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Solitary Keratoacanthoma at the Recipient Site of a Full-Thickness Skin Graft: A Case Report and Review of the Literature

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Abstract

A 57-year-old man presented with a pigmented papule, 0.4 cm in diameter, on the left lower eyelid. Skin biopsy revealed a basal cell carcinoma, which was excised through a wide excision followed by a full-thickness skin graft (FTSG). Two weeks after the surgery, an erythematous nodule developed in the lower margin of the graft recipient site. The nodule size increased rapidly over 2 weeks, becoming dome-shaped with a central hyperkeratotic plug. A diagnosis of keratoacanthoma (KA) was made, and surgical excision was performed. Histological findings revealed a large, well-differentiated squamous tumor with a central keratin-filled crater and buttress. The human papilloma virus (HPV) genotyping results were negative.

Risk factors for KA include trauma, old age, exposure to ultraviolet (UV) radiation, immunosuppression, and HPV infection. KA has most often been reported to develop at the donor site. Although the pathogenesis of KA is unclear, trauma is believed to act as a second insult to a preceding oncogenic insult, such as exposure to UV radiation, resulting in a koebnerization. Herein, we report a case of solitary KA at a FTSG recipient site. This report presents information that may provide guidance during dermatologic surgeries.

Keywords

- keratoacanthoma
- koebnerization
- full-thickness skin graft

Introduction

The term, keratoacanthoma (KA) was first coined in the 1940s.[1] KA are historically considered to be a variant of squamous cell carcinoma (SCC); however, it has been suggested to be defined as a benign tumor due to the numerous cases of spontaneous regression.[2] Despite the controversy, KA remains classified as a variant of SCC in the 2018 World Health Organization classification.[3] KA typically presents as a rapidly growing dome-shaped umbilicated nodule with a central hyperkeratotic plug,[4] undergoing three stages: proliferative, mature, and regression phase.[2] The similarity of the triphasic nature of KA to the follicular morphogenesis of anagen, catagen, and telogen cycles, suggests that KA has a

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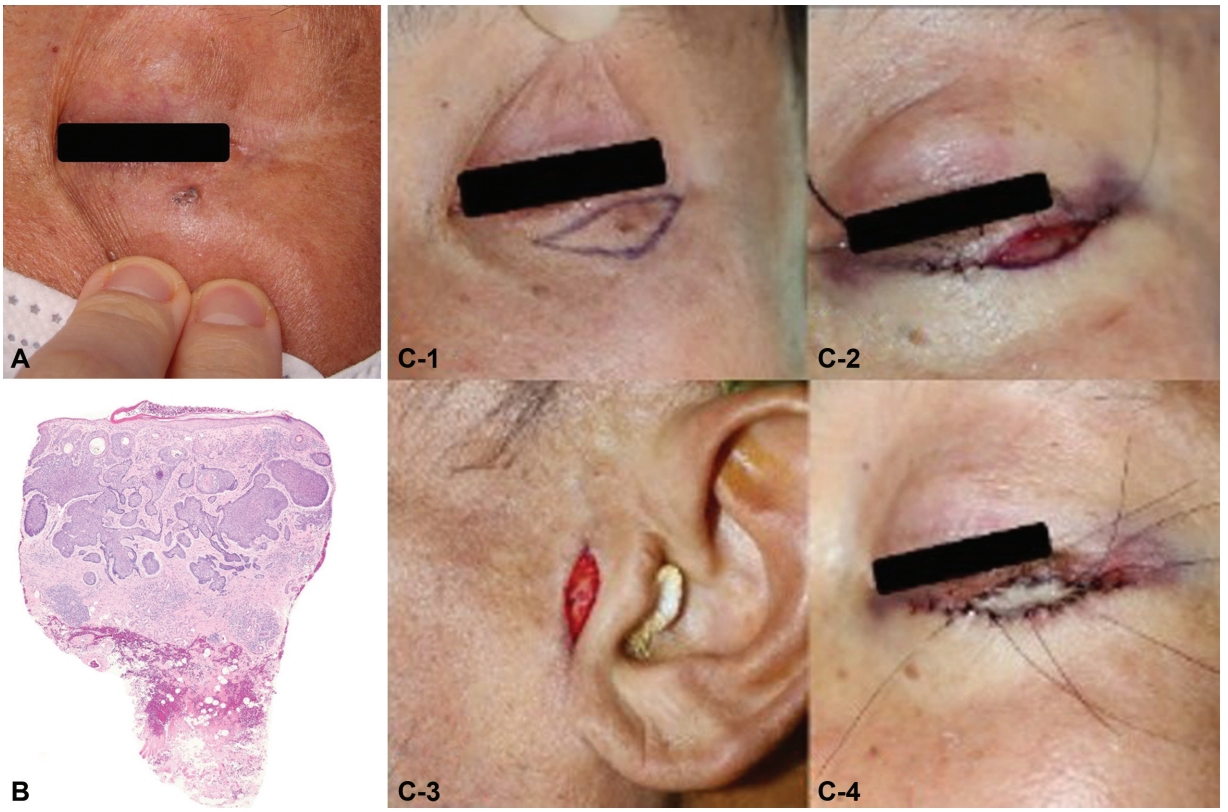

