Case Reports in Dermatology

Case Rep Dermatol 2020;12:19–24

DOI: 10.1159/000505530
Published online: February 4, 2020

Single Case

Transformation of Seborrheic Keratosis into Bowenoid Actinic Keratosis via Three Steps of Histological Change in a Patient with Rheumatoid Arthritis Treated with Multiple Immunosuppressants

Masahiro Oka[a] Yuki Yamamoto[b] Miki Fujii[c]

[a]Department of Dermatology, Kita-Harima Medical Center, Ono City, Japan; [b]Department of Pathology, Kita-Harima Medical Center, Ono City, Japan; [c]Department of Plastic and Reconstructive Surgery, Kita-Harima Medical Center, Ono City, Japan

Keywords
Actinic keratosis · Seborrheic keratosis · Squamous cell carcinoma · Transformation

Abstract
We report a case of seborrheic keratosis (SK) that transformed into bowenoid actinic keratosis (AK) via three steps of histological change in a 77-year-old woman. The patient presented with a multiple-year history of a brownish lesion on the right cheek. She reported that some months earlier she had noted a pinkish lesion developing within the brownish lesion. She had also been treated with several immunosuppressants for rheumatoid arthritis for many years. Physical examination revealed a nodule measuring 13 × 12 mm on the lateral side of the right upper cheek. The lesion comprised three regions: a brownish hyperkeratotic region in the upper portion; a pinkish region in the lower portion; and a slightly dented, band-like region between the other two regions. Histopathologically, the specimen consisted of four zones: SK comprising basaloid cells; SK composed of squamoid cells; atrophic AK; and bowenoid AK. The zones of SK with basaloid cells and squamoid cells clinically corresponded to the brownish hyperkeratotic region. Atrophic and bowenoid AK zones corresponded to the dented, band-like region

KARGER

Masahiro Oka, MD, PhD
Department of Dermatology
Kita-Harima Medical Center, 926-250 Ichiba-cho
Ono City, Hyogo 675-1392 (Japan)
E-Mail masahiro_oka@kitahari-mc.jp

and pinkish region, respectively. Collectively, the nodular skin lesion was diagnosed as SK associated with atrophic and bowenoid AK within the SK lesion. The present case suggests that bowenoid AK developed from SK by malignant transformation via three steps of histological change. The facts that our patient had received treatment with several immunosuppressants and that no other AK lesions were evident around the AK support the notion that in this case, bowenoid AK developed from SK by malignant transformation.

Introduction

Seborrheic keratosis (SK) has generally been considered a benign tumor, without any apparent potential for malignant transformation. On the other hand, although rare, cases of SK associated with squamous cell carcinoma (SCC) in situ arising within the SK have been reported [1–10]. Here, we describe a case of SK that transformed into bowenoid actinic keratosis (AK) via three steps of histological change in a 77-year-old woman.

Case Report

The patient was referred to us by her attending physician in the Division of Rheumatology at Kita-Harima Medical Center for evaluation of a skin lesion on the right cheek in December 2018. The patient had been diagnosed with rheumatoid arthritis at a clinic at the age of 42 years and had been treated with several medicines, including methotrexate, salazosulfapyridine, prednisolone, tacrolimus, abatacept, and tofacitinib citrate, which were changed depending on the symptoms and the appearance of side effects at the clinic until June 2017 and thereafter in the Division of Rheumatology at Kita-Harima Medical Center. The patient reported that the skin lesion had been present for many years as a brownish lesion, and some months prior to her referral she had noticed a pinkish lesion developing within the brownish lesion. Physical examination revealed a well-circumscribed, round, slightly raised nodule measuring 13 × 12 mm on the lateral side of the right upper cheek (Fig. 1a). The lesion consisted of three regions: a brownish hyperkeratotic region with fine unevenness on the surface of the upper part; a pinkish, glossy region with tiny brown dots on part of the surface skin in the lower portion; and a slightly dented, narrow, band-like region with a normal-looking skin surface between the brownish hyperkeratotic and pinkish glossy regions. The nodular lesion was resected en block with a 1- to 2-mm margin. Tissue sections were made to include all three regions (Fig. 1b). Histopathologically, the specimen consisted of four zones (A–D in Fig. 1c). Zones A and B clinically corresponded to the brownish hyperkeratotic region. The epidermis of zone A showed hyperkeratosis, acanthosis, and hyperpigmentation in the basal cell layer and comprised mainly basaloid keratinocytes (Fig. 1c, d). The epidermis of zone B showed hyperkeratosis and reticulated acanthosis mainly comprising squamoid keratinocytes, with interspersed pseudohorn cysts filled with keratin (Fig. 1c, e). The epidermis of zone C, which clinically corresponded to the dented, narrow, band-like region, was slightly hyperkeratotic and atrophic and showed irregular buds extending to the dermis (Fig. 1f). Atypical cells with large hyperchromatic nuclei were found both in and directly above the basal cell layer. Prominent infiltration of inflammatory cells and solar elastosis were present in the upper dermis. Zone D, which clinically corresponded to the pinkish, glossy region, showed acanthotic epidermis with hyperkeratosis and parakeratosis (Fig. 1g). The entire epidermis

was occupied with atypical keratinocytes with a disorderly arrangement, together with atypical mitoses. Severe infiltrates of inflammatory cells and solar elastosis were present in the upper epidermis. Based on these clinical and histopathological findings, the nodular skin lesion was diagnosed as SK associated with atrophic and bowenoid AK within the SK lesion.

