

The Management of Actinic Keratosis and Squamous Cell Carcinoma

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Abstract

Background: Actinic keratosis or solar keratosis is a common skin lesion caused by sun damage that progresses to squamous cell carcinoma. It has been suggested that actinic keratosis is in fact SCC in situ.

Objective: This literature review was conducted to investigate the differences between actinic keratosis and squamous cell carcinoma and whether actinic keratosis should in fact be managed as squamous cell carcinoma.

Methods: A literature review was conducted to assess the differences between actinic keratosis and squamous cell carcinoma. We conducted searches of Pubmed, Cochrane and Medline for articles published between January 1, 2000 and April 30, 2014, using the following search terms: actinic keratosis, solar keratosis, skin cancer, squamous cell carcinoma, dermoscopy, sun exposure, ultra violet radiation, and dysplasia.

Studies published in English were selected for inclusion in this review as were additional articles identified from bibliographies.

Results: It is difficult to distinguish between both actinic keratosis and squamous cell carcinoma. Perhaps a classification system for actinic keratosis including early in situ SCC type AK1, early in situ SCC type AK2 and in situ SCC type actinic keratosis is needed.

Conclusion: Actinic keratosis invades the basement membrane and as such may progress into invasive SCC. Superficially actinic keratoses are not distinguishable from a superficial SCC and as such may go unrecognized or inaccurately diagnosed.

Keyword: actinic keratosis; solar keratosis; common skin lesion

Introduction

Actinic keratosis also known as solar keratosis or senile keratosis are names given to intraepithelial keratinocyte dysplasia. As such they are a pre-malignant lesion or in situ squamous cell carcinomas and thus a malignant lesion. [1]

Actinic keratosis is a common skin lesion caused by sun damage which commonly progresses to squamous cell carcinoma (SCC). The prevalence of actinic keratosis in Australia has been estimated as 40-50% in those aged 40 years and above. [2] Squamous cell carcinoma is the second most common type of skin cancer [3] and it has been suggested that actinic keratosis is in fact SCC in situ. [4]

Actinic keratosis arises from long term sun exposure and is an indicator of sun damage and ultraviolet light exposure. The development of SCC in sun damaged skin is a gradual process and the majority of invasive SCC's result from actinic keratosis. [5] As such some studies have recommended an alternative classification system for actinic keratosis. Early in situ SCC has been recommended for type AK1, early in situ SCC for type AK2 and in situ SCC for type AK3. [6]

Risk factors for the development of actinic keratosis include, fair skin or light pigmentation status, caucasian individuals, freckles, light colored eyes (blue or green), blonde or red hair, male gender, older age, severe baldness, increased sun exposure, skin wrinkling and in those that work outdoors and have a high tendency of sunburn. [7,2]

Actinic keratosis presents as a rough, itchy and scaly lesion that can occur singly but usually grows as multiple dry, fleshy colored, erythematous papules or plaques with telengectasia, that are usually covered in brown or yellow adherent scales. [2] The distribution of actinic keratosis depends on a number of factors such as ethnicity, socioeconomic status, age, skin type, occupation, sex, and birth place.

Studies have shown that skin type is a major factor influencing the prevalence of actinic keratosis and skin cancers. [8] Actinic keratosis have been shown to be more common in those that have a skin phototype of 1-3. Furthermore, 60% of individuals over the age of 40 with skin phototype 1-3 will present with at least one actinic keratosis and this increases to 80% in those over the age of 60. [2] 5 to 20% of these lesions will progress in 10 to 25 years to SCC. [2]

There are a number of known risk factors in the development of SCC. These include the patient's skin type, the amount of photo damage the patient has been exposed to and a history of immunosuppression. [9] Furthermore, studies have shown that, ultraviolet radiation induced mutations and changes in gene expression are present in SCC, actinic keratosis and sun exposed skin. [5]

Actinic keratosis, is usually the first lesion in a disease continuum that progresses to invasive SCC. The risk of progression from actinic keratosis to SCC depends on a number of patient factors. The risk of transformation is enhanced in patients with increased solar damage, immunosuppression, and those of advanced age. [5] The presence of actinic keratoses is a risk factor for non melanoma skin cancers and they are precursors of squamous cell carcinoma. [10]

Disease progression depends on a number of clinical features such as the size of the lesion, the amount of ulceration, bleeding and induration, enlargement in diameter and erythema. [9,5] Studies have shown that patient's with actinic keratosis with an increased risk of malignancy have lesions that are indurated, inflamed, have a diameter greater than 1cm, are rapidly enlarging, bleeding, erythematous and ulcerated. [9]

Karyometric assessment can provide a numeric measure in the progression of sun damage. [11] Analysis using micro assay profiling has revealed that there are nine different genes expressed between both actinic keratosis and squamous cell carcinoma [1].

