Editorial: From actinic keratosis to squamous cell carcinoma – answers to some open questions

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EDITORIAL

From actinic keratosis to squamous cell carcinoma – answers to some open questions

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In the current issue of the *BJD* Schmitz *et al.* present a histological study on the correlation between squamous cell carcinoma (SCC) and actinic keratoses (AKs).[1] They discovered that SCCs were associated with basal proliferation and not with the degree of upward cellular atypia of the AKs.

AK is a very common skin disease. More than 50% of the light-skinned population is affected during their lifetime. With increasing awareness of AK being a precursor of SCC, more research has focused on its pathophysiology. Nevertheless, many questions remain unanswered. It is still unclear whether AK is precancerous or carcinoma *in situ*. Some AKs progress into SCC, others spontaneously regress. The term field cancerization indicates that the detectable keratosis is only the tip of the iceberg. An accurate and reliable AK lesion count, often performed in clinical studies, is difficult, as AKs are not discrete entities. Definition, description and quantification of field cancerization have not been precise or consented until now.

The clinical classification of Olsen considers solely the degree of hyperkeratosis, which can vary markedly over time.[2] Histologically, the established grading system of Röwert-Huber *et al.* assigns atypical cells in basal layers to AK I, in basal two-thirds to AK II and in the entire epidermis to AK III.[3] However, these clinical and histological grading systems are not well evaluated regarding their prognostic validity and clinical relevance. Furthermore, both classifications only assess single lesions and not the entire affected field, therefore limiting the overall picture. The current British Association of Dermatologists' guidelines reflect the diagnostic and prognostic uncertainty by stating that the clinical assessment of AK does not allow a reliable conclusion to be drawn on the further development into SCC.[4]

Thomas Dirschka, Lutz Schmitz and colleagues' research has focused on the open questions of how to better assess the severity of AKs and the risk of progression. They have investigated 892 AKs clinically and histologically, finding no match between both scores. Consequently, they stated that it is not possible to predict the histological extent of atypical keratinocytes by clinical assessment of the severity of hyperkeratosis.[5] Taking inspiration from other dermatological scores such as the Psoriasis Area and Severity Index, they developed the Actinic Keratosis Area and Severity Index (AKASI) for assessing AKs located on the head. Improving upon the Olsen grading system, which only considers the thickness of the keratosis, the AKASI also takes into account the affected area, distribution and erythema. This score was validated by 13 dermatologists, investigating 18 patients and two healthy controls. A strong correlation between the AKASI and the Physician's Global Assessment (PGA) of severity of AK was found. It was suggested that this score could be used for assessing field cancerization and evaluating the efficacy of treatment.[6]

In addition, they performed a retrospective analysis of 210 patients who underwent excision of skin lesions after assessment with the AKASI and PGA. A total of 26 patients were histologically diagnosed with a SCC, 82 with a basal cell carcinoma (BCC) and the rest with noninvasive findings such as AK and Bowen disease. Again, the AKASI correlated well with the global assessment. The AKASI was significantly higher in patients with SCC compared with patients with BCC or noninvasive skin cancer. They summarized that the AKASI can be used for risk stratification for SCC in patients with AK.[7]

Fernandez-Figueras *et al.* published a study in 2015, grading the AK on top of a SCC histologically after Röwert-Huber.[8] The most common type of AK above a SCC was AK I, only affecting the basal layer of the epidermis. This finding contradicted the former hypothesis of a stepwise progression from AK I to AK II, AK III and then to an invasive SCC. They suspected that there are two different ways of progression: a stepwise route and an alternative from AK I directly to invasive SCC.

Following these speculations, Schmitz *et al.* looked at the basal proliferation of AK without considering atypical keratinocytes above.[9] They described, developed and evaluated a new histologic scoring system, PRO I to III. PRO I describes crowding of basal keratinocytes, PRO II budding and PRO III papillary sprouting. In total, 246 AKs were assessed histologically using both scoring systems. There was no correlation between the upwards-directed scoring system after Röwert-Huber and the PRO classification. Other features such as adnexal structure involvement and increased number of vessels were found to be independent positive predictive markers for PRO III.[9] As a consequence of the above-mentioned findings, they repeated the study by Fernández-Figueras *et al.* and have published, in this issue, their study on the correlation between the PRO classification and SCC.[1]

A total of 307 lesions were investigated, assessing the adjacent and overlying AKs associated with an invasive SCC.[1] They confirmed that the most common AK above and adjacent to a SCC was graded as AK I. In contrast, PRO III was the most common finding applying the new PRO system, also of AKs extending into adnexal structures. As a result of these findings, they have assumed that the downward proliferation of basal keratinocytes has greater importance regarding risk of invasive growth in comparison with the degree of intraepidermal dysplasia.

The results of their studies, and this article in particular, suggest that we should abandon the theory of the upward-directed spread of atypical keratinocytes correlating to progression risk. It is more likely that basal proliferation and adnexal involvement have a greater influence. The PRO classification should replace the histological Röwert-Huber grading and the AKASI the clinical Olsen score. Thanks to the findings of Dirschka, Schmitz and colleagues we have now gained a clinical and a histological scoring system for AKs, both estimating the risk of invasiveness and further progression to SCC. Many questions, especially on the interaction between collagen tissue and epithelial cancer, remain. Nevertheless, these studies are a big step towards more reliable risk assessment, leading to better care for our patients with AK.

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Conflicts of interest

None declared.

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