Fig. 1 Clinical and histopathological features of preceding skin lesion. (**A**) Solitary rodent-ulcer like pigmented papule on the left lower eyelid. (**B**) Histopathological specimen was compatible with basal cell carcinoma, showing numerous nests of basaloid tumors with peripheral palisading and peritumoral cleft. (**C-1**) Preoperative design on the left lower eyelid. (**C-2**) Photograph immediately after tumor removal. **(C-3)** Preauricular donor site. (**C-4**) Photograph immediately after skin graft.

follicular origin and may be associated with Wnt signaling.[2] Representative KA types include solitary, centrifugum et marginatum, and giant.[2] Excluding solitary KA, all other types are reportedly associated with human papilloma virus (HPV) infection.[2]

In addition to the SCC-associated risk factors, trauma, including surgery, is also a potential risk factor for KA.[2,4] There are few reports on trauma after skin grafting. If KA occurs after skin grafting, it may be misdiagnosed as SCC without consultation with a dermatologist, which in turn can lead to invasive treatment such as wide excision. This report highlights a case of KA that occurred at the recipient site of full-thickness skin graft (FTSG), which has educational value.

Case

A 57-year-old Korean man without any contributory medical history visited the dermatology department with a solitary pigmented papule, 0.4 cm in diameter, on the left lower eyelid (►**Fig. 1A**). Skin biopsy revealed a basal cell carcinoma (BCC) with peripheral palisading and peritumoral cleft (►**Fig. 1B**). After wide excision, FTSG from left preauricular area was used for reconstruction during plastic surgery (►**Fig. 1C**).

Two weeks postoperatively, an erythematous nodule developed in the lower margin of the skin graft recipient site. The nodule rapidly attained a dome shape with a central hyperkeratotic plug over the following 2 weeks (►**Fig. 2A**). During

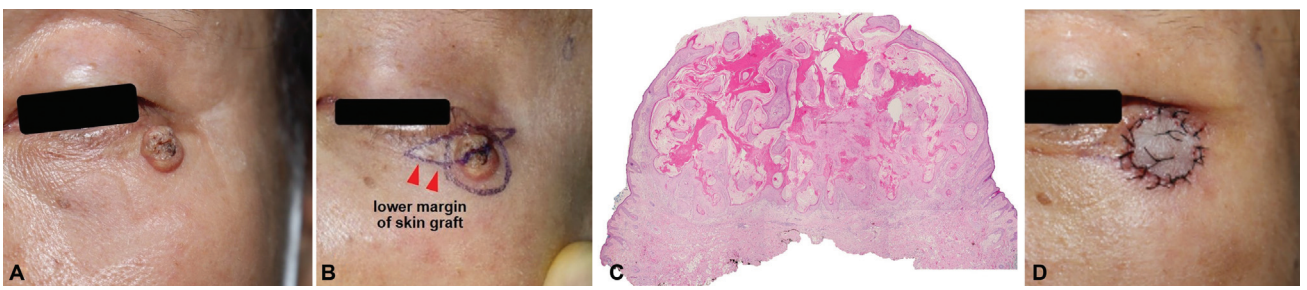

Fig. 2 Clinical and histopathological features of keratoacanthoma (KA). (**A**) Solitary dome-shaped nodule with central keratotic plug on the left lower eyelid. (**B**) The center of nodule located on the lower margin of skin graft (red arrow head). (**C**) Large, well-differentiated squamous tumor with central keratin-filled crater, consistent with KA. (**D**) Excision with split-thickness skin graft was performed.

dermatologic consultation, the patient was diagnosed with KA, and a surgical excision with 3 mm margin was performed (►**Fig. 2B**). Histopathological findings revealed a large, well-differentiated, squamous tumor with central keratin-filled crater (►**Fig. 2C**). A buttress of normal epidermis surrounded the crater. Keratin horn pearls, bland squamous cells with abundant eosinophilic or glassy cytoplasm with minimal atypia, were also observed. The tissue tested negative for HPV genotyping. The remaining defect was closed with a split-thickness skin graft harvested from the left lateral thigh (►**Fig. 2D**). No signs of recurrence were observed 3 months postoperatively.

