Infant's Rare Gaucher Defies Classification, Intrigues Experts, May Spur Research

Hannah's Story

Hannah Ostrea was born on July 25, 2008 with a rare form of Gaucher disease – at the time, physicians were unsure whether to classify it in the Type 2 or Type 3 category. In fact, some medical professionals have speculated that Hannah may have a hybrid version of both conditions, or even a wholly new form of the malady. Hannah's mother, Carrie Ostrea, explained how "at birth [Hannah] presented with an enlarged spleen, an enlarged liver [at her 2-mo hematology appointment], and low platelets (6000)." Her daughter's Gaucher disease (which actually presented but remained undetected *in utero* when an ultrasound image revealed Gaucher-related abdominal swelling) has "never been documented or seen before." In fact, said Carrie, "we just thought she had a big stomach."

Finding a Diagnosis

Hannah spent the first two weeks of her life in the intensive care unit. For the next 5 months, Carrie and her husband were consumed with trying to discover the root cause of their child's symptoms. Her search led to the Texas Children's Hospital, Houston, where after a skin biopsy, Hannah was diagnosed with Gaucher disease. Having researched the disease, Carrie recalled the fearful uncertainty she felt at that juncture. She "hoped that it was type 1" knowing it had better odds and outcomes and can often be effectively treated with Cerezyme® (imiglucerase), an enzyme replacement therapy (ERT).

Unfortunately, type 1 Gaucher disease was soon ruled out as a possibility. Carrie explained, "We were referred to Dr. Schiffmann who was at the NIH for many years studying Gaucher disease and who moved to Dallas shortly before Hannah was diagnosed. He was referred to us by Dr. Neal Weinreb, another Gaucher expert and scientific board member of the National Gaucher Foundation." According to Carrie, Dr. Schiffmann "noticed the presence of abnormal eye movements; so at that point, we knew that Hannah had type 2 or 3 Gaucher disease."

Types of Gaucher Disease

Gaucher disease is divided into types (1, 2, and 3), with varying degrees of prevalence, central nervous system (CNS) involvement, and symptom onset (**Figure**). In non-neuronopathic disease (type 1) multiple organs and tissues can be involved, but not the brain. In neuronopathic disease (types 2 and 3) the brain is also involved. Typically, when Gaucher disease is mentioned within the pages of *Horizons*, the text is referring to type 1 disease, since the overwhelming majority of those afflicted with the disease (approximately 90% to 95%, depending on the data source), are suffering from type 1.

Type 1 is the most common form of Gaucher disease, can present at any age, and has no CNS involvement. Perhaps the most common sign of type 1 is enlargement of the spleen. This is often the initial finding and may be first recognized in childhood. Skeletal symptoms of bone involvement can occur at any time in life, are very common, and present in the majority of patients at the time of diagnosis.

Type 2 Gaucher disease is a very rare, rapidly progressive form of the disorder that affects the brain as well as the organs affected by type 1. Type 2 is characterized by severe neurological involvement in the first year of life. Fewer than 1 in 100,000 newborns have this type. These infants typically appear normal during the first few months of life before developing the neurological signs and symptoms associated with type 2. A child afflicted with type 2 Gaucher disease does not usually live past the age of two years owing to the severe CNS involvement.

Figure. Gaucher Disease Types

	Non-neuronopathic	Neuronopathic	
Type	Type 1	Type 2	Type 3
Prevalence	*General Population:* 1 in 40,000-60,000 *Ashkenazi Jews:* 1 in 850	<1 in 100,000	< 1 in 100,000
CNS involvement	None	Severe	Moderate to severe
Symptom onset	Any age	First year of life	Childhood

CNS = Central nervous system.
Types of Gaucher disease. Available at: www.gauchercare.com/en/patient/about/TypesOfGaucher.aspx. Accessed January 25, 2010.

Type 3 is also very rare, and is characterized by slowly progressive brain involvement, in addition to severe disease of the other organs of the body. Signs and symptoms of type 3 Gaucher disease appear in early childhood. Other than the CNS involvement, many of the type 3 signs and symptoms are the same as those for type 1. If brain dysfunction is still subtle at diagnosis, children with type 3 disease may appear to have type 1 Gaucher disease. A clear diagnosis may be made only after neuronopathic signs and symptoms progress and are confirmed with clinical testing. Type 3 individuals who reach adolescence may survive into their 30s.

