A Rare Disease Identified and a Sister's Hope

OnMedicalGrounds

PODCAST 4

Jill Sellers:
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Jill Sellers:
We provide perks to all posted podcast by linking content so you can drink in more if you so choose. Our guest today is Heidi Edwards. Heidi is the president and founder of the Sister's Hope Foundation, a nonprofit organization supporting families struggling with hereditary diffuse leukoencephalopathy with spheroids or HDLS, and she is the caregiver for her twin sister Holly who has the disease. Welcome, Heidi.

Heidi Edwards:
Thank you, Jill.

Jill Sellers:
Some of our listeners will know what HDLS is and some may know it by its new name, adult-onset leukoencephalopathy with axonal spheroids and pigmented glia or ALSP. But tell us about HDLS and how the new name of ALSP came about.

Heidi Edwards:
ALSP was previously known as two diseases, hereditary diffuse leukoencephalopathy with spheroids, HDLS, and pigmentary orthochromatic dystrophy, POLD. After the discovery of the CSF1R gene mutation, these two diseases have become known as one entity, and that is ALSP. Some patients may also hear the term CSF1R-related leukoencephalopathy. Scientists have come together and decided to rename the disease. We still have all four diagnoses out there, but we're trying to get on the same page with calling it just ALSP.

Jill Sellers:
It's a mouthful, regardless of what you call it. I'd like to know how prevalent is ALSP, and is there a certain age where it is more likely to be diagnosed?

Heidi Edwards:
ALSP is just one of a group of adult-onset leukodystrophy disorders. There are over 50 different leukodystrophies. Because it is a rare disease, the actual number of cases are unknown. The scientific community believes there may be as many as 10,000 people living in the United States with the disease. Many are and will be misdiagnosed. ALSP makes up about 10 to 25% of adult-onset leukodystrophy, and the average age of diagnosis is 43 years old. That does vary from family to family.

My family, my mom, uncle and aunt were diagnosed in their early fifties to mid-fifties, and they passed away mid to late fifties, where my sisters were both diagnosed around the age of 42 to 43.

Jill Sellers:
With this being such a rare disease and much unknown about it, how did it become the focus of your foundation? I know you've alluded to the family members that had it. Let's tell your story.

Heidi Edwards:
My journey with this disease started 20 years ago when my aunt Ruth was diagnosed with a neurodegenerative disease. At the time, she was clinically diagnosed with Pick's disease, and we were told that no other family members would have to worry about this disease because it was not hereditary. She passed away in 2005. By 2009, my mom started showing similar symptoms and we started to get concerned that this may be a hereditary condition.

My mother went to the same doctors as her sister, my aunt Ruth, and they said, "We are now convinced it is a hereditary condition, but we do not know what that condition is." Because in 2009, there was no mutation that they were aware of that connected the two siblings. My mom was diagnosed clinically with corticobasal degeneration, because her first symptoms were apathy, personality changes, and losing the ability to walk. By 2012, my mother passed away. Her brother, my uncle Chuck, was also symptomatic.

Heidi Edwards:
He passed away in March of 2013. And by that time, the Mayo Clinic in Jacksonville found the CSF1R gene mutation. Luckily, my family donated brain tissue to the brain bank at the University of Pennsylvania. So they were able to go back and check each family member for this rare mutated gene. My family had the CSF1R mutation and was diagnosed with HDLS. Now, in 2013, when the third relative passed away, we thought we had time, because here is a disease that was affecting our family in the fifties. In the age of around 52, 53 is when they were diagnosed.

My mom passed away at the age of 57. But by August of 2019, my two sisters became symptomatic. We all of a sudden have... I have two siblings that are 42 and 43 years old that are symptomatic for a disease that we thought we had another 10 years to worry about. Holly and Heather both went to the same doctors that the other family members went to at the University of Pennsylvania, and they started the genetic testing and it was confirmed that they carried the mutation.

Now, there was an experimental bone marrow transplant taking place at the University of Minnesota, so Heather, my older sister, went to Minnesota. This was just about one year ago. It was May 22nd, 2020. Heather was admitted to the hospital to start the bone marrow transplant procedure. I was her donor. I was a 100% match to be her bone marrow donor. Heather suffered a heart attack 15 days after the transplant. She spent 22 days in the ICU. She was released back to the bone marrow transplant unit, but she never recovered.

