Actinic Keratoses: Reclassification Spurs Debate

BY BRUCE JANCIN
Denver Bureau

AMSTERDAM — Recent European guidelines classifying actinic keratoses as in situ squamous cell carcinoma came under fire in a panel discussion at the 11th World Congress on Cancers of the Skin.

"Since our histopathologist started calling AKs carcinoma in situ I've had four patients in my outpatient clinic crying because they were given the diagnosis of cancer. They had to wait 3 weeks for a follow-up appointment to have somebody explain the situation to them, and it was 3 weeks of hell. They were afraid of dying. So I think from the patient's point of view this classification is a big mistake," said Dr. Alexis Sidoroff of the Medical University of Innsbruck (Austria).

Dr. Eggert Stockfleth, lead author of the published guidelines (Eur. J. Dermatol. 2006;16:599-606) developed by the European Dermatology Forum and accepted by the Union of European Medical Specialists, defended the classification scheme on the basis of the histopathologic changes and genetic mutations shared by actinic keratoses (AKs) and squamous cell carcinomas (SCCs).

"Actinic keratosis is an early stage of cancer. It is not a precursor lesion," declared Dr. Stockfleth, director of the skin cancer clinic at Charité University Hospital, Berlin.

With the incidence of nonmelanoma skin cancer climbing worldwide by 7%-10% per year, the guidelines committee felt that routine treatment of AKs is warranted to combat the problem, he said.

Dr. Irene Leigh, however, argued that categorizing AKs as carcinoma in situ implies an inevitability of progression that bears no relation to reality. The chance that any individual AK will transform into invasive SCC is extremely low, so it is better to view AKs as markers of increased risk of SCC. These AKs arise and often regress in a field of sun-damaged, dysplastic skin that is undergoing a process called field cancerization or simply field change, out of which most SCCs arise, she said.

Categorizing AKs as carcinoma in situ implies an inevitability of progression that bears no relation to reality.

DR. LEIGH

"I don't call these lesions carcinoma in situ. I call them AKs. I don't think every AK is going to progress to squamous cell carcinoma. There's evidence for regression of AKs, and there's not much evidence for anything else," said Dr. Leigh of the University of Dundee (Scotland).

Dr. Hywel Williams expanded on this theme. "We are dealing with a field change. Surely what we see physically is like mushrooms in a mycelium of squamous metaplasia. The mushrooms pop up and others go down. To me, the idea that by freezing or otherwise treating a single lesion of AK we're dealing with the problem seems delusional," said Dr. Williams, professor of dermatology at the University of Nottingham (England).

"We are still in 2007 deluding ourselves about the value of destructive therapies for visible lesions and playing into the agenda of an enormous industry with vested interest in maintaining this ritual that we have," he added at the congress cosponsored by the Skin Cancer Foundation and Erasmus University, Rotterdam, the Netherlands.

Dr. Jean-Jacques Grob agreed that the case for routinely treating AKs to prevent SCC is weak in immunocompetent patients. Nor is there any persuasive evidence as yet that invasive SCCs can be prevented by treating the field cancerization process itself, although clinical trials involving imiquimod, photodynamic therapy, and other treatments are ongoing, noted Dr. Grob, professor of dermatology at the University of Marseille (France).

"Let's face it, aside from a few studies showing regular use of sunscreens prevents AKs, the field is a mess," Dr. Williams agreed. "There's a shocking lack of good-quality evidence to inform the debate. That's especially painful to see in a condition as common as this." ■

Australian Study Shows High Turnover of Actinic Keratoses

BY BRUCE JANCIN
Denver Bureau

AMSTERDAM — The natural history of actinic keratoses involves high turnover and far greater lability than generally recognized, according to a first-of-its-kind study.

"When you count three or four AKs on a person at time zero and come back and find three or four at time one you may think you're looking at the same AKs, but this study shows you're not. You're probably looking at six or seven different AKs—three have regressed and three others have taken their place," Dr. Adele C. Green said at the 11th World Congress on Cancers of the Skin.

Indeed, she compared AKs to whitecaps arising in a sea of dysplastic skin, then ebbing below the point of detection before reforming.

"It's striking how high the turnover is. This is such a dynamic population. The more frequently you look at patients and count their AKs, the more turnover you see," added Dr. Green, head of the cancer and population studies group at the Queensland Institute of Medical Research, Brisbane, Australia.

