. Given the rare nature of conditions, such as Edwards syndrome and encephalocele, it is difficult to anticipate the range of outcomes.

What's important for families to know including recommendations and "good to know" resources?

Parents want information they can use, information that provides both sides, the positive and the not so positive. At this time, parents have access to social media to learn about their child's rare diagnosis and the range in outcomes. They also seek objective recommendations. Recommendations not colored by the bleak view taken by some professionals, especially those in the medical field. Finding answers can be particularly difficult when it comes to rare diseases. This also makes it difficult for early intervention providers, as they too may have very limited experience with a particular child's rare diagnoses.

Yet, early intervention providers do need to be knowledgeable of resources that can help parents make the most appropriate decisions on behalf of their children. To this end, online sources are plentiful but must be used with caution. There are informational websites that provide informative articles and related materials. Yet, some of the available sources are written with complicated jargon and not necessarily aimed at parents and others may include information that is not entirely accurate or up to date. This too is where early intervention providers can assist families with "translating" and deciphering the information that is most pertinent to their needs and interests.

Early intervention providers can also offer parents connections with other parents and families. Connections can be made with local and regional hospitals, neonatal intensive care units specifically, and associated follow-up clinics. Pediatric specialists will also be involved in their children's care. While they

Consultation Corner (continued)

cannot directly connect parents due to HIPPA restrictions, a directory or similar compendium can be developed or accessed through established organizations that include state level groups of larger organizations focusing on children with specific rare diagnoses. The Support Organization of Trisomy 18, Trisomy 13 and Related Disorders (SOFT) is one example. Chapter Chairs in each state provide outreach to parents with newly diagnosed children. Information to assist with daily and medical care is available for download on SOFT's website (see http://trisomy.org/wp-content/uploads/2014/08/Carebook-updated-8-15-14.pdf). In addition, an annual conference brings together 50-75 families with both living and deceased children for family activities, information exchange and support. The resources below are also recognized trustworthy links to help parents and providers learn more about rare diseases.

What are some go to resources for understanding more about rare diseases?

- **National Organization for Rare Disorders (NORD) (**http://rarediseases.org**) -** NORD includes a searchable data base of rare diseases. Under the tab for patients and families, a drop down alphabetical listing of rare disorders provides detailed descriptions of disorders, frequently asked questions are reviewed, state health insurance information is listed and links to news about patient recruitment (for clinical trials) is available. There is also information for physicians, patient support (opportunities for patient assistance programs and workshops), and advocacy opportunities. Families may find this a good place to start as they investigate a newly given diagnosis.

- **Global Genes (**https://globalgenes.org**) -** Global Genes is a patient advocacy organization with a mission to build awareness, provide education, and link people with resources. This site also includes fact sheets, webinars, podcasts and a host of other resources on rare diseases.

- **Genetic and Rare Diseases Information Center (GARD) (**https://rarediseases.info.nih.gov/**)** - GARD is part of the U.S. Department of Health and Human Services and the National Institutes of Health (NIH). It is an information center aimed to help people who have rare diseases, their family members and friends as well as the medical community and other community members and leaders. GARD helps answer questions, drawing from research and experts in the field of rare diseases. It includes a database of diseases by name and by disease category, and many other useful resources. One particularly helpful resource is video and resource guide on "Tips for the undiagnosed" located at: **(**https://rarediseases.info.nih.gov/resources/pages/24/tips-for-the-undiagnosed**)**

- **Orphanet (**http://www.orpha.net**)** - Orphanet is a reference portal on rare diseases and orphan drugs. This site provides information about diagnostic testing, research trials, patient organizations, and more. It includes a search tool that provides links to specific condition resources.

- **Support Organization for Trisomy 18, 13, and Related Disorders (SOFT) (**http://trisomy.org**)** - SOFT is a network for families and professionals involved in supporting and understanding Trisomy 18, 13, and related disorders. It includes a vast array of resources as well as video links to related topics.

On the WWW

The Mighty is a resource aimed at helping families of individuals with rare diseases. This site provides a different type of information. It provides material that is the upbeat and insightful. It shares stories and accounts of the joyful moments that are also part of having a child with a rare condition. The Mighty is working toward building a community that can be accessed for support and shared to build awareness. All too often, the pessimistic outcomes and devastation of a diagnosis becomes the focus. The Mighty, on the other hand, shares the reality that life does not end when a child is diagnosed with a rare disease. The Mighty provides a platform for sharing stories that can inspire people. Check out the family stories and much more at The Mighty.

https://themighty.com

Continuing Education for KIT Readers

The Comprehensive System of Personnel Development (CSPD) is offering a continuing education opportunity for KIT readers.

In line with the focus on *Supporting Families Through the Diagnosis Process—Looking Closer at Rare Conditions,* readers are invited to receive continuing education contact hours for reading the monthly KIT publications (September - December 2016) and completing a multiple-choice exam about the content covered in these KITs.

KIT readers will receive the exam in January 2017. There is no need to register for the CEUs. Rather, if you are interested complete the exam online at www.edis.army.mil

Upon successful completion of the exam, you will receive a certificate of non-discipline specific continuing education contact hours.

KIT Newsletters are available online at **www.edis.army.mil**

Thank you for your continued interest in the KIT.