Hope for hypothalamic hamartomas—Cofounders stories

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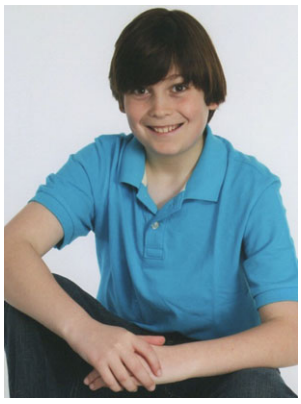

CJ… As Jon Soeby was cutting the umbilical cord, his newborn son CJ stared making a grunting noise, and the doctor commented "What do you know, I've never had one try to talk this early before." He didn't assume anything was wrong, just something new. But Jon and Lisa both looked at each other and thought sometimes new isn't good! Over the next several days, they noticed these episodes of grunting occurred around the clock every 15 min. Over the next 3 months, three doctors told them they we were just nervous parents and CJ probably had colic. Finally, a magnetic resonance imaging (MRI) study revealed a tumor and exploratory brain surgery confirmed a diagnosis of a hypothalamic hamartoma (HH). They were told there was nothing that could be done for CJ and they would just have to go home and live with CJ's 100–300 seizures a day.

For the next 3 years, the Soebys searched medical libraries, consulted doctors, and turned to the Internet for information. Unfortunately, because HH was so rare, information was sketchy at best. One day, while searching every corner of the Internet, they came across e-mails from a couple of families who had children with the same diagnosis. One family from Australia indicated in an e-mail that their daughter was going to be operated on by a neurosurgeon in Melbourne who had been working on cadavers for 6 months to try to go deep into the brain to remove the tumor without damaging critical structures in the process. Her surgery was hugely successful. The Soebys approached doctors in the United States to perform this same operation for CJ. Unfortunately, they believed it was too risky and were not willing to do it.

The Soebys traveled to Australia. CJ's 4-h surgery was a complete success. He was seizure-free with no complications. When the Soebys returned home, they pressed the U.S. team to reconsider their decision. Six months later, their surgeon from Melbourne came to Barrow Neurological Institute to demonstrate the technique on six children. All six patients were children from the online support group that had grown to >100 families from all over the world.

CJ was seizure-free for almost 3 years. However, at age 8, the seizures returned. CJ was a candidate for surgery at Barrow to remove the last bit of tumor that remained. This would not have been possible if the doctors at Barrow had not embraced the approach and taken it to the next level with the high-tech surgical equipment available today. Again, the surgery was a success; however, two small slivers remained. CJ had a fourth and final HH surgery in May of 2011. At age 16, CJ still has the occasional gelastic seizure but all visible HH is gone. He is doing well in high school, but he does continue to have challenges with his short-term memory, thyroid, and weight.

GRACE… A few months after Grace's first birthday, her mother, Erica, was changing her diaper and noticed blood. The pediatrician ordered a bone age test, which indicated an

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age of 2.5 years versus her chronological age of 15 months. A sonogram showed that Grace's uterus was maturing to puberty. An MRI was ordered to determine if a tumor was responsible for these endocrine issues. The MRI results showed a huge tumor, hypothalamic hamartoma, measuring 3.6 × 3.0 × 3.0 cm. Grace's parents, Erica and Perry, were told the tumor was causing the precocious puberty and the bone age issues Grace was experiencing and they should also be aware that this type of tumor could cause seizures and behavioral problems. Within 6 months, Grace was having >14 gelastic seizures per day and multiple complex partial seizures per week. She was also displaying the cognitive impact of the seizures, particularly in her expressive speech, and she was spending much of her day in "recovering mode" as a result of seizures. Grace's progression through the symptoms of HH continued, and in July 2006, she began to have hypothalamic rages. The onset of these rages were the turning point for the family in making the decision to move forward with surgery.

