ADA2 is a specific biomarker for MAS in systemic JIA

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According to new research findings presented at the 2019 ACR/ARP Annual Meeting, adenosine deaminase 2 (ADA2) in the peripheral blood is a sensitive, specific biomarker for macrophage activation syndrome, a potentially life-threatening complication of systemic juvenile idiopathic arthritis (systemic JIA) (Abstract #920).

About one child in every 1,000 develops some type of chronic arthritis. These disorders can affect children at any age, although rarely in the first six months of life. It is estimated that around 300,000 children in the United States have been diagnosed with the condition.

Macrophage activation syndrome (MAS) is characterized by a vicious cycle of immune cell activation and dysregulated cytokine production that can result in multi-organ failure and is a life-threatening complication in systemic JIA. Clear biomarkers are needed for prompt diagnosis of MAS to initiate treatment and better understand the pathogenesis of the disease. To address this, a group of researchers conducted a study of peripheral blood ADA2 activity levels to determine if it is a useful biomarker for MAS.

"Children with deficiency of ADA2 are known to develop early onset vasculitis and stroke, but the function of ADA2 and how it is regulated is not entirely clear," said Pui Y. Lee, MD, Ph.D., attending physician at Boston Children's Hospital and one the study's lead authors. "We conducted this observational study to understand whether ADA2 enzyme levels are different in various childhood rheumatologic diseases. To our surprise, the levels were very high in children with systemic JIA complicated by MAS. It is important to find useful biomarkers for MAS, because many of the existing markers are not very effective in distinguishing MAS from systemic inflammation. Early detection of MAS is extremely important, because mortality of the condition remains quite high and treatment should be started as soon as possible."

Researchers established normal levels of peripheral blood ADA2 levels in 175 healthy children and compared these values with 25 children with Kawasaki's disease, 13 with systemic lupus erythematosus (SLE), 13 with juvenile dermatomyositis and 120 with various forms of JIA. While they found mild elevation of ADA2 in some patients with SLE and juvenile dermatomyositis, ADA2 levels that were above the upper limit of normal were largely restricted to children with systemic JIA who had clinically diagnosed MAS.

The study's results show that in children with active systemic JIA, ADA2 activity beyond the upper limit of normal is strong evidence for concomitant MAS.

"Our findings show that ADA2 is a valuable diagnostic marker to distinguish MAS from other forms of systemic inflammation," said Dr. Lee. "While there are many markers currently used for evaluation of MAS, many of them lack specificity unless the cut-off is raised significantly to distinguish MAS from general inflammation. In contrast, elevation of ADA2 levels above the normal limit of healthy individuals has good sensitivity and specificity for diagnosing MAS. This is likely related to the biology of ADA2 as a direct product of activated macrophages. It is our hope that ADA2 testing will be become more available as a clinical test to help diagnose MAS rapidly, which will in turn facilitate treatment initiation and improve patient outcomes."

More information: Study: Adenosine Deaminase 2 as a Circulating Biomarker of Macrophage Activation Syndrome

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