Heather passed away on August 28th, 2020. In the meantime, Holly was going through the process of starting the bone marrow transplant. Luckily, Holly was only to be admitted to the hospital on the actual day Heather passed away. Holly made the tough decision to come home and live out the rest of her life with her family by her side, because she didn't think she could handle that her body wasn't strong enough and she was too progressed in the disease to be able to survive the transplant.

Jill Sellers:
For clarity, Heather passed. She had the gene mutation, so she had the disease. She also had a heart attack. She survived the bone marrow transplant, but then was it the disease that took her, or was it the heart condition combined with the disease, or just the heart?

Heidi Edwards:
So going into the transplant, they do extensive baseline testing and they check every organ, because the chemotherapy that you must go through is so hard on the body that healthy people can struggle with this. You need to have 10 days of intense chemotherapy. After the 10 days, which was on June 1st, 2020, Heather received my bone marrow and she was doing really well. We were shocked at how well she went through the chemotherapy. June 1st, she starts the transplant process.

On June 15th, we received a call that Heather was being taken to the ICU because she wasn't doing well. We had seen for a few days she wasn't eating. She had mouth sores that were really bad from the chemo, and she was really tired, which we expected, but she had lost the ability to swallow, which is part of the disease, not the chemotherapy or the bone marrow transplant. But she lost the ability to swallow. We had known going into this that the chemo would be hard on her body and a transplant actually is going to progress the disease before it actually stops it.

Well, Heather was at this point where her disease was so progressed already that when they did the transplant, she stopped walking. She stopped getting out of bed. She was so tired. She was sleeping all the time. She wasn't eating, and she couldn't even swallow her own saliva. They took her to the ICU that day and she suffered a heart attack in the wheelchair in the ICU. Now, going into this, she had no heart problems, but the chemotherapy is so hard on the heart that her body just couldn't handle anymore. It was the perfect storm and she suffered a heart attack.

After 25 minutes, they were able to revive her, but she was on life support for the next 22 days. They did wean her off of that, and she was able to go back to the transplant unit. And in that time her husband was able to visit with her. Now, she was admitted during COVID, so she was alone during all of this. COVID's protocols allow you to see the family member if they have died, which she technically did, or if there is no chance that they will survive. Her husband had a chance to see her.

Mid-August of 2020, the doctors met with her husband and I and the decision was made that Heather would not want to live out her life in a nursing home and on tubes, because she wasn't able to survive on her own. She was on feeding tubes, and she couldn't move at all on her own. The decision was made to have the children fly to Minnesota and say their goodbyes. Holly and I and my mom's sister, my aunt Barb, were there to spend a few days with Heather and get to say our goodbyes as well.

At the end, she had the bone marrow transplant had progressed her farther into the disease. We had known that that could happen and she would not be able to get back anything that she had already lost. The other part of this is you asked me, did she pass away from the heart attack, the disease, the bone marrow transplant? On June 13th, which was 12 days into her bone marrow transplant, she actually started the engraftment. She accepted my cells and two days later suffered the heart attack.

At the end, she started to need platelets, red blood cells. And at the very end, she was also starting to reject the white blood cells, they told us. For a period of time, she accepted the new cells. It was just too much

for her body to handle. It was too progressed with the disease. The other part I would like to let you know is that Heather and Holly are my two siblings. Holly is my twin sister. We are fraternal twins. And in 2014, I had found out through predictive genetic testing that I do not carry the mutated gene.

Heather and Holly decided they did not want to know because there is no cure. And at that time, there was no treatment options. I was the only family member to find out, and I did know, and to this day I know I do not carry the mutation.

Jill Sellers:
Wow. It's all very interesting how that occurs, isn't it?

Heidi Edwards:
Mm-hmm (affirmative).

Jill Sellers:
It makes me wonder if you were identical twins, most likely that mutation would have occurred. You would have that gene mutation. That's my understanding of genetics. Is that your understanding?

