

UV Exposure Tied to Dermatomyositis in Women

BY JEFF EVANS

The intensity of exposure to ambient ultraviolet radiation appears to determine the prevalence of dermatomyositis and an autoantibody specific to the disease in women, based on a study published in *Arthritis & Rheumatism*.

The UV Index across geographical regions of the United States also significantly correlated with the presence of an autoantibody unique to dermatomyositis (DM)—known as anti-Mi-2—and not to autoantibodies more commonly found in polymyositis (PM).

The association between UV radiation and DM was strongest in a collective group of white, Hispanic, and Asian American women, but it also was significant among black women.

This is the first study to show evidence of the influence of sex on the association between UV radiation and autoimmune disorders, commented Dr. Victoria P. Werth, professor of dermatology at the University of Pennsylvania, Philadelphia, and chief of dermatology at the Philadelphia Veterans Affairs Medical Center.

"This is the best study that I've seen so far in reference to dermatomyositis" and exposure to UV radiation, she said.

The study brings up many



The intensity of UV radiation exposure may be tied to the prevalence of dermatomyositis in women, such as this hand involvement.

COURTESY DR. VICTORIA P. WERTH

"intriguing kinds of things that we don't totally understand," such as differences in risk factors and responses to UV radiation between men and women and between polymyositis and dermatomyositis.

These types of "interesting epidemiologic observations" may help in the future to understand more about the differences in pathogenesis, Dr. Werth said in an interview.

In the cross-sectional, retrospective study, Dr. Lori A. Love of the National Institute of Environmental Health Sciences and her coinvestigators gathered clinical data and serum samples from 202 PM and 178 DM patients at referral centers across the United States.

The investigators detected

myositis-specific autoantibodies in 172 patients (45%), some of which were found in both polymyositis and dermatomyositis patients, whereas others were found only in each particular phenotypic type of myositis, such as anti-SRP in 21 PM patients and anti-Mi-2 in 23 DM patients.

Polymyositis occurred in a significantly greater proportion of black patients (66%) than among nonblack patients (48%), the study showed.

Most (86%) of the patients with anti-SRP antibodies were black, Dr. Love and her associates reported (*Arthritis Rheum.* 2009;60:2499-504).

The proportion of patients in the study who had anti-Mi-2 autoantibodies was significantly

associated with the UV Index for the seven regions (comprising 37 states) that the investigators categorized according to shared geoclimatic factors. However, the UV Index was not associated with the proportion of patients with DM. Both of these comparisons proved to be significant for women but not for men.

Evidence from a previous study has shown that the dose of UV radiation required to induce immunosuppression is three times higher in women than in men, which may mean "other mechanisms would need to be operative to potentially explain how UV radiation preferentially results in the development of dermatomyositis and anti-Mi-2 autoantibodies in women," the investigators wrote.

They noted that "it is tempting to speculate that the development of DM and DM-specific anti-Mi-2 autoantibodies, which are associated with certain major histocompatibility loci, is related to UV-induced increased expression of target autoantigens combined with altered immune responses in genetically susceptible individuals."

The fact that not all dermatomyositis patients have anti-Mi-2 autoantibodies but still develop dermatomyositis means that other environmental risk factors outside of UV radiation must be operating to contribute

to the development of the disease, said Dr. Steven Ytterberg of the division of rheumatology at the Mayo Clinic, Rochester, Minn.

It would be worthwhile to determine if DM patients with anti-Mi-2 autoantibodies are more likely to get clinical disease flares from UV radiation exposure than are those who do not have the autoantibodies. Dermatomyositis patients who are negative for anti-Mi-2 may have a different environmental risk factor, Dr. Ytterberg said in an interview.

The investigators noted that the study may be limited by the following: referral bias, because patients with myositis who are seen at referral centers may not be representative of the larger population of patients with myositis; the use of state-level UV radiation intensities, which can vary considerably from one part of a state to another; the lack of accounting for individual-level exposure; differences in UV radiation exposure at different locations over time; and the use of personal photoprotective measures.

The study was funded in part by the intramural research programs of the National Institute of Environmental Health Sciences.

Dr. Werth and Dr. Ytterberg said they had no relevant disclosures. ■

Diagnostic Test for Kawasaki Disease Is Closer at Hand

BY BRUCE JANCIN

VAIL, COLO. — By far the greatest need in Kawasaki disease is for a diagnostic laboratory test—and recent encouraging developments suggest that gene expression testing may be the answer.

"I don't think we're going to have a diagnostic test tomorrow, but with refinement I'm hopeful that gene expression profiling might be the basis of a diagnostic test," Dr. Marsha Anderson said at a conference on pediatric infectious diseases sponsored by the Children's Hospital, Denver.

"We really, really, really need a diagnostic test," added Dr. Anderson, a pediatric infectious disease specialist at the University of Colorado, Denver.

The need is desperate because it's clear that patients who meet the original Kawasaki disease case definition are just the tip of the iceberg.

That was acknowledged 5 years ago in the revised American Heart Association Kawasaki disease guidelines, which highlighted the diagnosis and treatment of what has come to be termed incomplete

Kawasaki disease (*Circulation* 2004; 110:2,747-71).

Patients with incomplete Kawasaki disease—that is, with fewer than four of the standard criteria—are at increased risk of coronary artery complications, just like patients who meet the original diagnostic criteria, and they too respond to intravenous immunoglobulin.

But familiarity with the revised guidelines isn't all that great outside the centers of expertise in Kawasaki disease, and the lack of a diagnostic test results in delays in diagnosis and treatment, which can have critical long-term impacts.

"I suspect that once we get a diagnostic test, we're going to quadruple the number of patients. We're going to have patients we never dreamed had Kawasaki disease who turn out to have very mild forms of it. That's been seen in many other diseases once a diagnostic test was available," Dr. Anderson observed.

Strong evidence suggesting that genetic predisposition plays a role in the development of Kawasaki disease comes from Japan, where the disease incidence is 10- to 15-fold higher than in white populations. Japanese studies indicate that

within 1 year after a first case occurs in a family, the incidence of Kawasaki disease in a sibling is 2.1%.

Moreover, Kawasaki disease is twice as common in children

whose parents had the disease.

Investigators at Stanford (Calif.) University are pursuing this genetic connection. They are using DNA microarray technology to examine patterns of gene expression in whole blood from patients with acute and convalescent Kawasaki disease.

These investigators demonstrated that patients with Kawasaki disease had increased expression of clusters of genes associated with platelet and neu-

trophil activation, including genes coding for cell adhesion, innate immunity, and B-cell activation, whereas interferon-gamma was turned off.

They also reported that gene clusters that were turned on in Kawasaki disease were, by and large, turned off in adenovirus infection, whereas those that were turned off in Kawasaki disease were turned on in adenovirus infection.

Whole-blood samples from patients with group A streptococcal infection showed a gene expression profile somewhat similar to that of Kawasaki disease, whereas samples from patients with systemic drug reactions were more akin to the adenovirus infection pattern.

When blinded evaluators were asked to use a set of 38 gene transcripts to categorize 23 Kawasaki disease patients and 8 with adenovirus infections, they got the diagnosis right in 21 of 23 Kawasaki disease patients and in 7 of 8 with adenovirus (*J. Infect. Dis.* 2009; 200:657-66).

This is the most promising lead to date in the effort to develop a diagnostic test for Kawasaki disease, in Dr. Anderson's view. ■

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