Infant's Condition Defies Easy Classification

At just over 18 months old (at the time of this writing), Hannah Ostrea has typical and atypical symptoms and an uncharacteristic progression when compared with other children who presented with symptoms before 3 months old. For example, Hannah recently lost the involuntary reflex to blink her eyes. As Carrie pointed out, "This is not a typical Gaucher symptom." The slower-than-expected pace of disease onset has "fooled the earlier doctors . . . who predicted that Hannah would require breathing tubes and feeding tubes at this point."

Carrie said, "We went to the National Institutes of Health in July 2009 and are going back in March 2010." According to Carrie, "Dr. Goker-Alpan and Dr. Sidransky cannot classify Hannah as type 2 or type 3 either. She is called a 'puzzle of sorts.'" If Hannah were type 2, "she should be sicker because she presented at birth. She's unique. This is new." So new, in fact, that according to Carrie, "the NIH is interested in meeting with her." (Since this interview occurred, a meeting at NIH headquarters in Bethesda, MD, has been finalized.)

Hannah's Disease Progression May Unlock Gaucher Mysteries

Several experts who have treated Hannah are optimistic that the peculiar nature of her disease presentation, progression, and symptoms may yield new insights into Gaucher disease care. For example, Hannah's lack of blinking reflex would make more sense in the context of Parkinson's disease (PD), as it is a symptom that is closely associated with PD but not associated with Gaucher disease at all. This has led researchers to explore potential links between these two diseases.

Another enticing avenue currently being explored is the modification of Cerezyme® ERT so that it will be able to cross the blood-brain barrier. If Cerezyme® can be reconfigured in this manner, then it might have the potential to be an effective treatment option for type 2 and/or type 3 Gaucher disease. Researchers are currently testing alternate Cerezyme® formulations in mouse models.

A Mother on a Mission

Carrie Ostrea has become a tireless advocate on behalf of her daughter. "I'm on a mission to find a treatment for her," asserted Carrie. "I spend all day talking to researchers and scientists and working with other moms who have kids (with Gaucher disease and other similar lysosomal storage diseases). That's my day job." Aside from her own personal battle against her daughter's illness, Carrie is also fighting to raise awareness and funds for other children with neuronopathic Gaucher disease. By coordinating her efforts with other parents of children with the disease, Carrie hopes they can provide one another with a support network and fundraising infrastructure.

"I don't want any parent to feel alone out there!" said Carrie. "The more parents we have fighting for our kids, the stronger we can be. These kids (children with type 2 or type 3 Gaucher disease) need to be helped, supported, and cared for. I believe that [Neuronopathic] Gaucher disease is underfunded and under-researched . . . the individuals with this disease aren't given a chance."

Equally as troubling as the scarcity of funding, according to Carrie, is the piecemeal, uncoordinated approach that currently characterizes most neuronopathic Gaucher research. "We don't have one centralized

initiative in which all findings are shared and built upon. Researchers are investigating bits and pieces of this disease. We need to start thinking of this in terms of solving the problem, finding a treatment or a cure, not throwing together bits and pieces of research," asserted Carrie.

Special Support for Special Patients

"If you have a type 2 or type 3 child, this is a very lonely disease. You think you are out there alone," Carrie explained, but Genzyme representatives have helped mitigate those feelings of isolation. She cited Genzyme as an invaluable resource, praising the company for providing stalwart support and demonstrating a willingness "to go out of their way (for Hannah and others like her)." One particular Genzyme representative was singled out for special praise: Kathleen Coolidge, Associate Director, U.S. Patient Advocacy. "Prior to dealing with Genzyme, I had my face slammed in so many doors. Ever since I [connected] with Kathleen, she has been amazing," declared Carrie. "She's helped me contact researchers and other parents (of children with Type 2 and Type 3 Gaucher disease)."

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As *Horizons* goes to press, Carrie will continue to battle for her daughter and others like her with all means at her disposal. Hannah is continuing to battle as well; each day for her is a triumph over staggering odds and expert calculations. As her caregivers continue to observe and examine Hannah's rare manifestation of Gaucher disease, they hope to gain insights that are significant enough to yield care advances. They "hope that Hannah holds some new answers," because as Carrie succinctly summarized: "She's here for a reason."

Hannah's continued and vigorous resistance against her disease has provided her mother with encouragement and hope. Carrie concluded her *Horizons* interview with an appeal to the readership, urging anyone who is interested in getting involved in any way to contact her through Hannah's website (www.littlemisshannah.com). ■