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Life and death after transplants

Alexis' and Jashaia's battles end, while the Bihns adjust to their 'new normal' back home

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Craig and Nichole Markowich of Amherst and Ken and Julie Bihn of Olmsted Falls started the year hopeful that an unconventional treatment for the rare, fatal genetic disease their daughters shared would save them. After months of medical complications and raw determination, the reality of their daughters' fates came home.

Alexis Markowich died at 1:35 a.m. Thursday, Sept. 14, with a tube down her throat. She was 5.

She died on Day 258 on the calendar that began last December, when she underwent a cord-blood transplant at Duke University Medical Center in Durham, N.C. She died on Day 32 of the Markowiches' return to their Amherst home.

It happened so fast, said Alexis' mom, Nichole.

Alexis spiked a high fever. Her mom and her dad, Craig, took her to one hospital, which sent her to another in a speeding ambulance. A few hours later, she was dead. Nichole said Alexis didn't suffer in the end.

Dakota Bihn is the surviving member of the trio that Bihn family members nicknamed the "Tri-Angels." The girls, all with juvenile Tay-Sachs disease, had received cord-blood transplants within weeks of each other. It was the first time Dr. Joanne Kurtzberg, a pediatric hematologist at Duke, had tried transplants on children with the juvenile form of the rare genetic fatal disease.

Alexis was the first to get the procedure: chemotherapy, then new stem cells harvested from a stranger's umbilical cord, then strong anti-rejection drugs to help her body accept the new cells.

Jashaia Small, a 3-year-old from Connecticut, was the first to die. She had been on life support for weeks before her parents disconnected her Aug. 26.

Dakota came home to Olmsted Falls Aug. 24. Today marks Day 285 since her transplant. Every day she has grown stronger, more in tune with her surroundings. Improving, said her parents, Ken and Julie Bihn.

Alexis' death in September rattled the Bihns. Alexis and her family had visited the Bihns the Sunday before she died. She looked so much better, Ken said. Everyone was so happy, Julie said.

Dakota's progress had tracked Alexis' fairly closely. Now, Ken and Julie wondered how long Dakota had.

Alexis was recorded as a "positive death," said Kurtzberg, the doctor who performed the transplant.

Kurtzberg looks at this procedure in terms of cellular changes. From a transplant point of view, the doctor said Alexis' worked: 100 percent of the donor's cells established themselves in her body. She survived the transplant long enough to leave the hospital, and she showed minimal signs of rejecting the donated cells. Kurtzberg said tests showed her body was producing the missing enzyme that characterizes Tay-Sachs.

Dr. K, as the Bihns and Markowiches call her, said Alexis died from transplant complications. She said that the girl died too soon to tell if the transplant helped her disease but that she thought Alexis may have benefited from the procedure.

"I think based on the way she was when we saw her initially, we felt like within a few months she was going to deteriorate quite a bit and wouldn't be communicating anymore -- which happened anyway to some degree," Kurtzberg said.

In her opinion, Alexis might not have lived through the year without the transplant.

As it turned out, Alexis died 10 months after the procedure.

Kurtzberg said parents faced a choice that offered some hope though no guarantees.

"I think I sometimes say to parents, You have two bad choices. It's not like you have one good choice that's definitely going to work and make your child well with no risks," Kurtzberg said.

She said the Markowiches made a choice.

"I didn't put a sign out front that said, Come to me. I can cure Tay-Sachs," Kurtzberg said. "Alexis' parents found me."

Kurtzberg said she doesn't think the transplant harmed Alexis.

"I've seen untreated kids progress, and the disease is as bad or worse than treatment," she said. "In fact, I think worse."

She said "the jury's out" on whether the transplant did any good. She said she probably would not perform transplants on other children like Jashaia, who arrived at Duke with significant neurological damage.

So did Alexis and Dakota, according to developmental tests performed before their transplants. Kurtzberg's own research on other metabolic storage diseases suggested that the more neurologically devastated a child is, the less likely a transplant would help. Many experts have voiced grave doubts that transplants can help any Tay-Sachs kids.

There is much to learn, Kurtzberg said, and transplants alone probably won't be enough to make big strides in Tay-Sachs. "We're probably going to have to combine a transplant with some other targeted cell therapy when it's available," she said.

One technique Kurtzberg said she is exploring in animals is injecting cells directly into the brain at the time of a transplant. Meanwhile, she said she collects data on the children who undergo cord-blood transplants at Duke for a national registry of donors. Information has been submitted on Dakota's, Jashaia's and Alexis' transplants. The doctor said she plans to write up their cases.

Kurtzberg also will examine Alexis' brain, which the Markowiches donated to her.

The doctor said she hoped to learn from Dakota, who she said "is making a lot of progress now."

When Alexis died, Ken wanted to move his family back to Duke. Dakota would be taken care of there. Safer. He wanted Kurtzberg to ask them to return to Duke. He wanted her to tell them that everything was going to be OK. That Dakota's falling white-blood-cell and platelet counts didn't mean she was getting worse. Worse like Alexis.