Yes. Yes. If we were identical twins, we would either both have the mutated gene or both not have the mutated gene. Because of being born in 1977, and my mom always told us we were fraternal twins, but we wanted to make sure because here we have twins who want two different things, and this is a life-changing event. I want to know if I have the gene, but knowing that there's nothing I can do about it, and Holly does not want to know if she has the gene because she just wants to live her life the way it was going the best she could and not worry about having this disease.

We actually had testing done to make sure... We had DNA testing done and make sure that we were definitely fraternal twins. Before I went to have predictive genetic testing done, they did confirm that we were fraternal twins, because I didn't want to find out if I had the disease, if I had that mutated gene, it would automatically tell Holly if she had it too.

Jill Sellers:
Right. Okay. Understood. Before we move on to Holly, I'd like to state an observation from your story. It appears that your aunt Ruth went through quite a bit of testing and diagnostics, and they really never figured it out. Then your mom started having similar symptoms and she seemed to have... It took about three years, right, from the start of her symptomatology to her passing. And then your uncle around a year.

And then Heather maybe a year as well. It seems like the signs and symptoms were coming faster, and the rate at which the disease was progressing became faster, or is it just that we knew more, you knew more?

Heidi Edwards:
And that's something we have talked to the neurologist about as well. It seems that each person has progressed a little bit more rapidly than the one before them. With aunt Ruth, she seems to have been around like the three years from time of diagnosis to death. My mom was two years. Uncle Chuck was a year and a half. Now, Heather's situation is a little different with the bone marrow transplant because she passed during that procedure. But with Holly, from time of diagnosis... Holly is end-stage stage right now.

She's a fighter. I don't even know how her body keeps going. She is such a fighter, but it'll be definitely less than two years. Typically from time of diagnosis, they say it's around two years until you'll pass away from the disease.

Jill Sellers:
Okay. Wow. Let's talk about Holly a little bit. Holly, again, as we stated is your fraternal twin, and she is in the end stage of this disease and she chose not to have the bone marrow transplant. Is that correct?

Heidi Edwards:
That is correct.

Jill Sellers:
And is that because of what she saw Heather go through, or she just decided that she wanted a better quality of life with what she has left?

Heidi Edwards:
She was 100% going to have the bone marrow transplant. She got down to her final day, the decision day, where... I was not a match for Holly, believe it or not. We are fraternal twins, so a lot of people assume that I would have to be her genetic match as well. I was Heather's genetic match, but not Holly's genetic match. They had to find a donor from Europe. We were four days away from the donor having harvest, and Holly decided after seeing Heather laying in a hospital bed with feeding tubes, tubes coming out of her nose.

She had a trach. She couldn't go to the bathroom on her own. She couldn't even turn in bed without the assistance of others. Holly decided that that was not the way she wanted to live out the end of her life. We live in Pennsylvania. Heather had to go to Minnesota. Holly would have to be in Minnesota alone without family because of COVID. Holly decided that when she saw Heather, and it was hard to watch Heather in that state, that Holly could not and didn't want to live out the rest of her life in a hospital away from her family.

What she did say was... Her decision. She made her decision and she said, "I want to come home and live out the time that I have left with the people I love and enjoy my time with my son Mason." Holly's goal was always... Even before she would admit that she had the disease and was sick, she always just said, "I will deal with it when Mason graduates from high school." And Mason graduates from high school in two weeks.

Jill Sellers:
Oh wow.

Heidi Edwards:
Yeah. And all she ever wanted to do was see her son graduate, and that is what she keeps saying, "I want to see Mason graduate." And now we're two weeks away. We almost lost Holly in March. March 1st, I didn't think she'd get out of the hospital. She came home on hospice and I worried that we would not get to spend our last birthday together. Holly and I celebrated our 44th birthday on March 31st. She pushed herself and we had a party. And now she is still pushing herself and she's going to get to graduation.

Jill Sellers:
She has set goals for herself. I believe that when we have goals, no matter where we are in life, that it does drive us. It keeps us moving forward. Wow. Going on away from your personal story, let's tell our listeners a little bit more about ALSP and how would you summarize the signs and symptoms of this disease.

