Clinical Recognition of Actinic Keratoses in a High-Risk Population

How Good Are We?

Suraj S. Venna, MD; Dennis Lee, MD; Miguel J. Stadecker, MD, PhD; Gary S. Rogers, MD

Background: Actinic keratoses (AKs) are dysplastic epidermal lesions considered to be potential precursors of squamous cell carcinoma. Most AKs are diagnosed clinically and are rarely confirmed histologically. High interobserver variation exists among dermatologists for the diagnosis of AKs. Previous studies of the positive predictive value of the diagnosis of AKs have yielded rates as high as 94%. This study evaluates the rate at which histologic analysis confirms the clinical impression (positive predictive value) of AKs in patients with a history of skin cancer.

Observations: Seventeen (74%) of 23 lesions with classic features of AKs, as determined by 3 dermatologists, were confirmed as AKs histologically. These were lesions that would ordinarily not be biopsied. Of the 6 misdiagnoses, 5 (83%) were skin cancer, most often squamous cell carcinoma.

Conclusions: The positive predictive value of 74% for the diagnosis of AKs in this study is substantially lower than that of 2 previous studies, suggesting that physicians may be misdiagnosing many patients with classic features of AKs. Most misdiagnosed cases were forms of skin cancer. These preliminary data suggest that the threshold for biopsy of suspect lesions in patients with a history of skin cancer should be low and warrant further evaluation.

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Medical Center for definitive surgical treatment of skin cancer were consecutively examined by a team of dermatologists for the presence of AKs during a 6-week period. The examiners included 2 board-certified dermatologists and a second-year dermatology resident. Every patient presenting for surgery was examined, and the first 18 patients who satisfied the inclusion and exclusion criteria (Table) underwent a biopsy of the presumed AK. All members of the team had to agree that the lesion represented a classic AK, a lesion that would not ordinarily warrant a biopsy examination. A classic AK was defined as an erythematous papule 2 to 5 mm in diameter, with an adherent scale and a palpable rough surface (Figure). Lesions that were indeterminate or hypertrophic were not included.

For each patient, skin examinations of sun-exposed areas were performed, with special attention to the scalp, face, and dorsal hands. Patients were made aware of the purpose of this pilot study and agreed to have suspect lesions biopsied after informed consent was obtained.

A spreadsheet was devised that included the patient’s medical record number, date, site of biopsy, site of skin cancer, clinical impression, and pathologic diagnosis. All 23 lesions were histologically evaluated by a single dermatopathologist (M.J.S.). Two lesions, which were acquired from a Tufts–New England Medical Center satellite office, were submitted to another dermatopathologist. All the lesions that were initially read as AK were then reread in a masked manner, with 100% intraobserver concordance.

### Table. Inclusion and Exclusion Criteria

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<thead>
<tr>
<th>Inclusion Criteria</th>
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<tr>
<td>• A history of skin cancer</td>
<td>• Immunosuppression</td>
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<td>• Current surgical treatment of skin cancer</td>
<td>• Organ transplantation</td>
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<td>• AKs with classic clinical features</td>
<td>• Current treatment with chemotherapy</td>
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<td>• Genetic disorder associated with an unusually high rate of skin cancer, such as xeroderma pigmentosa or basal cell nevus syndrome</td>
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<td>• AKs occurring within 1 cm of a surgical scar or the site of skin cancer</td>
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<td>• AKs with previous treatment (liquid nitrogen, fluorouracil, or photodynamic therapy)</td>
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<td>• Hypertrophic AKs</td>
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<td>• Indeterminate lesions</td>
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Abbreviation: AKs, actinic keratoses.

The present pilot study of 18 high-risk patients (skin phototype I or II) with 23 lesions yielded a PPV of 74% for diagnosing AKs in which only lesions with clinically classic features of AKs were biopsied. In a population of patients with a high prevalence of skin cancer, we would expect to have more than 95% PPV for the diagnosis of AKs. Physicians are misdiagnosing a substantial proportion of patients with classic features of AKs. In addition, of the lesions that were not AKs histologically, 5 (83%) of 6 were forms of skin cancer (3 SCC, 1 BCC, and 1 lentigo maligna).

The differential diagnosis of a classic AK includes seborrheic keratoses, stucco keratoses, arsenical keratoses, developing keratoacanthoma, discoid lupus erythematosus, acantholytic acanthoma, psoriasis, acrokeratosis verruciformis, SCC, BCC, and Bowen disease. This broad differential underscores the highly nonspecific clinical features of AKs. The present pilot study shows that in a population of patients with a high prevalence of skin cancer, it would be prudent for physicians to have a lower threshold to biopsy suspected lesions rather than repeatedly treating them with liquid nitrogen or other methods.

Weinstock et al examined the reliability of dermatologists to count AKs and found a substantial degree of interobserver variation, even with experienced dermatologists. Whited et al examined the ability of primary care physicians to diagnose AKs and NMSC using der-
matologists’ clinical impressions as the gold standard and found again that for the diagnosis of AKs, the interobserver variability among dermatologists was unreliable.

Marks et al11 examined the presence of AKs as a predictive factor for a person’s potential to develop NMSCs. Most AKs were diagnosed clinically, except in doubtful cases, when a biopsy was performed. The examiners, including a consultant dermatologist, a dermatology registrar, and a medical student, were tested for their ability to correctly diagnose AKs in a previous study.12 Their PPV was 94% (34/36). One lesion was found to be a seborrheic keratosis, and the other showed normal histologic findings except for solar elastosis.

The only other data examining PPV for the diagnosis of AKs were collected in a study13 investigating the reduction of AKs with the regular use of sunscreen. Of 588 patients with clinically diagnosed AKs, 48 were chosen at random for biopsy examination as a measure of diagnostic accuracy. Thirty-nine of the 48 lesions, or 81% PPV, were histologically confirmed AKs. None of the missed lesions were skin cancers. The histologic findings of the 9 lesions that were not AKs were as follows: 1 each spongiform dermatitis, hemangioma, and benign papilloma; 2 stucco keratoses; and 4 with severe solar damage and inflammatory changes in the dermis.

Although various prevalence rates of AKs are quoted in the literature, the true rate cannot be determined unless histologic confirmation is made. Moy14 makes the statement that “there is no definite way to distinguish between an actinic keratosis and a squamous cell carcinoma without performing a biopsy . . . many lesions thought to be actinic keratoses are actually squamous cell carcinomas but are treated as actinic keratoses.”

Most epidemiologic studies are based solely on the clinical skin examination. At least 8 epidemiologic studies in Australia and 5 studies outside of Australia (3 in the United States, 1 in Ireland, and 1 in Wales) have examined the prevalence of AKs. All were limited owing to a lack of histologic validation of the clinical impression.6

The presence of AKs not only is a measure of sun damage but, more importantly, also identifies a high-risk group of patients predisposed to the development of invasive SCC and BCCs.15,16 and, to a lesser extent, melanoma.17,18 A larger multicenter study is needed to further validate these observations.

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REFERENCES