Ken checked flights to Raleigh, N.C.; schools for the couple's older daughter, Bailey; and whether they could re-rent the apartment near Duke where they had lived for six months after Dakota left the hospital. He looked online for houses to buy. Julie thought he was overreacting.

"We're not moving, Ken," she said.

Julie worried and was not sleeping well, up and down all night checking Dakota. But she'd had enough of being isolated at Duke. Olmsted Falls was home. She wanted life to settle down and wanted some consistency for Bailey.

When all this started, Ken had imagined the Tri-Angels with their moms on "Oprah," telling her how their transplants cured juvenile Tay-Sachs. He imagined Oprah interviewing Kurtzberg.

Now he just wanted Dakota's hair to grow back the way it was -- long, blond and full. He wanted her swollen face and body to return to normal.

Not so she'd look good on "Oprah." So she'd look better in her casket.

Dr. Maria Escolar is a pediatrician at the University of North Carolina at Chapel Hill who specializes in inherited diseases that affect development. When she evaluated Alexis and Dakota before their transplants, she was blunt. She warned the Markowiches and Bihns that Tay-Sachs had inflicted too much damage to their brains to make any difference. She told them the toxicity of the drugs used throughout the procedure would hasten the girls' decline. She said it might put them in a vegetative state.

At the time, Escolar's words stung. But just about everything she predicted would happen had.

Before Alexis returned to Amherst in August, Escolar examined her and told the Markowiches that the transplant had not stopped the Tay-Sachs progression.

Escolar also evaluated Dakota before she came home. The doctor said Dakota showed neurological regression, but she couldn't tell if it was because of the disease or the transplant.

"Dakota is worse in her gross motor, her expressive language and a little bit in her fine motor," Escolar said.

She said three things could happen: One, Dakota could die from infection, because the transplant process suppressed her immune system. Two, she could do well and get better and then neurologically recover some function only to regress a couple of years later. Three, she could maintain her neurological status for years, never gaining more skills.

"We just have to wait and see," the doctor said.

Escolar said she would deem Dakota's transplant a success if she was able to learn new things, beyond what she could do before the transplant.

The pediatrician continues to collaborate with Kurtzberg, assessing transplant patients' neurological outcomes. The doctors sometimes disagree. For one, Escolar disputes Kurtzberg's contention that cord-blood transplants for Tay-Sachs are the standard of care, an established and accepted therapy.

"I don't think we can just say this is the treatment for any kid" who has Tay-Sachs, Escolar said. "It's not like leukemia, that, OK, this is how you treat leukemia because we have done it thousands of times.' "

Escolar said that for metabolic storage diseases like Tay-Sachs and Hurler syndrome, many factors must be in a child's favor for doctors to believe a transplant will help.

"For one, how neurologically devastated the child is, that is very important," she said. "And that's what should determine whether these kids get this treatment or not -- not just because you have the disease and that is your treatment. I think treating a child that is neurologically devastated is not the standard of care, because there is nothing that is going to come out of that."

"Gabs! Ria!" Dakota yelled at the neighborhood kids she recognized, managing to say only part of their names. Julie pointed to another child and said her name. Dakota repeated it and laughed, loud, deep, from her belly.

Dakota has a long way to go physically to catch up to where she was before the transplant. She sits without support and can shimmy off the couch. She walks the length of the kitchen, with Julie hovering closely.

But Dakota is unsteady. She can't crawl up the stairs the way she could before the transplant.

She enjoys being pushed outside on her special tricycle. She no longer is coordinated enough to pedal, so Julie and Ken manipulate the trike with its large, black handle. She must be belted in, her feet strapped to the pedals, to ensure she doesn't topple off.

Whenever she goes outside, she's surrounded by a swarm of neighbor kids. She smiles widely, and her head swings from face to face.

With all the attention she and Dakota receive when they're outside, Julie said she feels a bit like a freak show.

There is no status quo for Ken and Julie. In the two months they have been home, Dakota seems to improve for a day or two; then the next three days, she vomits and is listless.

The Bihns struggle to manage Dakota's needs while maintaining some routine for Bailey. Their "new normal," Ken and Julie said.

Everything's changed. Their family life, their social life, Ken's life at work.

Health insurance rates for his family-owned automotive supply business doubled because of the high cost of Dakota's care, Ken said.

Dakota's care monopolizes Julie's day. She must feed Dakota every two hours, pumping her full of formula through a line that months ago had seemed like such a milestone to Ken in Dakota's

decline. In between, she must give Dakota more than eight medicines. Weekly doctor appointments eat up most of Wednesdays. Daily therapy sessions and visits from a special-education teacher four times a week occupy the other days. Julie can't leave Dakota, even to use the restroom, without Dakota crying for her.

It is almost impossible for Julie to take a walk, work in the garden or sit on the patio and chat. Much like having a newborn, Julie said.

They can live with all that. What stresses them out most is Dakota's constant vomiting. At the hospital, Ken and Julie piled her soiled sheets in a bin and the staff changed her bed. At the temporary apartment they moved into when Dakota left the hospital, Ken and Julie did the laundry, but the floors were uncarpeted, the furniture rented. Ken didn't care if she threw up on either.

