Therapy helps regenerate child's undeveloped bones

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Janelly Martinez-Amador is responding to treatment for a rare genetic disorder that caused her bones to become soft. Credit: Daniel Dubois

Four years ago, Janelly Martinez-Amador was confined to a bed, unable to move even an arm or lift her head. At age 3, the fragile toddler had the gross motor skills of a newborn and a ventilator kept her alive.

She was born with thin, fragile bones, and by 3, she had no visible bones on X-rays. Initially, doctors weren't sure she would survive her first birthday. In May, Janelly will turn 7, and is developing bone with the

help of an experimental drug therapy and her care team at the Monroe Carell Jr. Children's Hospital at Vanderbilt.

Janelly has a rare genetic disorder called hypophosphatasia (HPP), a metabolic disease that affects the development of bone and teeth. An enzyme deficiency causes the bones to become soft because they can't absorb important minerals such as calcium and phosphorus, increasing the risks for pain, broken bones and bone deterioration.

"Imagine your child laying all the time in bed, not being able to lift herself, not being able to move herself, making sure she is not falling or tripping on things," her father, Salvadore Martinez, said through a Spanish interpreter.

"The treatment has worked very well but it has been a compilation of doctors, nurses, assistants … everyone that has been a part of her care that has helped her make a meaningful recovery."

HPP affects about one in 100,000 babies born in the United States. While there are varying degrees of severity, the most severe forms of HPP occur before birth and early infancy. More than half of babies born with the disease don't survive beyond their first birthday.

Janelly has the more severe form of the disease, which was diagnosed when she was 3 months old after failing to grow and gain weight. Doctors initially thought she might have cancer. With a thorough blood analysis at Children's Hospital, they diagnosed her with HPP.

"If you saw her in 2009 and see her now, it's not the same Janelly," said her mother, Janet Amador. "She used a ventilator, an oxygen mask – many machines to help her breathe."

Janelly is one of 11 children, age 3 years and younger, to participate in a

clinical trial to receive an enzyme-replacement drug therapy, asfotase alfa, for the life-threatening form of HPP. She had the worst case of the group.

Michael Whyte, M.D., the lead investigator of the study, which published results in March, 2012, in the *New England Journal of Medicine*, visited Janelly and her family at Children's Hospital last week. It was the first time he had met the family and her physician, Jill Simmons, M.D., a pediatric endocrinologist at Vanderbilt.

"It's wonderful that you had the faith that a treatment might come along. For many years, it seemed there was nothing that was very helpful for this disorder," said Whyte, medical-science director of the Center for Metabolic Bone Disease and Molecular Research at Shriner Hospitals for Children in St. Louis.

"We were fearful that her bone disease was so terribly severe that it might not work. But by looking at the X-rays and hearing about her visits, we were thrilled to hear about her progress."

About eight months into the treatment, Janelly's parents felt her fingers—which had been completely soft and boneless—and they could feel traces of developing bone. Her head also began to develop bone. At 18 months into therapy, X-rays showed, for the first time, the visible development of her rib cage.

Janelly now sits in a wheelchair. Recently, dressed in her Easter best and bright pink bows, she was able to turn her head to gaze at a room of onlookers.

She smiled and waved her hand excitedly, a feat she never would have accomplished before the drug therapy. She is also able to attend school at Harris-Hillman Special Education School, not far from Children's

Hospital.

This spring, doctors hope to be able to remove her tracheostomy tube, which has prevented her from speaking. Her developmental and cognitive abilities will be tested in July.

Improvement continues each day, each week for Janelly.

"This is why we get into medicine in the first place: to truly make a difference in the life of a child," said Simmons, her physician. "My goodness, to go from no bones to bones. That's the most impressive thing I have seen as a physician. It's incredible."

Provided by Vanderbilt University Medical Center