Cardiovascular Disease, Psoriasis Link Questioned

BY BRUCE JANCIN

BUDAPEST — The last word on the relationship between psoriasis and cardiovascular disease may not be in, according to the results of a new study.

Contrary to earlier studies, psoriasis was found to not be an independent risk factor for hospitalization for ischemic heart disease in a large Dutch study, Dr. Marlies Wakkee reported at the annual congress of the European Society for Dermatological Research.

Even after subdividing the 15,820 Dutch psoriasis patients in the study into those who used only topical therapy versus patients with more severe disease—as defined by use of systemic therapies or hospitalization for psoriasis—the more severely affected patients did not have a higher rate of ischemic heart disease (IHD) hospitalization, said Dr. Wakkee of Erasmus University Medical Center, Rotterdam.

The same held true when the analysis was narrowed to hospitalization for acute myocardial infarction. The psoriasis patients, even those with more severe skin disease, did not have a greater rate of MI than controls, she added.

The study relied upon hospital and pharmacy linked databases covering 2.5 million Dutch patients. The 15,820 psoriasis patients and 27,577 nonpsoriatic controls (mean age 48 years) were followed for a mean of 6 years.

The IHD hospitalization rate was 611 cases per 100,000 person-years in psoriasis patients and 599 in controls. MI hospitalization rates were also similar: 234 per 100,000 person-years in psoriasis patients and 235 in controls.

At study entry, the psoriasis patients had slightly, but statistically significantly, higher rates of antihypertensive drug therapy, compared with controls (19.4% vs. 16.4%, respectively), lipid-lowering drugs (7.0% vs. 6.2%, respectively), and antidiabetic medications (4.4% vs. 3.6%, respectively). This was not surprising, said Dr. Wakkee, given that prior studies have shown the prevalence of metabolic syndrome to be elevated in psoriasis patients.

In the absence of definitive data, physicians will have to help psoriasis patients minimize risks.

DR. WAKKEE

Psoriasis patients also had more hospitalizations for reasons other than psoriasis in the prior 6 months.

In a multivariate analysis adjusted for age, gender, medications, and hospitalizations in the prior 6 months, the relative risk of IHD hospitalization during 6 years of follow-up was 5% higher in psoriasis patients, and the MI hospitalization risk was 6% lower than in controls. These differences were far from statistical significance, she said.

Dr. Wakkee noted that her study findings are at odds with those of a much-publicized analysis of the U.K. General Practice Research Database (JAMA 2006;296:1735-41), which concluded that psoriasis patients had a small but significantly increased risk of MI. It is possible, she said, that the earlier finding was due to detection bias. This potential confounder could occur because psoriasis patients have greater consumption of health care, as shown by the Dutch patients' higher hospitalization rate.

Further muddying the waters, investigators at the University of Basel in Switzerland recently analyzed the U.K. General Practice Research Database and found no overall increased risk of MI, stroke, or transient ischemic attack in patients with recently diagnosed psoriasis, although there was a suggestion of a possible small absolute increase in MI risk in patients younger than age 60 with severe psoriasis (Br. J. Dermatol. 2009;160:1048-56). And no increase in cardiovascular mortality was identified in an earlier long-term follow-up study of PUVA-treated patients.

So the question remains: Is psoriasis as a systemic inflammatory state an independent risk factor for cardiovascular events, or does the increased risk, if present, result from psoriasis patients' increased prevalence of obesity, smoking, metabolic syndrome, and other cardiovascular risk factors?

Dr. Wakkee said the only way to resolve the controversy is to move beyond case-control studies and conduct a large, detailed, long-term prospective study. In the absence of definitive data, physicians will have to help patients minimize their risks. ■

Five Newer or Atypical Exanthems Call for Reassurance

BY ROBERT FINN

While most exanthems are self-limiting, some are not, making it important to establish a specific diagnosis, according to Dr. Anthony J. Mancini.

Parents want to know how long it's going to take to go away, Dr. Mancini said in an interview. "If you can characterize it … at least they may have some answers. They know that it's going to take a while to resolve, and that saves you from follow-up phone calls and visits to the office when they're frantic because it's still there 4 weeks later."

Clinicians have learned to keep an eye out for the bad actors, like oral mucosa necrosis that could signal Stevens-Johnson syndrome, or the centripetal spread of exanthem with petechiae from a tick bite that could signal Rocky Mountain spotted fever, he said at a women's and pediatric dermatology seminar sponsored by Skin Disease Education Foundation (SDEF). Dr. Mancini—head of pediatric dermatology at Children's Memorial Hospital in Chicago—reviewed these five newer or atypical exanthems:

Arcanobacterium haemolyticum

Often masquerading as scarlet fever, *A. haemolyticum* typically appears in adolescents and young adults as a sore throat with a scarlet fever–like rash. It is important for physicians to recognize and diagnose *A. haemolyticum* because it can be treated, noted Dr. Mancini.

