

Trauma Linked to Arthritis in Psoriasis Patients

BY KATE JOHNSON

MONTREAL — Occurrence of injury, heavy lifting, severe infection, or other forms of trauma were associated with the progression of psoriatic arthritis in a study presented at the annual meeting of the Canadian Rheumatology Association.

“All we’re talking about here is an association; we can’t infer causation,” Dr. Dafna Gladman, the study’s principal investigator, told RHEUMATOLOGY NEWS.

Previous, less rigorous studies have

spectively). The mean duration of PsA was 3 years.

A questionnaire was administered to all patients to assess their environmental exposure over the past 10 years, including occupational trauma, infection, immunization, smoking status and history, and psychological stress.

Univariate and multivariate logistic regression analysis was used to determine the odds ratio of each exposure prior to the diagnosis of PsA. “We actually examined all the patients with psoriasis to make sure they didn’t have psoriatic arthritis,” she said.

Univariate analysis revealed that a history of infection requiring hospitalization was the strongest risk factor for the development of PsA, with an OR of 11.7. (Infective diarrhea carried an OR of 2.11.)

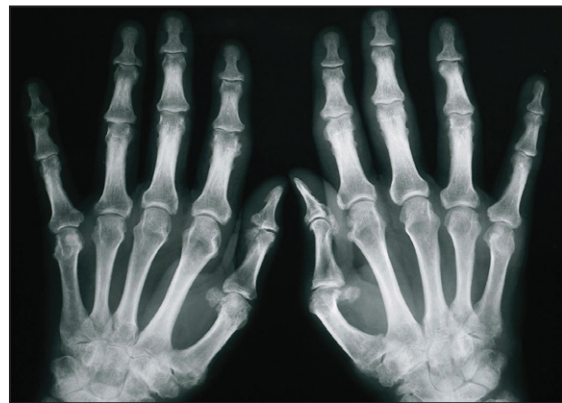
The second-highest risk factor was in the category of occupational exposure. A history of work involving cumulative lifting of at least 100 lb/hr carried an OR of 2.9, and pushing cumulative loads of at least 200 lb/hr

carried an OR of 1.8. And the third-highest risk factor was any injury requiring medical attention (OR, 2.43).

Multivariate analysis revealed that injuries requiring medical attention but excluding fracture and motor vehicle accident (OR, 2.3; $P = .03$), occupations requiring the lifting of heavy loads (OR, 2.7; $P = .002$), and severe infection requiring hospitalization (OR, 10.6; $P = .03$) were significantly associated with progression from psoriasis to PsA.

“For exposure to immunizations we found no risk, but another group [of investigators] has found that immunization was higher in those who got arthritis,” said Dr. Gladman.

“And psychological stress had no impact, although it has been reported that psoriatic patients without arthritis have a lot of stress; in fact, they may even have more because it turns out that patients with psoriasis and no arthritis actually have worse psoriasis.”



Changes in the interphalangeal joints are shown in this x-ray of a patient with PsA in both hands.

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suggested the association between trauma and psoriatic arthritis (PsA), said Dr. Gladman, professor of medicine at the University of Toronto and deputy director of the Centre for Prognosis Studies in the Rheumatic Diseases in that city.

“This study supports that notion—that environmental factors are important—but we think genetic factors are also involved,” as well as immunologic factors, she said, explaining that at most, 30% of psoriasis patients go on to develop PsA.

Her study, which was presented as a poster at the meeting, compared 159 patients who had PsA with the same number of control patients who had psoriasis alone, in order to identify risk factors for progression to PsA. Men accounted for a similar percentage of both groups (46% in the PsA group and 44% in the controls).

The mean age of participants in each group was similar (45 years and 48 years, respectively) as was the mean duration of psoriasis (17.5 years and 18.5 years, re-

After the multifactorial analysis, smoking appeared to be associated with decreased risk, she added. Current smoking had an OR of 0.4 ($P = .01$), and past smoking had an OR of 0.5 ($P = .04$).