Discussion/Conclusion

When a malignant cutaneous tumor arises within or in close proximity to SK, there has been a debate over whether the malignant tumor has actually originated from SK or instead represents a collision tumor. In previously reported cases of SK associated with SCC in situ, the region of SCC in situ has been seen on histopathological examination to be in direct contact with the SK region and most authors have considered that SK transforms directly to SCC in situ [1–10]. On the other hand, in the present case, we have observed two different histopathological regions between the main SK region and the region of bowenoid AK. This observation suggests that SK transformed to bowenoid AK via at least three steps of histological change.

Our patient had been treated with several immunosuppressants before the AK lesion had developed, and immunosuppression has been reported as a risk factor for developing SCC in SK [8, 10]. In addition, our patient showed no other AK lesions beyond that arising within the area of SK, whereas AK usually develops as multiple lesions. These observations support the idea that, at least in the present case, bowenoid AK developed from SK by malignant transformation.

Statement of Ethics

Informed consent was obtained from the patient. The study complied with the Declaration of Helsinki.

Disclosure Statement

The authors declare no conflict of interest.

Funding Sources

None of the authors received any financial support for the present study.

Author Contributions

All authors have contributed significantly. Dr. Oka conducted the dermatological examinations of the patient and wrote the manuscript. Dr. Yamamoto performed the histological analyses. Dr. Fujii treated the patient surgically. All authors are in agreement with the content of the manuscript.

References

1 Bloch PH. Transformation of seborrheic keratosis into Bowen's disease. J Cutan Pathol. 1978 Dec;5(6):361–7.
2 Rahbari H. Bowenoid transformation of seborrhoeic verrucae (keratoses). Br J Dermatol. 1979 Oct;101(4):459–63.
3 Baer RL, Garcia RL, Partsalidou V, Ackerman AB. Papillated squamous cell carcinoma in situ arising in a seborrheic keratosis. J Am Acad Dermatol. 1981 Nov;5(5):561–5.
4 Monteagudo JC, Jorda E, Terencio C, Llombart-Bosch A. Squamous cell carcinoma in situ (Bowen's disease) arising in seborrheic keratosis: three lesions in two patients. J Cutan Pathol. 1989 Dec;16(6):348–52.
5 Sloan JB, Jaworsky C. Clinical misdiagnosis of squamous cell carcinoma in situ as seborrheic keratosis. A prospective study. J Dermatol Surg Oncol. 1993 May;19(5):413–6.
6 Rajabi P, Adibi N, Nematollahi P, Heidarpour M, Eftekhari M, Siadat AH. Bowenoid transformation in seborrheic keratosis: A retrospective analysis of 429 patients. J Res Med Sci. 2012 Mar;17(3):217–21.
7 Shankar A, Choudhary S, Manjunatha YA. Seborreic keratosis with Bowenoid transformation. Indian Dermatol Online J. 2012 Sep;3(3):225–7.
8 Boyd AS, Su PF, Shyr Y, Tang YW. Squamous cell carcinomas in situ arising in seborrheic keratoses: an association with concomitant immunosuppression? Int J Dermatol. 2014 Nov;53(11):1346–50.
9 Wu YH, Hsiao PF, Chen CK. Seborrheic keratosis with bowenoid transformation: the immunohistochemical features and its association with human papillomavirus infection. Am J Dermatopathol. 2015 Jun;37(6):462–8.
10 Conic RZ, Napekoski K, Schuetz H, Piliang M, Bergfeld W, Atanaskova Mesinkovska N. The role of immunosuppression in squamous cell carcinomas arising in seborrheic keratosis. J Am Acad Dermatol. 2017 Jun;76(6):1146–50.