Heidi Edwards:
Everyone's journey with ALSP is different. ALSP can present with symptoms within the same family. ALSP is a progressive neurodegenerative disease that is characterized by issues with judgment, personality, and psychological changes, and problems with movement like shuffled gait, loss of mobility. Symptoms often begin with mild psychological changes and eventually develop into loss of movement and overall function. The early signs of ALSP can be very hard to distinguish from other neurological disorders.

These symptoms usually include poor judgment, depression, personality changes, and limited movement problems. As ALSP progresses, the disease can lead to mental decline, severe depression, apathy, anxiety, irritability, and dementia.

Jill Sellers:
What kind of assessment or laboratory tests are done to diagnose ALSP?

Heidi Edwards:
You start with a neurological exam. Sometimes there is a CT scan done first, especially if you end up in the emergency department like my mom, Heather, and Holly ended up in the emergency department because they had such strange symptoms that it almost mimicked a stroke because of the left side weakness they were experiencing. And then the neurologist ordered an MRI. That MRI shows white matter changes. Your doctor will want to rule out other diseases like MS.

Anyone with white matter changes or an undiagnosed leukodystrophy should have genetic testing done to rule out ALSP or to confirm a diagnosis of ALSP.

Jill Sellers:
Genetic testing is done relatively quickly, like once the white matter degeneration is seen. It seems like with you, you had your genetic testing done because of the family history. But then in someone that they're trying to diagnose that maybe doesn't have a family history, should they request gen genetic testing right off the bat. Or is that something that's automatically done that's part of the protocol?

Heidi Edwards:
Right now it is not part of any protocol, unless you have a family history of ALSP. There's two ways it'll play out for symptomatic and asymptomatic patients. I was asymptomatic, and I decided I have a family history. I have a 50% chance of inheriting this disease. I wanted to find out through predictive genetic testing if I was carrying the mutation. Holly and Heather were symptomatic. Also, we knew of the 50% chance that they were carrying this mutated gene. Their process was just a little different. They already had symptoms. So for them, they had their neurological exam. The doctor ordered an MRI, scheduled genetic testing because of our family history. The process is only a little different if you're symptomatic or asymptomatic. You have to meet with a geneticist. You have to have some counseling done. Let's talk about a little bit if you don't have a family history yet. You don't know if this disease runs in your family. Then the process is you go to your neurologist. They're going to do the standard testing.

If they see these white matter changes on the MRI, then they're going to want to order genetic testing. And that's where Sisters' Hope is trying to educate more clinicians, geneticists, neurologists on ordering genetic testing to determine if you carry the CSF1R mutation. It is not a standard test that's ordered, but we're seeing that so many people are being misdiagnosed or have been misdiagnosed with MS or other white matter diseases. That it's a simple test to rule out this disease. In Heather's case, she went to the doctor at University of Pennsylvania.

And during the visit, they wrote out a script and said, "I want you to go downstairs to lab and have blood drawn. And in a few weeks, we'll receive the results back. We'll have you come into the office, and we will let you know if you have the mutated gene or not." Now, they were 99.9% sure based on symptoms she was carrying this mutated gene. In Holly's situation, COVID happened. They already knew she was symptomatic. They, again, were almost certain she had the mutated gene. But because of COVID, they sent the kit, it's a cheek swab, to her house.

And all she had to do was rub it in her cheeks and mail it back to them. In a few weeks, we did another virtual meeting with the geneticists and the doctors and they confirmed the diagnosis that way. It's not a hard process. I know there's other family members now in my family that have done the cheek swab. it's fairly easy to have this testing done.

Jill Sellers:
It's good that the testing is easy because the disease is not. What is the current plan of treatment for ALSP?

Heidi Edwards:
Currently the only treatment option is a bone marrow transplant. In order to have a bone marrow transplant, you must be diagnosed early or before you become symptomatic. Since this is a rapidly progressing disease, time really matters. The longer you wait to get a confirmed diagnosis, the less likely you'll be able to have a bone marrow transplant. If you cannot have a bone marrow transplant, your only option is to treat the symptoms.

