Actas Dermosifiliogr. 2017;108(1):31–41

ACTAS Dermo-Sifiliográficas

Full English text available at www.actasdermo.org

PRACTICAL DERMATOLOGY

Precancerous Skin Lesions☆

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Received 26 April 2016; accepted 28 July 2016
Available online 6 December 2016

KEYWORDS
Precancerous skin lesions;
Actinic keratosis;
Bowen disease;
Evaluation;
Diagnosis;
Treatment

Abstract Certain clinically and histologically recognizable skin lesions with a degree of risk of progression to squamous cell carcinoma have been traditionally grouped as precancerous skin conditions but now tend to be classified as in situ carcinomas. This consensus statement discusses various aspects of these lesions: their evaluation by means of clinical and histopathologic features, the initial evaluation of the patient, the identification of risk factors for progression, and the diagnostic and treatment strategies available today.

PALABRAS CLAVE
Precáncer cutáneo;
Queratosis actínica;
Enfermedad de Bowen;
Evaluación;
Diagnóstico;
Tratamiento

Precáncer cutáneo

Resumen Bajo el término de precáncer cutáneo se han englobado tradicionalmente distintas entidades, clínica e histológicamente reconocibles, asociadas a un cierto riesgo de evolución a carcinoma escamoso cutáneo invasivo aunque en la actualidad se tiende a interpretarlas como carcinomas *in situ*. En este documento de consenso se abordan distintos aspectos de estas lesiones como son su evaluación a través de las características clínicas e, histopatológicas de las mismas, la evaluación inicial del paciente afecto, la identificación de los factores de riesgo para su desarrollo, los distintos métodos hoy día existentes para su estudio y diagnóstico así como las diferentes estrategias terapéuticas.

☆ Please cite this article as: Ferrándiz C, Malvehy J, Guillén C, Ferrándiz-Pulido C, Fernández-Figueras MT. Precáncer cutáneo. Actas Dermosifiliogr. 2017;108:31–41.
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1578-2190/

Concept and Types of Precancerous Lesions

The term *precancerous skin lesion* has traditionally been used to refer to a set of clinically and histologically recognizable lesions with a degree of risk of progression to invasive squamous cell carcinoma of the skin. Today, these lesions are generally classified as in situ carcinomas, that is, as the intraepidermal stage of the neoplasm.[1] The 2 main types of precancerous lesions are actinic keratosis (AK) and Bowen disease (BD). Much less common forms include arsenical keratoses, radiation keratoses (caused by ionizing radiation), and hydrocarbon keratosis. Other forms, which we have not discussed in this article because they affect the mucous or semi-mucous membranes rather than the skin, are leukoplakia, erythroplakia, and actinic cheilitis.

Actinic Keratoses

Introduction

AKs are a type of skin lesion commonly encountered in routine clinical practice. In Spain, AK is considered to be one of the 5 most common dermatological diagnoses.[2] The recent EPIQA study estimated the prevalence of AK among Spanish patients aged 45 years or older attending outpatient dermatology clinics to be 28.6%.[3] Moreover, if we take into account increasingly longer life expectancy, changes in behavior relating to sun exposure that began several decades ago, and the increase in the practice of outdoor sports and recreational activities, there is no doubt that the incidence and, therefore, the prevalence of AK will continue to grow in the coming years, along with the incidence and prevalence of skin cancer. Thus, it is not surprising that nonmelanoma skin cancer, including AK, has become a public health problem and a growing financial burden for national health systems and society as a whole.[4]

Definition and Nomenclature

AK can be regarded as a form of cutaneous squamous cell carcinoma in situ. However, some authors consider AK to be a precancerous lesion representing the first step in a continuum that starts with dysplasia of the basal keratinocytes and can progress to invasive squamous cell carcinoma (the cancerization process). In that case, AK would be the first stage in the carcinogenesis of epidermal keratinocytes caused by actinic radiation, primarily UV.[5] It does not, in any case, appear to be advisable, at least when talking to patients, to use the term carcinoma in situ. The reason for this precaution is simply to avoid the unnecessary alarm and psychological and emotional impact on patients and their families that would result from the use of the term *carcinoma* to describe a lesion that can almost certainly be cured relatively easily and has only a very low risk of becoming an invasive tumor.

Other synonyms for AK are solar keratosis, squamous cell carcinoma in situ AK-type, keratinocytic intraepidermal neoplasia, and senile keratosis, although this last is best avoided.[6]

Identification of At-Risk Patients

The chief cause of AK is exposure to nonionizing radiation, and in particular UV radiation, which directly (UV-B) or indirectly (UV-A) induces characteristic mutations in the DNA and RNA of epidermal keratinocytes as a result of photo-oxidative stress and the formation of cyclobutane dimers.[7,8] The principle cause of these lesions is therefore chronic exposure to sunlight (more than 80% of AKs are located in chronically sun-exposed areas), and at-risk patients can be identified by exploring the factors and variables associated with chronic and intense exposure to sunlight, greater vulnerability to UV radiation, and possible defects in the ability of the patient's skin to repair damaged DNA. The following are all factors of particular interest[9]:

a. advanced age, masculine sex, outdoor occupation (farming, fishing, marine occupations, etc.), outdoor sports and recreations (tennis, golf, etc.), residence in a country with a hot climate or in a latitude close to the equator, use of artificial UV lamps. All of these factors increase the patient's long-term exposure to UV radiation.
b. Skin phototype. Patients with a type I or II skin phototype are more vulnerable to UV radiation.
c. Genetic syndromes characterized by alterations in DNA repair mechanisms, chromosomal instability, and photosensitivity (xeroderma-pigmentosum, Rothmund-Thomson syndrome, etc.).
d. Immunocompetence. Another at-risk group is that of immunocompromized patients, particularly solid organ transplant recipients, who are chronically immunosuppressed as a result of the therapy they receive to prevent transplant rejection.

Initial Assessment of Patients with AK

Medical History. As with any other disease, the initial assessment of a patient with AK should include a general medical history supplemented by a series of additional questions to gather information that may prove important in the design of the treatment and follow-up strategy. In the case of AK, the following additional information is of interest[10]:

1. Prior treatments to determine the effectiveness and tolerance profile in the patient.
2. Past history of nonmelanoma skin cancer.
3. Exposure to sunlight at work and/or in the course of outdoor leisure activities, and UV-A sun lamp use.
4. Past or current immunosuppressant therapy for any reason.
5. Symptoms (itching, pain, burning, etc).
6. The motive for the consultation (symptoms, concern about skin cancer, cosmetic issues).
7. It is also essential to include questions in the medical history aimed at identifying any signs or symptoms indicative of progress to invasive squamous cell carcinoma (Table 1).[10]

Physical Examination. The procedure for the physical examination of a patient with AK is as follows:

1. Complete dermatological examination, paying particular attention to areas of the skin usually exposed to sunlight (face, balding scalp, ears, upper chest or neckline, and the dorsum of hands and forearms). Patients usually have multiple AKs rather than a single lesion. Patients with AKs