A CASE STUDY

IDENTIFYING GENE LEADS TO IBD CURE

VEO-IBD patient Garrett, age 5

THE MULTIDISCIPLINARY APPROACH TO DIAGNOSE AND CURE VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE

By Judith R. Kelsen, MD

Children who present with inflammatory bowel disease (IBD) <6 years old are categorized as having very early onset inflammatory bowel disease (VEO-IBD). These children can have a more severe and refractory disease course than older children and adults. While older pediatric and adult-onset IBD is a complex and polygenic disease, the role of genomics is more pronounced in this younger age group. Identification of monogenic defects can radically change the therapeutic approach, and in some cases, can be curative.

The following case is an example of a patient seen in the CHOP VEO-IBD multidisciplinary clinic who presented with neonatal-onset, fistulizing, severe IBD and diffuse large B-cell lymphoma (DLBCL). Through genetic sequencing and functional validation, she was found to have a homozygous *IL-10RA* mutation.

Case

A newborn presented with bloody diarrhea and fever on day 1 of life. During the next 2 years, her disease course was complicated by severe bloody diarrhea and development of rectovaginal fistulae. She was diagnosed with duodenal and ileocolonic Crohn's disease and was treated with multiple conventional medical therapies including steroids, mercaptopurine, Humira®, Remicade®, and methotrexate. She ultimately underwent a diverting ileostomy at 9 years of age and a mass was detected intraoperatively that was consistent with diffuse large B-cell lymphoma (DLBCL). She underwent chemotherapy and was successfully induced into remission. We met her in our multidisciplinary VEO-IBD clinic when she was 13 years old.

While her DLBCL was in remission, her IBD remained active, including recurrent oral ulcers, intermittent abdominal pain, and watery ostomy output without blood. In addition, she had severe growth failure and lifelong steroid dependence. Infectious history was notable for 20 to 25 episodes of sinusitis, 1 pneumonia, 14 episodes of otitis media, and 1 pelvic abscess. The combination of DLBCL and fistulizing IBD, known to be consistent with *IL-10R* defects, prompted genomic evaluation using whole exome sequencing. Indeed, we detected a homozygous mutation in *IL10RA*. Our

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collaborative team worked quickly to functionally validate this mutation. She underwent a hematopoietic stem cell transplantation as the definitive therapy and is now cured. She has completed a steroid taper, is in school, and leads a very active life.

This case highlights the critical importance of a multidisciplinary approach. Integrating the phenotypic, immunologic, and genomic data can allow for identification of monogenic defects in these children and the potential for a targeted, life-saving therapeutic approach.

LEARN MORE ABOUT OUR VEO-IBD PROGRAM

CHOP's VEO-IBD Program delivers a personalized evaluation and care plan for each child. Our team includes pediatric gastroenterologists, immunologists, IBD nurses, registered dieticians, behavioral psychologists, and social workers with expertise in VEO-IBD.

Our team works closely with other divisions including Immunology, Microbiome, and Genetics to deliver quality care and discover new breakthroughs. We have:

- Vast experience incorporating nutritional management and therapies: Nutrition is a key component of our treatment recommendations, and the overall nutritional status of our patients is critical to maintaining health and disease remission.
- Quick scheduling of appointments: When VEO-IBD is suspected or diagnosed, which can be difficult in a young child and a trying time for their families, our expert coordinators will gather patients' initial information and schedule a clinic visit as expeditiously as possible. We encourage second opinion visits as well.
- State-of-the-art pediatric endoscopy and infusion suite: Our experienced endoscopy team performs more than 4,500 procedures annually.
- Unparalleled patient access to research trials
- In-person support for the whole family: Our center offers emotional and social support to meet the unique needs of all family members experiencing a VEO-IBD diagnosis. Each year we have an IBD Education Day, where hundreds of family members join us for ongoing education, panels, and support. We also offer a quarterly support group geared at young children, siblings, and their parents facing this diagnosis.

See how we can make a difference to your patients. Learn more about CHOP's Center for Pediatric IBD in this video: **chop.edu/ibd-video.**

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To refer a patient or request a second opinion:

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