Clinical Recognition of Actinic Keratoses in a High-Risk Population

How Good Are We?

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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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ACTINIC KERATOSSES (AKS) are dysplastic epidermal lesions that are precursors of invasive squamous cell carcinoma (SCC). Various studies during the past 15 years have determined a rate of conversion of AKs to SCC of 0.1% to 10%. In 2002, more than 1 million cases of nonmelanoma skin cancers (NMSCs) were diagnosed in the United States. Squamous cell carcinoma accounts for more than 20% of NMSC and most metastatic disease and death due to NMSC. Therefore, the ability of the physician to distinguish precancerous lesions with a high degree of accuracy is invaluable and will decrease the morbidity and mortality of SCC.

The diagnosis of AKs is frequently made by dermatologists. Feldman et al determined that in a 4-year period, there were 127 million office visits to dermatologists, of which 14.6 million (11.5%) were for the evaluation and treatment of AKs. Yet, most AKs are diagnosed clinically, with few histologic confirmations. The clinical features of AKs are nonspecific, usually described as red, scaly papules or plaques, 2 to 5 mm in diameter, occurring in sun-exposed sites. They may bleed or become hypertrophic, at which point a biopsy is generally performed to evaluate for progression to SCC. The diagnostic accuracy or positive predictive value (PPV) of the clinical diagnosis of AKs would require biopsy confirmation.

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Although a variety of studies have examined the rate of misclassification of AKs as suspected skin cancers, no study has exclusively examined the accuracy of the clinical diagnosis of AKs as confirmed by histologic examination. The question we are asking is how often the skin biopsy findings confirm the clinical impression of AK in a population at risk for NMSC.

METHODS

Patients who were seen at the Department of Dermatologic Surgery at Tufts–New England
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 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.

RESULTS

In this pilot study, 23 lesions with classic clinical features of AKs were identified in 18 patients (6 women and 12 men) presenting for surgical treatment of skin cancer. The mean age of the cohort was 67 years, and the most common presenting skin cancer was basal cell carcinoma (BCC) (n=11), followed by SCC (n=6) and melanoma in situ (n=1). The 23 lesions presumed to be AKs were histologically evaluated. Seventeen of these lesions were confirmed histologically to be AKs, yielding a PPV of 74%. Of the 6 lesions that were not AKs, 3 were SCC, 1 was BCC, 1 was lentigo maligna, and 1 was a collision lesion of an irritated seborrheic keratosis with an AK.

COMMENT

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 al. 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. Their PPV was 94% (34/36). One lesion was found to be a seborrhoeic 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 study 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 spomiotic 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. Moy 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.

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 and, to a lesser extent, melanoma. A larger multicenter study is needed to further validate these observations.