There is a lot of exciting work being done in the ALSP space and soon we will see more treatment options available. But unfortunately, if it's too late for our bone marrow transplant, your only options are physical therapy, occupational therapy, which eventually the disease just continues to progress past where it's helping you. And in Holly's case now, she's on hospice and you will have just comfort measures to help you until the end of life.

Jill Sellers:
As a caregiver for your sister, Holly, I know you're heavily involved with the hospice caregivers as well, but I imagine you have had some difficult days. Has anything surprised you about being a caregiver? Do you have any words of advice for other caregivers when you know what the ultimate outcome is going to be?
Heidi Edwards:
Being a caregiver for this disease is the hardest job I've ever had. I have watched four family members die from the disease, and I've helped my mom and Heather along the way. And now I was Holly's 100% full-time caregiver. I was it for a little while, until we were able to hire more help. I try to remind myself that this is harder for Holly and the patient than it is for me. They have no ability to cope with the changes they are experiencing. As a caregiver, I still have coping skills, and I need to use those skills to help myself get through each day.

Like dementia patients, ALSP patients have no filter. They can be extremely agitated, and this can take a toll on the strongest caregiver. ALSP patients can also be the sweetest people you meet. Each day we get to see a glimpse of the person Holly was before the disease. I just take one day at a time. I remember it is the disease talking, not my loved one. I try as hard as I can to enjoy each moment. In my case, I definitely remind myself that these are the last days I will get to spend on this earth with Holly, who is also my best friend.

Every day when I leave her, I make sure I did everything I could to enjoy our time together, and I make her happy because it may be the last day I have with her on this earth. I make sure she always knows how much I love her.

Jill Sellers:
That's important. That's very important. She is very fortunate to have you. I believe that being a caregiver of a family member is difficult and especially in something that there's not a lot you can do for her at this point, but comfort measures, reassurance, and celebration for Mason's graduation when the time comes. Let's transition to the Sister's Hope Foundation. You mentioned it previously, but what kind of research is being done in the area of ALSP? How are you involved with that, and how does the foundation help?

Heidi Edwards:
I started Sister's Hope so I could find a cure or a treatment for my family and other families. It was a lonely road for many years. There was not a lot of information or research about the disease. I want to make sure when a family receives a diagnosis of ALSP, they have one place to go and have everything they need to navigate this diagnosis. I want more doctors, researchers, scientists, clinicians, and families to hear ALSP and immediately think Sister's Hope Foundation.

Through Sister's Hope, I have had the opportunity to meet with and will continue to meet with experts in the field, and I am connecting with more families who have ALSP. We will be launching a new website in the next few weeks. We will continue to provide support group meetings. We are rolling out a newly diagnosed kit for families receiving this diagnosis. We will continue to work with neurologists to understand the symptoms and discuss CSF1R genetic testing.

Sister's Hope is working alongside the best and the brightest, so that one day we have our first survivor of ALSP.

Jill Sellers:
That will be a great day. And for our listeners, there is a link to the Sister's Hope Foundation website, which is sistershopefoundation.com, in the show notes. And this website has a plethora of great information, as Heidi mentioned, including published studies on ALSP, resources for caregivers, a sign up to volunteer your time if you're in that area, and a couple of easy ways to make a financial contribution, if you're not. Be sure to check out sistershopefoundation.com.

Heidi, before we close, is there anything that you would like to share with our listeners that perhaps we haven't covered in our discussion?

Heidi Edwards:
I just went to say, we are no longer alone in our fight to save our family and friends affected by ALSP. Together, we are going to make a difference. Sister's Hope is extremely grateful to have your support and thanks to everyone who has continued to support our mission.

Jill Sellers:
Before we close, I want to offer a sincerest heartfelt thank you, Heidi, for being part of the *On Medical Grounds* podcast. I know talking about this disease and its devastating effects on your family is not easy. Thank you for being so open about your family's story, educating us on ALSP, and establishing the Sister's Hope Foundation as it is playing an important role in bringing awareness to this disease.

Heidi Edwards:
Thanks, Jill.

Jill Sellers:
And thank you for listening to the *On Medical Grounds* podcast. We know your time is valuable. The resources that were referred to in this podcast can be found at onmedicalgrounds.com. In addition, please be sure to click the subscribe button to be alerted when we post new content.