Severe Psoriasis Appears to Be Potent Risk Factor for Stroke

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K YOTO, J APAN — 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. Five percent have severe disease as defined by a need for systemic therapy or phototherapy.

She and her coinvestigators had previously 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, according to Dr. Azfar.

The working 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 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.

A German dermatologist in the audience questioned the reliability of psoriasis diagnoses in the GPRD. In his country, he added, general practitioners get it wrong at least 30% of the time.

Dr. Azfar replied that she and her coworkers have formally validated the ability of U.K. general practitioners to reliably diagnose the disease. In any event, severe psoriasis was typically diagnosed by a consultant dermatologist.

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, Dr. Shin said.

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.)

There was, however, one glaring exception to the broad trend. Why the lack of association between severe psoriasis and increased peripheral vascular disease? “I’ve asked some of my colleagues in cardiovascular medicine, and they think peripheral vascular disease is significantly underdiagnosed,” explained Dr. Joel M. Gelfand, senior investigator in the GPRD studies and medical director of the clinical studies unit in the department of dermatology at the university.

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