The surgery indicated a 90–95% resection. Although the year of recovery following surgery was tough, the good news was that Grace had not had a single seizure or a hypothalamic rage since leaving Arizona. The postoperative struggles continued with diabetes insipidus, uncontrollable hunger, and a decreased metabolism. Grace suffered surgical damage to her hypothalamus, which regulates the ability to control appetite. She did not feel full and therefore her parents had to measure/ration her food to prevent her from overeating. Instead of tracking seizures, Erica and Perry now measured all fluids in and out, weighed Grace daily, measured all food, and provided food on a strict time schedule. Grace's weight gain was a constant struggle. Grace's drive for food continued, and eventually she was diagnosed with the acquired form of Prader-Willi syndrome as a result of surgery.

Two years later Grace's parents again began noticing "episodes" of odd behaviors and blips of aggression from Grace. The next year was reminiscent of life before surgery. Grace's parents were working closely with her neurologist to find a balance of antiseizure medications to help decrease the frequency and the progression of her seizures, as well as trying to find the right antidepressant to help with her depression.

Soon after a routine follow-up MRI showed a sliver of the hypothalamic hamartoma and another surgery was recommended. However, before a final decision on surgery was made, Perry and Erica found Grace one early morning in her room having a seizure. Grace was unresponsive, and they knew something was terribly wrong. They called 911 and administered her clonazepam, which was for seizures lasting longer than 3–5 min. Grace was breathing and continued throughout the trip to the hospital. However, as soon as the ambulance pulled up to the doors, she went into cardiac arrest. Grace passed away on December 11, 2011, at 8:14 a.m. with Perry and Erica at her side.

MARK… As a toddler, Mark was quick to smile and laughed often. He seemed happy, but his parents Craig and Ilene had a feeling something was amiss. Mark often made swallowing motions and had frequent, but brief, moments where he "spaced out." Their pediatrician diagnosed him with reflux and assured them he was fine.

One day Mark and Craig went ice-skating. Mark had been ice-skating proficiently since he was 2 years old; mid-skate stroke, Mark froze. After a minute, he tried to skate but kept falling down and could not stay upright. Suddenly, Craig, an orthopedic surgeon, realized that Mark was experiencing the disorienting state that follows a seizure. Mark had an MRI just before his fifth birthday. At first, the radiologist reported that Mark's MRI was normal. However, after his parents conveyed the strange "staring spells" and "unusual giggling" episodes Mark experienced, the radiologist reviewed the MRI again. He concluded that Mark had a very small hypothalamic hamartoma (HH). The giggling was a "gelastic" seizure.

HH is a one in 200,000 diagnosis, and most radiologists would have missed it. Suddenly Mark's peculiar symptoms began to make sense. However, the information created new anxiety because many children diagnosed with HH are severely handicapped due to frequent seizures and are physically, cognitively, and behaviorally challenged. Mark's symptoms worsened and he began having daily gelastic, absence, complex partial, and grand mal seizures. Mark's parents tried antiepileptic drugs, even though gelastic seizures do not respond to medicine. Also, they sent Mark's records to over 20 neurosurgeons worldwide. Some doctors declared that Mark did not have an HH; others were convinced he did. Some thought Mark needed surgery; others advised his parents to "watch and wait." The diversity of medical advice from top neurosurgeons was overwhelming.

At age 5½, Mark underwent gamma knife surgery (GKS; radiation targeted at the tumor with the goal of killing it to make the seizures cease), which at the time was considered "experimental." Because Mark was high functioning and his seizures were few, he was deemed a good candidate for this procedure; it could take up to 3 years to determine whether it was effective. Five years postsurgery, Mark was still experiencing seizures. He has memory deficits and processes information more slowly than his peers. Like other HH parents, Craig and Ilene were forewarned that the effects of HH worsen as children age. Recently, Mark was recommended for another experimental procedure—an MRI-guided laser ablation, which has demonstrated success in a small but growing number of patients with HH. In preparation for this surgery just before Mark's 11th birthday, his epilepsy medications were switched (from Depakote [divalproex sodium] to Zonegran [zonisamide]—given Depakote's incompatibility with brain surgery). Mark has been unexpectedly seizure free now for 6 months on this new drug regimen, despite the fact that gelastic seizures are typically refractory to medications. Therefore, Mark's parents

continue to "watch and wait" for Mark to begin seizing again or show signs of digression before they intervene again with another surgical procedure.

