Diagnosing Kawasaki Disease

Researchers at the Rady Children’s Hospital in San Diego are testing a new tool to help in the earlier diagnosis of children with KD.

By Ronale Tucker Rhodes, MS

IT IS ESTIMATED that the number of kids who are accurately diagnosed with Kawasaki disease (KD) is just the “tip of the iceberg,” says Adriana Tremoulet, MD, MAS, a pediatric infectious disease specialist at Rady Children’s Hospital in San Diego, Calif. In the U.S., there are approximately 5,000 to 7,000 cases of KD diagnosed annually, but there are many people who present later with conditions that likely are a result of KD being misdiagnosed or undiagnosed. One of the most common conditions is a high risk of heart disease. Specialists like Dr. Tremoulet and her colleagues know that if KD could be diagnosed when symptoms present, the risk of serious outcomes is greatly reduced. And, they may be very close to developing such a diagnostic tool.

What Is KD?

KD, a form of vasculitis, is a rare childhood disease in which the walls of the blood vessels throughout the body become inflamed. In some cases, KD affects the coronary arteries that carry oxygen-rich blood to the heart, which causes some kids with KD to develop serious heart problems.

It’s unknown what causes KD, but it’s believed to be a trigger combined with genetic factors, even though no trigger in kids diagnosed with KD has been found. The disease affects children of all races, ages and genders, although it occurs most often in children of Asian or Pacific Island descent. It is also more likely to affect boys than girls, and most cases occur in children younger than 5 years old.

During the acute phase of KD, one of the main symptoms is a fever that lasts longer than five days, which remains high even after treatment with standard medicines. Also during this phase, a child may be irritable, have a sore throat, joint pain, diarrhea, vomiting and stomach pain. Other classic signs of the disease include swollen lymph nodes in the neck; a rash on the mid-section of the body and in the genital area; red, dry, cracked lips and a red, swollen tongue; red, swollen palms of the hands and the soles of the feet; and redness of the eyes.

Unfortunately, not all kids have classic signs of KD. And, some kids with classic signs may actually have other illnesses that present with similar signs. Therefore, many of these kids go undiagnosed until long-term damage has occurred. This damage, which can present after two to three weeks of the start of symptoms, includes the peeling of fingers and toes, sometimes in large sheets, as well as damage to their coronary arteries.

Rady Children’s Hospital

The Kawasaki Disease Clinic at Rady Children’s Hospital, follows the health status of more than 1,200 children with KD and treats 80 to 90 new patients per year. The clinic is directed by Jane Burns, MD, who was involved with the first intravenous immune globulin (IVIG) study with KD patients (IVIG is a U.S. Food and Drug Administration-approved indication for KD).

The cutting-edge Kawasaki Disease Research Center supports clinical, laboratory and epidemiologic investigation into the etiology, pathophysiology and natural history of the disease. Currently, the center is conducting a number of studies, including the long-term outcome for adults who suffered from KD in childhood, the epidemiology of KD, and genetics and gene expression of KD, among others. But, the newest study launched this year focuses on diagnostics.

A KD Diagnostic Tool in the Works

For approximately five years, researchers at the Kawasaki Disease Research Center have been working to develop the right combination of physical biomarkers and clinical indications to diagnose KD. To do this, they have collected clinical and lab data, as well as blood and urine, from the repository of kids with KD and without, and then combined them to show which combination increases the likelihood that a child has KD. Just last year, they collaborated with researchers at Stanford University and developed an algorithm of that data that appears to be 80 percent accurate in distinguishing between kids with KD and kids with symptoms that are not KD. “Eighty percent is
Did You Know?

Great, but 100 percent would be better,” says Dr. Tremoulet. So, using that algorithm, they launched a diagnostic test validation study in September in the Rady Children’s Hospital emergency room. The clinical trial will include a total of 60 kids at the beginning of diagnosis and 60 kids who have a separate illness, and it will last for three to four years (three years of enrollment, and another year of analysis). After conducting the trial locally, it will have to be tested in nonchildren emergency rooms and then move on to a multicenter study conducted nationally. The ultimate goal is to use the algorithm to develop a tool that will diagnose kids with KD early and, hence, reduce the number of children and adults who suffer serious issues that occur as a result of a KD misdiagnosis.

“One of the hard parts about KD is you have to have a very good clinical eye,” explains Dr. Tremoulet. So, we’re testing [the algorithm] with clinicians who are ER physicians who see kids with a whole host of diseases. Ultimately, what we want is a test that is generalizable.”

A Highly Motivated Team

The researchers involved in this new study are highly motivated for good reason. “What’s motivated us to do this work is that, on a monthly basis, we see probably three to five children who develop significant peeling of their fingers, which is a sign of missed KD,” says Dr. Tremoulet. “Some of the most difficult cases to hear about are the young adults in their mid-30s who may be suffering a heart attack or die suddenly from having had missed KD as children. We are hoping that our diagnostic test will detect children early and prevent such devastating outcomes.”

RONALE TUCKER RHODES, MS, is the editor of IG Living magazine.

Sources


This KD Foundation poster shows the signs of KD and is available on the organization’s website at KDFoundation.org. Photo courtesy of the KD Foundation.