Case Reports in Dermatology

Case Rep Dermatol 2020;12:19–24

DOI: 10.1159/000505530

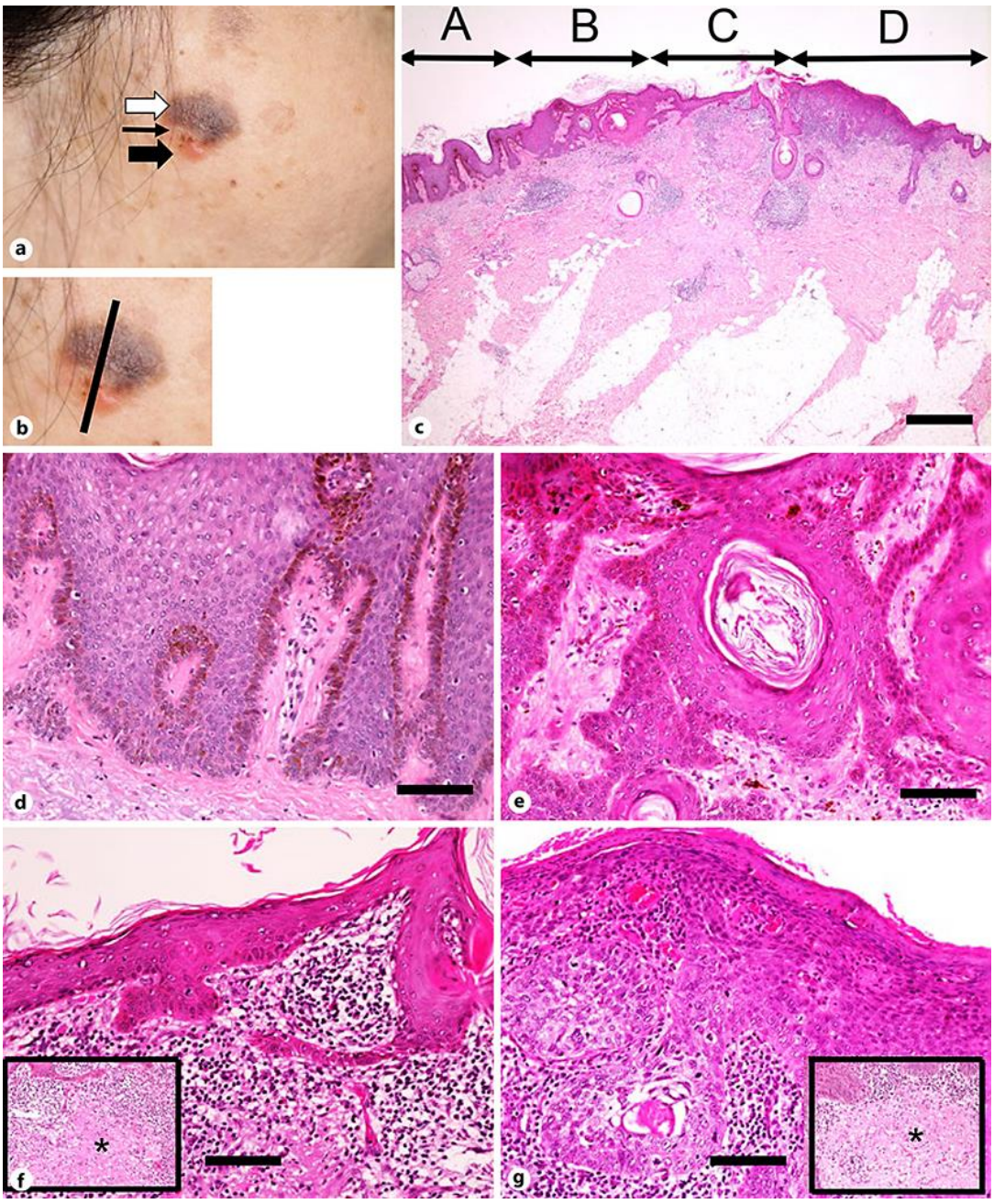

Fig. 1. **a** Clinical appearance of the skin lesion. The nodule consists of three regions: a brownish, hyperkeratotic region (white arrow); a slightly dented, narrow, band-like region with a normal-looking skin surface (thin black arrow); a pinkish, glossy region (thick black arrow). **b** Cutting line of the resected tissue. Tissue sections were made according to the cutting line to include all three regions. **c–g** Histopathological findings. The specimen consists of four zones (A–D) (hematoxylin and eosin, original magnification ×20) (**c**). Histopathological findings of zones A and B correspond to the brownish, hyperkeratotic region. The epidermis of zone A shows hyperkeratosis (**c**), acanthosis composed of basaloid keratinocytes, and hyperpigmentation in the basal cell layer (**d**) (hematoxylin and eosin, original magnification ×200). The epidermis of zone B shows hyperkeratosis (**c**) and reticulated acanthosis composed of squamoid keratinocytes with pseudohorn cysts filled with keratin (**e**) (hematoxylin and eosin, original magnification ×200). Histopathological findings of zone C correspond to the dented, narrow, band-like region. The epidermis of this zone is atrophic and shows irregular buds extending to the dermis (hematoxylin and eosin, original magnification ×200) (**f**). Atypical cells are found in and directly above the basal cell layer. The atypical cells have large hyperchromatic nuclei. Prominent infiltration of inflammatory cells is present in the upper dermis just under the epidermis. Solar degeneration is present in the upper dermis (* in inset). Zone D, corresponding to the pinkish, glossy region, shows acanthotic epidermis, the entirety of which is occupied by atypical keratinocytes with a disorderly arrangement and atypical mitoses (hematoxylin and eosin, original magnification ×200) (**g**). Most of the epidermis shows parakeratosis. Severe infiltration of inflammatory cells is present just under the epidermis. In the upper dermis below the infiltrate of inflammatory cells, solar degeneration is evident (* in inset). Bars indicate 250 μm in (**c**) and 100 μm in (**d–g**), respectively.