The other impressive finding from this AK substudy—conducted within the larger prospective, longitudinal, community-based Nambour Skin Cancer Study—was that a small percentage of individuals carry a disproportionate load of the total AK burden. While the risk that any individual AK will transform into invasive nonmelanoma skin cancer is extremely low, the high total AK count in this heavily burdened subgroup identifies affected individuals as being at high risk.

The AK substudy involved 96 randomly selected adults, equally divided between men and women, who underwent detailed skin examinations every 2-6 months during which every AK was stenciled onto a clear plastic-wrap body map for purposes of lesion comparison over time.

At baseline, 53 of the 96 participants had no prevalent AKs, while the other 43 had a total of 494 lesions. Twelve percent of subjects had 65% of all prevalent AKs.

During the first 12 months of follow-up, 549 new AKs occurred in men and just 65 in women. Meanwhile, 526 prevalent AKs regressed and 53 prevalent AKs regressed and then recurred. The result was a 1-year net 45% increase in the number of AKs in men and a 44% net decrease in women. Seventy-four percent of prevalent AKs regressed, as did 29% of incident AKs.

Participants with baseline AKs were more than sevenfold more likely to develop additional AKs in the next year, Dr. Green noted at the congress, cosponsored by the Skin Cancer Foundation and Erasmus University.

The clinical relevance of these findings about the natural history of AKs hinges on the fact that the full 1,621-subject Nambour study showed that regular use of a broad-spectrum sunscreen markedly reduced the incidence of both AKs and invasive squamous cell carcinomas. Since AKs arise and regress so frequently in a field of sun-damaged skin and there is no way to identify which ones will transform into skin cancer, it's illogical to treat individual lesions with cryotherapy, as many dermatologists persist in doing, she continued.

This argument struck a responsive chord with other speakers. "For field cancerization, we need field therapy," agreed Dr. Tobias Forschner of the skin cancer center at Charité University Hospital, Berlin.

"We have lots of treatment options—I would say an armada," Dr. Forschner added, citing the intense commercial interest in field therapy using photodynamic therapy, imiquimod, diclofenac, and 5-fluorouracil. ■

Some Topical Polyphenols May Have a Role in AK Treatment

BY DOUG BRUNK
San Diego Bureau

CORONADO, CALIF. — Topical red wine, green tea, and caffeine polyphenols may play a role as chemopreventive agents for actinic keratoses and photodamaged skin, results from a small pilot study suggest.

The first part of the study was designed to assess the safety and efficacy of the individual polyphenols. The second part of the study was designed to assess the efficacy of combination therapy (green tea polyphenols plus vitamin C or red wine polyphenols plus caffeine), Dr. Karen F. Han said at the annual meeting of the Pacific Dermatologic Association.

Seven of nine patients had significantly fewer actinic keratoses on the combination therapy side.

DR. HAN

Patients were eligible for the study if they had at least three actinic keratoses on each forearm, each dorsal hand, or the face/scalp/neck area, and were otherwise in good health.

In a double-blind, left-to-right placebo-controlled trial, the subjects were randomly assigned to one of the tested gels and a placebo gel. Patients were instructed to apply the gels twice a day for 12 weeks.

Before and after clinical photographs were taken, shave or 2-mm punch biopsies were obtained, and the patients were followed monthly for a total of four visits.

At each monthly follow-up visit, Dr. Han, a dermatologist in group practice in Palo Alto, Calif., mapped and counted actinic keratoses, took clinical photographs, and reviewed each patient's self-assessment form. The main outcome measure was the total number of residual actinic keratoses; the secondary outcome measure was an assessment of signs of photodamage, including dyschromia, wrinkling, texture, and telangiectasia.

In part 1 of the study, Dr. Han saw a statistically significant difference between the treatment sides and placebo sides in 11 of 14 patients. Of those 14 patients, 7 (50%) had reduced numbers of actinic keratoses that favored the treatment side. The reduction ranged from 60% to 100% clearance.

In part 2 of the study, Dr. Han observed a statistically significant difference between the treatment sides and the placebo sides in eight of nine patients who completed this component of the trial. Of those nine patients, seven (78%) had reduced numbers of actinic keratoses that favored the treatment side. The reduction ranged from 50% to 85% clearance.

Shantel Medical Supply Corp. supplied the gels used for the trial, but Dr. Han did not receive any financial support from the company. ■