No two HH patients are the same. Hypothalamic hamartomas (HHs) are a benign tumor-like malformation that causes a syndrome characterized by treatment-resistant epilepsy, beginning with gelastic (laughing) seizures, but later including other seizure types. Moreover, many patients have developmental and cognitive deficits and behavioral problems (including rage attacks), and endocrine disturbance (most commonly central precocious [early] puberty). There is a tremendous diversity of diagnostic challenges, intervention options, and outcomes among HH families. While CJ, Grace, and Mark offer quick glimpses into three lives affected by HH, there are many other stories that illustrate the hope of new interventions like MRI-guided lasers, as well as the challenges of targeting deep brain tumors.

Lisa Soeby, Erica Webster, and Ilene Miller all came to discover their children's HH in very different ways. But they all felt a strong calling to use their resources and experiences to help others, and in early 2010, they joined together to found a 501c3 nonprofit foundation—Hope for Hypothalamic Hamartomas (www.hopeforhh.org)—whose mission is to provide information and support to hypothalamic hamartoma patients, caregivers, and health care providers, and to promote research toward early detection, improved treatments, living with HH, and cure. Incorporated in Phoenix, AZ (U.S.A.), Hope for HH is the only 501c3 serving the HH patient and research community in the United States and abroad. Hope for HH is guided by a volunteer Board of Directors comprised of caregivers (parents, grandparents, relatives) of HH patients, as well as a Medical Advisory Board of the foremost international medical experts (neurologists, neurosurgeons, endocrinologists, neuropsychologists) on HH.

Hope for HH offers a dedicated Website (www.hopeforhh.org) full of articles and advice for newly diagnosed families, a monitored international forum (http://www.hopeforhh.org/community/), facebook page (https://www.facebook.com/pages/Hope-for-Hypothalamic-Hamartomas/177325282307083), blog http://hopeforhh.org/blog/), and an e-newsletter to keep families up to date on new research and other breakthroughs. In addition, Hope for HH has organized two family symposiums to bring together HH families and educate them on the latest interventions and research. The first forum was at Barrows Neurological Institute on November 10, 2012, and included 30 families from around the United States. The second forum was on September 21, 2013, in Marseille, France, and brought together families from the United States, England, France, Tunisia, and Ireland.

In September 2013, Hope for HH cosponsored the 2nd International Symposium on Hypothalamic Hamartomas in Marseille, France, bringing together thought leaders from around the world (nearly all seven continents) on this very rare form of epilepsy to discuss advances in research and surgical treatment, as well as to set a roadmap for HH for the years to come. HH is rare and our patients and practitioners are broadly dispersed. Patients can go through years of misdiagnoses, as well as improper treatment, before they are connected to an experienced doctor. Collaborating with *Epilepsia* to help educate practitioners worldwide on how to diagnose and treat HH, as well as making HH medical advances more widely available around the world, will dramatically change the course of this condition and the lives of the patients severely affected by this disease.

Hope for HH is a proud member of Vision 20-20—a collaboration of epilepsy advocacy organizations. Hope for HH also joined together with the Epilepsy Foundation and other rare epilepsy organizations to submit a research grant for a rare epilepsy registry grant. Furthermore, to increase research in HH, Hope for HH welcomes research proposals and considers them as received. Hope for HH is also participating in a gene sequencing project in collaboration with Duke University and Melbourne Brain Centre to sequence HH genes. Working with Hope's Medical Advisory Board, the foundation is working to increase multiinstitutional international collaborations.

More stories can be found on the Hope for HH Website (www.hopeforhh.org) and blog (http://hopeforhh.org/blog).

Disclosure

The authors declare no conflicts of interest. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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