Insulin Resistance Linked to Acanthosis Nigricans

BY DAMIAN McNAMARA

SAN FRANCISCO — Insulin resistance may be present in patients with acanthosis nigricans, particularly if they are overweight or obese, and research increasingly supports a link between these conditions.

A high level of clinical suspicion may be warranted, Dr. Jeffrey P. Callen said at a seminar on women's and pediatric dermatology sponsored by Skin Disease Education Foundation (SDEF). "Sometimes it is a very subtle finding."

Dr. Callen, chief of dermatology and professor of medicine at the University of Louisville (Ky.), cited the case of an overweight young woman he saw for acne treatment. She had no menstrual irregularities, which can signal polycystic ovary syndrome, a condition also linked with insulin resistance. "Basically the reason we were alert to the fact that she was insulin resistant is, during her complete examination, we noticed a velvety discoloration on the back of her neck, in a folded area of the skin."

The patient was referred to her primary care physician and tested positive for insulin resistance.

An insulin sensitizer such as metformin can help such a patient lose weight, after which their acanthosis nigricans would likely improve as well, said Dr. Callen. Some reports in the literature support use of insulin sensitizers to indirectly improve acanthosis nigricans (Ann. Pharmacother. 2008;42:1090-4), whereas others only point to modest benefits (J. Drugs. Dermatol. 2006;5:884-9).

The clinical association became stronger after researchers found 78 (36%) of 216 patients newly diagnosed with type 2 diabetes also had acanthosis nigricans on the back of their necks (Endocr. Pract. 2004;10:101-6). Investigators at the University of Texas Southwestern in Dallas found risk varied by body mass index and ethnicity in this retrospective study. "They found those who had acanthosis nigricans were most often insulin resistant, overweight, and more of them were people of color," Dr. Callen said. For example, 50 of 95 African American and 28 of 78 Hispanic diabetics in the study had acanthosis nigricans, compared with 1 of 39 whites and 0 of 4 Asians.

More recently, researchers found a higher prevalence of insulin resistance among obese women with acanthosis nigricans, compared with others without the skin hyperpigmentation (J. Dermatol. 2009;36:209-12). Specifically, 5 of 32 participants (16%) with acanthosis nigricans had insulin resistance, compared with none of the 34 women without the dermatologic condition.

Acanthosis nigricans is a clinical diagnosis and histopathology generally is not required. Affected patients often come to a dermatologist "because they've noticed this hyperpigmentation on folded areas of the skin—the back of the neck or under the arms." Although Dr. Callen sometimes orders fasting and postprandial insulin levels for patients with acanthosis nigricans, he thought most dermatologists would refer a patient for further work-up.

Dr. Callen disclosed no relevant conflicts of interest. SDEF and this news organization are owned by Elsevier. ■

To see a video of Dr. Callen discussing this association, visit www.youtube.com/SkinAndAllergyNews.

Radiation's Association to Skin Conditions Is Often Missed

BY AMY ROTHMAN SCHONFELD

BOCA RATON, FLA. — New guidelines for patient radiation dose management following neuroembolization procedures emphasize the need for physicians to inform and follow-up with patients about early and delayed adverse effects.

Often neither the patient nor a physician makes the association between the neurointerventional treatment the patient had months or years before and the skin rash, ulcer, or hair loss he currently has, according to Dr. Donald L. Miller, a coauthor of the guidelines, which were published by the Society of Interventional Radiology (J. Vasc. Interv. Radiol. 2009;20:S263-73).

"I think this will be a useful resource for clinicians," said Dr. Miller, a professor of radiology and radiological sciences at the Uniformed Services University of the Health Sciences, Bethesda, Md., referring to a table on radiation and the skin.

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The table describes immediate, early, midterm, and late reactions—and the extent of recovery—across five levels of radiation exposure. For instance, at 2-5 Gy exposure, transient erythema and hair thinning should produce no long-lasting effects. If the patient receives more than 15 Gy exposure, during the first 2 weeks the patient may exhibit transient erythema with possible pain, edema, and acute ulceration, which develops into hair loss, and thinning and weeping of the skin between 14 and 40 days. The condition may further deteriorate into skin atrophy, secondary ulceration, and dermal necrosis between 40 and 400 days after exposure, with skin breakdown and persistent wound atrophy evident more than a year after exposure and requiring surgical treatment.

