Psoriasis Independently Increases Stroke Risk

BY BRUCE JANCIN
Denver Bureau

KYOTO, JAPAN — Severe psoriasis appears to be a potent risk factor for stroke independent of the traditional stroke risk factors, Dr. Rahat S. Azfar said at an international investigative dermatology meeting.

She presented a case-control study drawn from the U.K. General Practice Research Database (GPRD) in which she found severe psoriasis was associated with an excess stroke risk amounting to one additional stroke per 530 patients per year attributable to the immune-mediated skin disease, beyond background levels of traditional stroke risk factors.

"Given the prevalence of psoriasis worldwide, these numbers carry a potentially significant impact on public health," observed Dr. Azfar of the University of Pennsylvania, Philadelphia.

Psoriasis affects roughly 2.5% of the population worldwide, including an estimated 4.5 million U.S. adults.

She and her colleagues previously had shown psoriasis to be an independent risk factor for acute MI, also using the GPRD. But the relationship between psoriasis and stroke had never before been studied.

The GPRD is an extensive electronic medical record including more than 9 million U.K. patients under the care of general practitioners/family physicians in 450 primary care practices. Dr. Azfar reported on 129,143 patients with mild psoriasis in 1987-2002 and 496,666 contemporaneous controls without psoriasis, along with 3,603 patients with severe psoriasis and 14,330 separate controls. The mean follow-up was about 4 years.

As found in other studies, patients with severe psoriasis had higher rates of obesity and smoking than did controls, while rates of these and other traditional cardiovascular risk factors were similar in patients with mild psoriasis and in controls.

After adjustment for the major stroke risk factors—diabetes, hyperlipidemia, smoking, obesity, hypertension, age, and gender—patients with mild psoriasis were found to have a statistically significant 6% per year increased relative risk of stroke. In contrast, the stroke risk in patients with severe psoriasis was increased by 43% per year, compared with matched controls.

The attributable risk of stroke in patients with mild psoriasis was 2.4 strokes per 10,000 person-years, and with severe psoriasis it was 1.9 strokes per 1,000 person-years.

A caveat: Data audit suggested up to 15% of patients categorized in the GPRD as having mild psoriasis may actually have had moderate disease. If so, truly mild psoriasis may not be associated with any significant excess in strokes, Dr. Azfar said.

The hypothesis is that the link between psoriasis and stroke—and MI as well—lies in Th1/Th17-mediated systemic inflammation, a prominent shared feature, she explained at the meeting, sponsored by the European Society for Dermatological Research, the Japanese Society for Investigative Dermatology, and the Society for Investigative Dermatology.

To examine the possibility that the excess stroke risk seen in severe psoriasis was a function of toxicities of treatments for the disease rather than being intrinsic to severe psoriasis itself, the investigators reanalyzed the data

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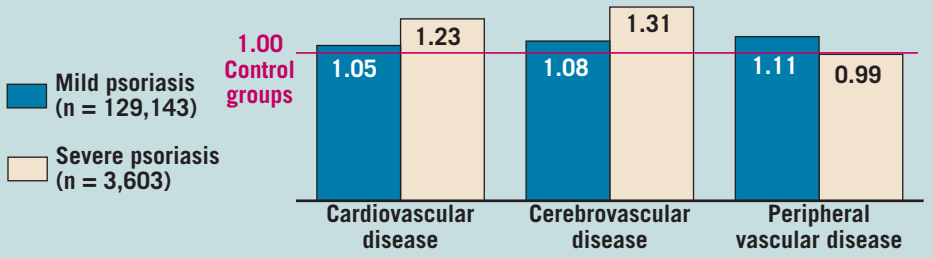
Odds Ratios of Atherosclerotic Diseases In Psoriasis Patients at 4-Year Follow-Up



Notes: Odds ratios adjusted for traditional factors. There were 496,666 controls for mild psoriasis and 14,330 controls for severe psoriasis.
Source: Mr. Shin

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after excluding methotrexate users or restricting the analysis to patients treated with oral retinoids. It didn't have any significant impact upon the results. Neither did exclusion of psoriatic arthritis patients.

Elsewhere at the conference, Daniel B. Shin, Dr. Azfar's coinvestigator, presented an analysis of the rates of cardiovascular, cerebrovascular, and peripheral vascular disease in the same study population. The rationale for this additional analysis was that MI and stroke are acute thrombotic events, and it would be informative to see if psoriasis is also associated with increased rates of chronic atherosclerotic diseases as reflected in the appropriate diagnostic codes, as well as procedure codes for coronary revascularization, carotid endarterectomy, and peripheral vascular intervention.

This indeed proved to be the case. As for stroke, the associated risks generally were greater with severe than with mild psoriasis, noted Mr. Shin, a medical student at the university. (See chart, page 14.)

The ongoing GPRD studies are partially funded by an unrestricted grant from Centocor. The investigators reported having no conflicts of interest.■

'Bridging' With Enoxaparin Or Heparin Appears Risky

BY MARY ANN MOON
Contributing Writer

For patients with cardioembolic stroke, "bridging" therapy with either enoxaparin or heparin until long-term warfarin treatment takes effect raised the risk of serious bleeding, compared with immediately commencing warfarin, a study shows.

In contrast, initiating warfarin shortly after cardioembolic stroke was found to be safe in this single-center retrospective review of 204 patients, according to Dr. Hen Hallevi of the University of Texas at Houston and associates (Arch. Neurol. 2008 July 14 [doi:10.1001/archneur.65.9.noc70105]).

Because this study was retrospective and nonrandomized, the results await validation; they should be viewed as "hypothesis-generating," and should be interpreted with caution, they noted.

Currently no consensus exists on when and how to institute long-term anticoagulation for secondary stroke prevention in these patients. "Bridging" with enoxaparin or heparin is common practice even though it is not endorsed in published guidelines, the investigators said.

Many clinicians also defer initiating warfarin for fear of precipitating a hypercoagulable state, which "may occur when warfarin is initiated without heparin and may lead to abnormal clotting and skin necrosis," they said. However, this is an uncommon occurrence in clinical practice, and is usually associated with protein C deficiency, they added.

In this study, all cases of cardioembolic stroke between April 2004 and July 2006 were reviewed. The decisions of whether to use bridging and, if so, whether to use enoxaparin or heparin were "based on clinical judgment and personal preference of the treating physician."

Thirty-five patients were given warfarin immediately, without any bridging. Forty-four received heparin bridging, and 29 received enoxaparin bridging. Another 8 patients received no anticoagulation therapy, and 88 received aspirin only.

The patients who received no anticoagulation or only aspirin fared poorly and were 12 times more likely to experience stroke progression than those in the other treatment groups.

Heparin bridging was significantly more likely to cause systemic bleeding, and enoxaparin bridging was significantly more likely to cause grade 2 parenchymal hematoma, compared with immediate warfarin.

There were no episodes of skin necrosis in the warfarin group, supporting the observation that this complication is very uncommon in clinical practice and that bridging specifically to prevent skin necrosis is unwarranted, Dr. Hallevi and his associates said

Moreover, there was a clustering of cases of late, symptomatic hemorrhagic transformation "composing an alarming 10%" of the enoxaparin group, with no cases in the warfarin and heparin groups. This suggests a pathophysiologic link between enoxaparin and hemorrhagic transformation, they added.

"Warfarin treatment appears to be safe and can be started at any point during the hospital stay, along with deep vein thrombosis prophylaxis. [In contrast], bridging with a full dose of enoxaparin or heparin may carry a high risk of intracranial and systemic bleeding," the researchers said. ■