The first clue that it is not scarlet fever or mononucleosis is a negative throat culture for strep and a negative Monospot. Most labs can test for *A. haemolyticum,* but only if they know to look, because they need to plate it on a different agar.

Although *A. haemolyticum* will probably resolve on its own with time, children can be treated effectively with a macrolide antibiotic such as an erythromycin, azithromycin, or clarithromycin. Patients do not respond well to penicillin antibiotics, an important distinction from streptococcal infection, he said.

Papular-Purpuric Gloves and Socks Syndrome

Caused most often by parvovirus B19, papular-purpuric gloves and socks syndrome is named for the characteristic rash appearing on a child's palms and soles, with sharp cutoffs at the wrist and ankle, according to Dr. Mancini.

The virus is self-limited and typically requires only symptomatic treatment, but it is important to establish a diagnosis because parvovirus B19 can cause fetal infections in utero and lead to a variety of complications.

Parvovirus B19 also causes Fifth disease, but there is an important difference, he pointed out. The "slapped cheeks" of Fifth disease are thought to appear only after the child is no longer viremic. A child with papular-purpuric glove and socks syndrome may still be viremic when they have a rash, however, and so should be kept away from pregnant women who are early in gestation.

Gianotti-Crosti Syndrome

Most physicians have heard of Gianotti-Crosti syndrome, but many have probably not diagnosed it because they have not looked closely at distribution. "This exanthem likes to involve the outer arms, the outer legs, the buttocks, and the face. It almost always spares the trunk, or at least the trunk will be much less involved than everywhere else," he said.

Physicians need to remember that, while they may have learned in residency that Gianotti-Crosti syndrome is associated with hepatitis B, that's rarely true in the United States. It is usually caused by the Epstein-Barr virus and requires no treatment. It will resolve, but it may take up to 2 months.

Unilateral Laterothoracic Exanthem

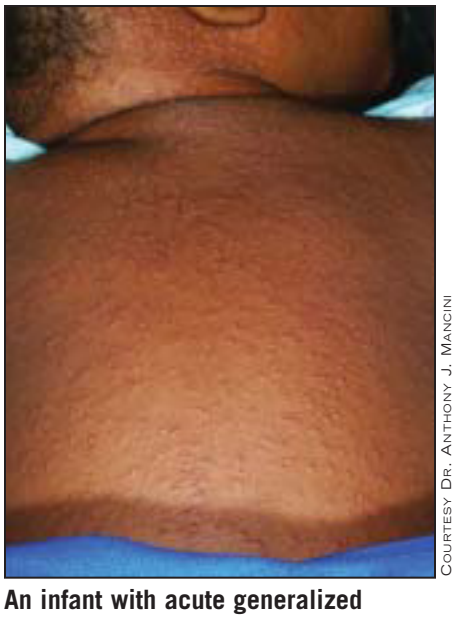
Most physicians "have probably seen unilateral laterothoracic exanthem, but they may have misdiagnosed it as contact dermatitis," Dr. Mancini said. Beginning on one side of the body, usually at the arm, armpit, or trunk, the exanthem may initially look like a contact dermatitis but then begins to spread. Even after spreading, the exanthem maintains predominance on the initial side of involvement.

The cause is unknown, but it is probably viral, he said. It requires no treatment and typically takes 6-8 weeks to resolve.

Acute Generalized Exanthematous Pustulosis (AGEP)

AGEP is often mistaken for drug-induced pustular psoriasis, and the literature is filled with a wide range of reported drug associations, including amoxicillin, erythromycin, NSAIDs, and even pseudoephedrine, but current thinking is that it is often viral, at least in children.

"It's an important entity to recognize, because AGEP can have a sudden onset,



COURTESY DR. ANTHONY J. MANCINI

An infant with acute generalized exanthematous pustulosis is shown.

with fevers and numerous widespread nonfollicular pustules, which can look a lot like pustular psoriasis," Dr. Mancini said. It's self-limited, but children do tend to appear more toxic with AGEP than with some of the other exanthems, especially if they are young. They may have low-grade fevers, and their white counts may be mildly elevated.

Treatment is supportive, with antihistamines, cool compresses, and topical steroids if patients are uncomfortable. AGEP will resolve over 2 weeks or so with desquamation.

Dr. Mancini disclosed being a consultant to SkinMedica and Galderma, and on the speakers bureau of Promius and Galderma. SDEF and this news organization are owned by Elsevier. ■