There is a greater likelihood of both early and delayed adverse events when risk factors such as medical history, previous radiation exposure, and patient/lesion characteristics are factored in, he said.

If the radiation dose administered during the procedure was high, the possible effects of radiation, and its management, should be discussed after the procedure, Dr. Miller said at the annual meeting of the Society of NeuroInterventional Surgery.

"Without these instructions, patients may go to a dermatologist, but neglect to mention that they have undergone an interventional procedure. I have heard of patients undergoing unnecessary skin biopsies. Not only is the biopsy not diagnostic, but it may result in a nonhealing ulcer. The correct diagnosis may be delayed for years," Dr. Miller said.

Radiation dose from some interventional procedures may be several orders of magnitude greater than that for simple studies. Also, dose may be increased when the lesion is difficult to access, the procedure is prolonged, or the patient is obese, Dr. Miller explained. Other factors, including diseases such as hyperthyroidism, ataxia, telangiectasia, collagen vascular disease, and diabetes mellitus make patients more prone to radiation-induced injury, as might therapy with actinomycin D, doxorubicin, bleomycin, 5-fluorouracil, or methotrexate.

Clinicians should also be aware of stochastic effects of radiation, meaning that its probability of causing damaging effects increases with increasing dose, but the severity of such effects is independent of the total dose.

After a procedure, the operator is responsible for noting radiation doses in the medical record. Clinicians can later consult the record to find out the level of radiation exposure if injury is suspected. The guidelines specify threshold values of significant radiation dose; surpassing the significant radiation dose initiates additional dose management actions, but does not imply that injury will result, Dr. Miller said. ■

Sensitivity Reaction Found To Cause Heparin Lesions

BY MICHELE G. SULLIVAN

Heparin-induced skin lesions are fairly common among patients receiving heparin for treatment or prophylaxis, especially among women, and those who are overweight or who have taken the drug for more than 9 days, a new study has determined.

Prior research had suggested that many cases were caused by heparin-induced thrombocytopenia. The study by Dr. Marc Schindewolf and colleagues contradicts those data: A delayed-type hypersensitivity reaction caused the lesions in all 24 of the cases they observed (CMAJ 2009 Sept. 28 [doi:10.1503/cmaj.081729]).

Dr. Schindewolf of the Hospital of the Johann Wolfgang Goethe University in Frankfurt, Germany, and his coauthors also postulated that heparin-induced skin lesions are probably much more common than currently believed. Their observed incidence of 7.5% far exceeded their expected findings of 2%, which were based on prior clinical observations. "During the study we were surprised by the high number of patients with [lesions]," they wrote. "For most of the patients, the diagnosis was made because of our study. Therefore, it is tempting to speculate that many cases of heparin-induced skin lesions are undiagnosed."

The study comprised 320 patients enrolled over a 12-month period, all of whom were taking some form of heparin as treatment or prophylaxis. The patients' mean age was 61 years; the median duration of heparin use was 9 days, but it ranged from 7 to 1,095 days. Most (60%) were taking enoxaparin; 31% were taking nadroparin. The remainder was taking other forms of heparin.

In all, 24 patients developed heparin-induced skin lesions. Most of the cases were small eczema-like plaques at the injection site. A few patients had generalized itchy erythematous plaques. In 23 patients, a delayed-type hypersensitivity response was the confirmed cause. One patient refused to consent to a punch biopsy or allergologic testing. Although all of these patients were screened for immune-mediated heparin-induced thrombocytopenia, it was detected in only one patient.

Compared with those who did not develop lesions, more of those who did were women (71% vs. 45%), had a higher body mass index (30 kg/m^2 vs. 26 kg/m^2), and had used heparin longer (19 days vs. 9 days). A linear regression analysis confirmed several significant risk factors: body mass index higher than 25 kg/m^2 (odds ratio, 4.6), female gender (OR, 3.0), and therapy duration exceeding 9 days (OR, 5.9).

The lesions should be viewed as a symptom requiring an investigation of some underlying etiology, they wrote: "We recommend obtaining a punch biopsy; comparing platelet counts before, during, and after therapy; and performing appropriate laboratory investigations to exclude heparin-induced thrombocytopenia."

The authors reported having no financial conflicts with regard to the study. ■