Now Dakota soiled and threw up on their carpet and furniture. The rug and couches in their family room have dark stains. Ken and Julie keep a large spray bottle of Febreze on the coffee table, but the odor remover doesn't help.

Julie and Ken don't understand why Dakota continues to vomit and poop so much.

Escolar said that in an ideal world, she would have parents talk to a committee before they proceed with a transplant for their sick child.

The committee would consist of a chaplain, an uninvolved physician and parents of children whose transplants succeeded and those whose didn't. A neutral board would make the decision for the parents.

"We're letting the parents make the decision, and it's a very tough one," Escolar said. "This is not just a medical decision."

The team of physicians on a case should routinely meet to discuss all aspects of the situation, because parents desperate to help their child can't always see how the decision will affect their lives, Escolar said. Sometimes "we should recommend they not do this, and we don't do it like that," she said.

Escolar is tracking the progression of children with metabolic storage diseases like Tay-Sachs so she can develop standards for measuring how kids do, with and without a transplant. A separate study funded by the National Institutes of Health is charting Tay-Sachs as it progresses. Much remains unknown about the disease.

"I don't think we should sit down and wait until everything about the disease is understood and then somebody can come up with a treatment," Escolar said.

It is not unusual for terminally ill patients to travel to institutions like Duke, where cutting-edge clinical trials that try to move science forward can offer one last thing to try. The first phase of trials is dangerous and risky and often doesn't deliver, said Arthur Caplan, an ethicist at the University of Pennsylvania.

Kurtzberg said Alexis, Jashaia and Dakota were not part of a study. She said cord-blood transplants for Tay-Sachs were therapy, not research. But Caplan said, "The honest description is, you're in research, and even then, it doesn't work out. But the notion that [a transplant for Tay-Sachs] is being billed as therapy makes it even less acceptable because it is clear how experimental it is."

In the back row at Alexis' funeral, Ken stared forward, his right arm wrapped around Julie. She was inconsolable, dabbing tears with a crumpled tissue.

They had just celebrated their 13th wedding anniversary. They'd planned to see a movie for their first time out together in 10 months. They came to Alexis' funeral instead. They left Dakota with a friend who is a nurse.

From where he sat, Ken couldn't see the shiny white casket surrounded by flowers and stuffed animals. He preferred that. The casket, the pain on Craig's face, the pain in the room was almost too much for Ken to process.

Nichole had picked the funeral home before they left for Duke. Just in case, she said. Ken has several drafts of Dakota's eulogy, but he and Julie haven't made funeral arrangements. That is something they can't talk about yet.

With Alexis gone, Craig and Nichole didn't have to ask any more medical questions. They didn't have to wonder why she was eating or not eating, vomiting or not vomiting. They could go on vacation, go out to dinner, go shopping with Brianne, their 9-year-old daughter, who does not carry the Tay-Sachs gene. They no longer had to wonder when it was all going to end. Or how. They could make plans for their future. Ken envied Craig and Nichole.

Two weeks after the funeral, Nichole and Craig took a weeklong Hawaiian cruise. Jashaia's mother, Nadine Small, has been able to move forward, too. She is expecting a baby in December. Prenatal screening determined the baby does not have Tay-Sachs.

At Alexis' funeral, a recording of "Streets of Heaven" played over loud speakers. The singer, Sherrie Austin, pleaded with God:

"So tell me: What do you need her for? Don't you know one day she'll be your little girl forever. But right now I need her so much more. She's much too young to be on her own: barely just turned 7. So who will hold her hand when she crosses the streets of heaven?"

Ken listened intently and nervously adjusted his tie. He took a deep breath to keep from crying. He glanced out the window and watched the cars rush by. No one in those cars would know about Alexis. Unless she had beaten Tay-Sachs, the world would never know her struggle. Or Dakota's.

He wondered how God could let something like this happen.

He doesn't think God arbitrarily picked out Alexis and Dakota and gave them this disease. He doesn't think God works that way. But Ken couldn't just say "Let's pray" and hope for the best. He believed it was up to him to find Dr. K, get insurance to pay for it and get Dakota to Duke.

Julie believed God had it all worked out. Alexis' death had made her question everything: God. His so-called plan. The wisdom of subjecting Dakota to the transplant.

Julie thought she wouldn't be human if she didn't question their decision. Every time Julie watched Dakota struggle to stand or identify a pumpkin on a flash card, she questioned it. Every time Dakota got another infection, soiled herself or vomited, she asked: Did they do the right thing? If they hadn't done it, would Dakota still be able to go to school?

Would the disease already have killed her?

Ken thought Julie was silly to go through such mental gymnastics. How could they know what would have happened if they hadn't done the transplant?

Deal with it. Move on.

Julie hopes Dakota might live to see her 10th birthday.

Ken isn't that optimistic. He would be grateful for a few extra months, a year. That doesn't mean he regretted subjecting Dakota to it.

He had to do something.

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