Dr. Gladman said that the findings are too preliminary to inform clinical recommendations at this time, but psoriasis patients should know that “if you have a job that requires a lot of lifting, you are more susceptible to getting psoriatic arthritis. Whether it’s the only fac-

tor, we don’t know, because there are also genetic factors involved. It’s quite possible that in those people who are genetically predisposed, if they also do this work, they are more likely to get arthritis.” She said that the next step should be to look at genetic and environmental factors and see if they are independent or not. ■

Disclosures: Dr. Gladman declared no conflicts of interest.

Now We Need Prospective Trials

MY TAKE

The potential impact of trauma on the development of psoriatic arthritis was first proposed over 50 years ago, when the observation of acryo-osteolysis in an injured digit was labeled “deep Koebner’s effect.”

Two recent, retrospective, case-control studies analyzed the relationship between trauma and the onset of psoriatic arthritis. Corticosteroid use (in the first report) and immunization, moving house, and injury severe enough to require medical consultation (in the second report) were associated with incident PsA.

Dr. Gladman’s study provides additional support for the association between trauma and incident PsA.

In this study, individuals with PsA were matched to psoriasis patients, and investigators found that injury requiring medical attention, heavy lifting, and severe infection were associated with the development of PsA.

Of course, many important questions remain to be addressed.

Could the retrospective designs of these case-control studies be strongly influenced by recall bias? This is possible but unlikely to account for these findings, given that both RA and psoriasis subjects have been used as controls.

A second question centers on the

mechanisms that underlie this interesting association.

Two potential explanations have been suggested: the activation of proinflammatory molecules (such as nerve growth factor) that are produced in the psoriatic plaques, or high-level biomechanical stress to the synovial-entheseal complex, which triggers an innate im-

mune response and subsequent inflammation.

Evidence amassed from several different sources supports the concept that trauma may be associated with the onset of PsA.

An adequately powered prospective study of psoriasis patients, with strict case definitions and appropriate control groups, will be required to adequately test the hypothesis and to understand the magnitude of a particular risk factor. Genetic risk factors could also be analyzed in such a study.

In the meantime, we await the details of Dr. Gladman’s analysis, and we should make an effort to catalogue the events that are temporally related to the onset of inflammatory arthritis in our patients.

CHRISTOPHER T. RITCHLIN, M.D., is professor of medicine at the University of Rochester (N.Y.). He reports having no relevant conflicts of interest.



Hypothesis Challenges Current Wisdom on RA Pathogenesis

BY ROBERT FINN

A new “inside-out” hypothesis on the pathogenesis of rheumatoid arthritis suggests that joint damage may arise from within adjacent bone marrow, rather than—or in addition to—arising from outside via the synovial membrane, according to Dr. Georg Schett and Dr. Gary S. Firestein and published online in the journal *Annals of the Rheumatic Diseases*.

The conventional “outside-in” hypothesis holds that the primary pathogenic event in RA is the alteration of a synovial membrane. The altered membrane recruits immune cells, resulting in an onslaught of inflammation, cell accumulation from unbalanced proliferation and cell death, and perhaps a synovial immune response.

Either of two scenarios could lead to alterations in the synovial membrane. In one scenario, there’s a confluence of environmental and genetic factors and the breakdown of tolerance. Alternatively, the synovial membrane could be changed by systemic processes.

The inside-out hypothesis holds that lesions within the bone marrow could begin to destroy the inner cortical bone surface, eventually opening pathways to the synovium. Mesenchymal elements could migrate through these cortical pores, stimulating joint inflammation, wrote Dr. Schett, professor of internal medicine, rheumatology, immunology, and oncology at the University of Erlangen-Nuremberg (Germany), and Dr. Firestein, professor of medicine of the University of California, San Diego.

Lesions within the bone marrow have been observed with MRI in the earliest stages of the disease. Microscopically, these lesions are sites where bone marrow fat has been replaced by inflammatory tissue dominated by lymphocytes. Other studies have demonstrated that these lesions are associated with structural damage in joints. “Different forms of arthritis may preferentially use either the outside-in or inside-out mechanism. ... Preference for one of these two mechanisms may better explain some of the clinical differences of the various forms of arthritis.” (*Arch. Rheum. Dis.* 2010 March 18 [doi:10.1136/ard.2009.121657]). ■

Disclosures: The investigators stated that they had no conflicts of interest.