Actinic keratosis are considered pre-malignant and are believed to be the result of abnormal squamous cells caused by ultra violet mediated gene alteration. [12] With increased sun exposure the proportion of nuclei exhibiting changes in the nuclear chromatin pattern rises. Furthermore a large group of SCC's have characteristics that are similar to actinic Keratosis. [11]

Actinic keratosis invades the skin basement membrane and as such may progress to invasive SCC. [1] It is difficult to distinguish actinic keratosis and SCC as superficially they appear similar. This however means that there is an increased tendency for them to go unrecognized or to be inaccurately diagnosed. [1]

Results

Actinic keratoses are established as direct precursors of squamous cell carcinoma. Lesions are found in the epidermis and are caused by ultraviolet radiation. [13,14]

Studies following single actinic keratosis lesions have shown that there is an inherent risk of progression from actinic keratoses to SCC. [1] Progression rates from actinic keratosis to SCC ranged from 0 to 0.075% per lesion-year with a risk of up to 0.53% per lesion in patients with a prior history of non-melanoma skin cancers. Rates of regression of single lesions ranged from 15% to 63% after 1 year and recurrence rates 1 year after regression are approximately 15 to 53%. [1]

Another study showed that 60% of SCC's arose from a lesion diagnosed as solar keratosis in the previous year and the other 40% of SCC's from what had been clinically normal skin 12 months previously. [15] Annual rates of transformation from actinic keratosis to SCC have been reported from 0.025% to 20%. [16]

A study reported that the risk of progression from AK to primary SCC was 0.60% (95% CI, 0.44%-0.82% at 1 year and 2.57% (95% CI, 2.12%-3.12%) at 4 years. For primary invasive SCC the risk was 0.39% (95% CI, 0.26%-0.57%) at 1 year and 1.97% (95% CI, 1.58%-2.47%) at 4 years. transformation from actinic keratosis to SCC was < 1 in 1000 (0.075% or 0.096%) and a hospital based population study showed the risk of progression to be 0.53% a year in patients with a prior history of non melanoma skin cancers. [13]

Studies have shown that significant variation exists between actinic keratosis diagnosed by clinical criteria and those diagnosed by histology. A study showed that 5% of 22 clinically diagnosed actinic keratosis were identified histologically as BCC. [17] Another study showed that 12% of 514 presumed BCC's were diagnosed histologically as actinic keratosis. [18]

Studies have also shown that the majority of SCC's that arise from actinic keratoses arise in the same area or in close proximity to the actinic keratosis.

Studies have also shown that 65% of all SCC's arise in previously diagnosed actinic keratosis. Other studies have also indicated that 60% of SCC's occurred at a site where an actinic keratosis had been recorded previously. [18] An American study concluded that 10% of actinic keratosis progressed to SCC due to chronic sun exposure especially UVB sunlight. A retrospective study concluded that the length of time for an actinic keratosis to progress to an SCC was determined to be 24.6 months (95% Confidence interval, 21.04-28.16 months). [3]

Although the rate of malignant transformation varies in literature, actinic keratosis can commonly progress to invasive SCC and as such should be treated to avoid possible morbidity and mortality. [13] Some studies have shown a low risk of progression from actinic keratoses to SCC however the majority of SCC's do arise from actinic keratoses. [13]

Discussion

The burden of disease in relation to transformation of actinic keratosis may be much larger than previously appreciated. A previous study indicates that the aggregate value for willingness to pay for symptom relief for all individuals with actinic keratoses was \$2.4 billion [13].

The cost associated with actinic keratosis must be considered when considering this disease entity. A study concluded that there are an estimated 5.2 million actinic keratosis visits to health care professionals annually, 60% of these were made by patients that are on medicare. A total of 920 million dollars is spent on the treatment of actinic keratosis annually, 6% on topical therapy, 43% on office visits and 51% on destructive procedures. Studies showing the cost benefit analysis of treating actinic keratosis are lacking and are essential to guide the future management of this disease. The number of visits to a health care practitioner made by patients who have been diagnosed with SCC and the financial burden associated with managing those patients with SCC will allow for a better understanding and appreciation of whether solar or actinic keratosis should in fact be treated as SCC in the first instance. [19] Further studies estimating the prevalence, economic burden and impact on quality of life are required.

It has also been suggested that destructive procedures compared to topical therapies provide a better standard of care for patients, have a greater efficacy and furthermore provide better cost control. [19] As such actinic keratosis lesions should be treated with lesion or field directed therapy due to the potential for metastasis. [4] Furthermore, the overall spontaneous complete field regression of actinic keratosis is relatively low and the risk of subsequent reoccurrence is high.

