Genetic Variants May Confer Susceptibility to JIA

VITALS

Major Finding: Two genetic variants with known associations to type 1 diabetes or celiac disease also predispose to juvenile idiopathic arthritis.

Data Source: DNA from 1,054 patients with juvenile idiopathic arthritis was compared with that of 3,129 healthy controls. Thirteen single nucleotide polymorphisms (SNPs) that already had confirmed associations with type 1 diabetes or celiac disease were investigated.

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BY MICHELE G. SULLIVAN

FROM THE ANNALS OF THE RHEUMATIC DISEASES

Two genetic polymorphisms now appear to be associated with juvenile idiopathic arthritis as well as type 1 diabetes or celiac disease.

The finding lends credence to a growing idea that genetic variability in common loci can predispose a child to different autoimmune disorders, wrote Dr. Anne Hinks of the University of Manchester, England, and colleagues.

"The approach of targeting variants associated with other autoimmune diseases is already yielding insights into the genetic complexity underlying susceptibility to this serious childhood disease," Dr. Hinks and her coauthors wrote (Ann. Rheum. Dis. 2010;69:2,169-72).

The researchers compared DNA from a total of 1,054 patients with juvenile idiopathic arthritis with that of 3,129 healthy controls. All the subjects were white.

The study focused on 13 single nucleotide polymorphisms (SNPs) that had already had confirmed associations with type 1 diabetes or celiac disease, according to the researchers.

One SNP on the preferred translocation partner in lipoma (LPP) gene (rs1464510) was significantly associated with juvenile idiopathic arthritis. Another SNP located in the ataxin 2 (ATXN2) gene was marginally associated with JIA, but the association was not significant.

The IL12A gene exerts a number of important influences, including encoding a cytokine necessary for the differentiation of T cells and T cell–independent induction of interferon gamma.

The SNP lying in the LPP domain is particularly interesting, the authors noted, because that gene has a confirmed association with celiac disease.

LPP is integral in cell migration and adhesion and is a substrate of tyrosine phosphatase. In addition, LPP has been linked to Ras signaling, a process that is important to the functions of cell growth and differentiation, as well as survival.

A third SNP (rs17810546) located in the interleukin 12A gene (IL12A) was significantly associated with enthesitis-related arthritis. The IL12A gene has already been associated with celiac disease. The association with arthritis was a strong one, Dr. Hinks and her colleagues noted, but there were no other associations with any other JIA subtype.

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Although this gene has not been associated with ankylosing spondylitis, patients with enthesitis-related arthritis are prone to joint destruction in the spine and sacroiliac joints.

"It is important to note that the numbers in this subgroup are small (61), so this finding should be interpreted with caution and will require validation in an independent cohort," Dr. Hinks and her coauthors noted. ■