Patients who are receiving immunosuppressant therapy for organ transplant or autoimmune diseases and those that are on chemotherapeutic medication are at an increased risk of actinic keratosis and SCC as well as BCC. It is imperative that these patients are regimental with the application and re-application of sunscreen. Studies have shown that the application of sunscreen may prevent the development of further actinic keratosis and SCC as well as increasing remission in existing ones. [20,10] Controlled trials have shown the benefit of using sunscreen in the prevention of progression of actinic keratosis to SCC. [1] It has been established that regular sunscreen use suppresses actinic neoplasia.

Actinic keratosis varies in appearance over time and dermoscopy may aid in differentiating between actinic keratosis and SCC. However, histopathologic examination should be performed when the differential diagnosis is inconclusive. [19]

Sun exposure has shown to be to be one of the main risk factors in the progression of actinic keratosis to SCC; however, longitudinal studies are essential to allow for a better understanding of the progression of actinic keratosis to SCC. [9] Studies vary in the exact risk of progression of actinic keratosis to SCC, some indicating an overall risk of progression as 0.075% a year. [15] Discrepancies between studies may be a result of confounders such as having a prior history of non melanoma skin cancers, amount of sun exposure or radiation exposure to date, exposure to other proven risk factors, previous use of immunosuppressant's, and the use of sunscreen. This review indicates that variation exists in whether actinic keratosis should in fact be referred to as keratinocytic intraepithelial neoplasia or true epithelial neoplasia. Some studies have suggested that actinic keratosis is in situ intradermal squamous cell carcinomas which in 10% of the case can develop into SCC. [2]

The management of actinic keratosis is difficult as it is difficult to clearly distinguish actinic keratosis from squamous cell carcinoma. As such it is essential for clinicians to obtain histopathological information when unable to clearly identify the nature of a lesion. Perhaps initial management and monitoring of lesions should be aggressive with most studies showing actinic keratosis being a continuum of solar keratosis. Furthermore a cost benefit analysis in treating actinic keratosis is essential to aid in the economic burden associated with this prevalent disease.

References

1. Werner RN, Sammain A, Erdmann R et al. The natural history of actinic keratosis: a systematic review. *Br J Dermatol.* 2013; 169:502-518.
2. Rossi R, Mori M, Lotti T. Actinic Keratoses. *Int J Derm* 2007; 46:895- 904.
3. Fuchs A, Marmur E. The kinetics of skin cancer: progression of actinic keratosis to squamous cell carcinoma. *Dermatol Surg.* 2007; 33:1099- 1101.

4. Feldman SR, Fleischer AB. Progression of actinic keratosis to squamous cell carcinoma revisited: clinical and treatment implications. *Cutis*. 2011 Apr; 87(4):201-7.
5. Rowert-Huber J, Patel MJ, Forschner T. Actinic keratosis is an early in situ squamous cell carcinoma: a proposal for reclassification. *Br J Dermatol*. 2007 May; 156 suppl 3:8-12.
6. Flohil S, Van der leest RJT, Dowlatashahi E et al. Prevalence of actinic keratosis and its risk factors in the general population: The Rotterdam study. *J Invest Dermatol*. 2013 March. doi:10.1038/jid.2013.134.
7. Marks R, Ponsford MW, Selwood TS et al. Non-Melanotic skin cancer and solar keratosis in Victoria. *Med J Aust*. 1983 Dec 10-24; 2(12):619-22.
8. Quaedvlieg PJ, Tirisi E, Thissen MR, Krekels GA. Actinic keratosis: how to differentiate the good from the bad ones. *Eur J Dermatol*. 2006 Jul- Aug; 16(4):335-9.
9. Marks R. Epidemiology of non-melanoma skin cancer and solar keratosis in Australia: A tale of self-immolation in Elysian Fields. *Australas J Dermatol*. 1997 Jun; 38 Suppl 1:s26-9.
10. Krouse RS, Alberts DS, Prasad AR et al. Progression of skin lesions from normal skin to squamous cell carcinoma. *Anal Quant Cytol Histol*. 2009 Feb; 31(1):17-25.
11. Fuchs A, Marmur E. The kinetics of skin cancer: progression of actinic keratosis to squamous cell carcinoma. *Dermatol Surg*. 2007; 33:1099-1101.
12. Criscione V, Weinstock M, Naylor M et al. Actinic keratoses: Natural history and risk of malignant transformation in the veterans affairs topical tretinoin chemoprevention trial. *American Cancer Society* 2009. Doi 10/1002/cncr.24284.
13. Marks R, Rennie G, Selwood TS. Malignant transformation of solar keratosis to squamous cell carcinoma. *Lancet*. 1988 Apr 9; 1(8589):795-7.