Discussion

KA classically presents as a firm, dome-shaped nodule filled with a keratinous plug.[2,4] It has been associated with old age, HPV infection, immunosuppression, ultraviolet (UV) exposure, and cutaneous traumas such as surgery, laser resurfacing, and burns.[2] The patient in the present case tested negative for HPV deoxyribonucleic acid on polymerase chain reaction analysis. Considering his age and medical history, it is unlikely that the patient was immunosuppressed. ►**Table 1** summarizes the reported cases of KA after skin grafting according to the patient demographic and case data. The occurrence of KA at the skin graft site is rare, and in most of the 11 reported cases, the KA developed at the donor site.[5–7] Moreover, the cases that report KA development on the recipient site are recurrences of multiple KAs in the extremities of older patients.[5,9,11] The mechanism of KA formation after receiving a skin graft is unclear due to its multifactorial etiology.[10] A two-step pathogenesis, characterized by two triggering insults to the epidermis, has been proposed.[6,7,11] The first insult (initiator) may be oncogenic UV exposure of the epidermis or the mutation of cell-cycle regulators due from a chemical carcinogen. The KA in our patient also occurred in a sun-exposed area (lower eyelid) where BCC had previously presented. We believe that a potential first insult may have been a mutation in the cell-cycle regulator due to UV exposure. The trauma associated with surgery may have been the second insult (promoter) to induce epithelial proliferation. The local upregulation of cytokines and chemokines from recruitment of neutrophil, macrophage, and T cells may be involved in the acute wound healing process.[11] Helper T cells enhance skin carcinogenesis.[12] Fibroblast growth factor is involved in the Koebner phenomenon of psoriasis,[13] characterized by the appearance of skin lesions following trauma in a previously affected site. Therefore, epithelial proliferation and angiogenesis may be induced by these cells after acute epidermal injury.[11] Contrastingly, cytotoxic T cells are involved in KA regression. After skin grafting, microscarring reduces lymphatic regeneration, thereby decreasing local immunosurveillance; this factor places higher risk among older patients with immunosenescence.[11] In a previously reported case of recurrent multiple KA in older patients, local and systemic immunosuppression were presumably involved. Considering these findings and reports, the two-step pathogenesis presents an acceptable explanation for the koebnerization.[7,11]

In our case, the KA occurred at the FTSG recipient site following the surgical excision of a BCC in a relatively young patient. Without dermatological consultation, this pathogenic presentation may have been misdiagnosed as a SCC and treated invasively with wide excision margins. Since a possibility of KA

Table 1 Keratoacanthomas associated with previous skin graft

Author (year)	Age/Sex	Preceding lesion	Time interval between SG and appearance of KA	Type of SG	Location of KA
Dibden and Fowler (1955)[a]	76/M	Keratoacanthoma	2 mo	Unspecified	Donor and **Recipient** sites
Wulsin (1958)	unspecified	Unspecified	3 wk	Unspecified	Donor site
Schwartz (1979)[a]	59/F	Keratoacanthoma	Unspecified	Unspecified	Donor site
Soto-de-Delas et al (1989)	38/F	Melanoma	3 wk	Split-thickness	Donor site
Hamilton et al (1997)	61/F	Burn	1 mo	Split-thickness	Donor site
Taylor et al (1998)	55/M	Burn	3 wk	Split-thickness	Donor site
Tamir et al (1999)	54/M	Burn	4 mo	Split-thickness	Donor site
Vergara et al (2007)[a]	80/F	Keratoacanthoma	1 mo	Split-thickness	**Recipient site**
Nagase et al (2016)	78/F	Actinic Keratosis	23 d	**Full-thickness**	Donor site
Nishibaba et al (2017)[a]	89/F	Keratoacanthoma	2 mo	**Full- thickness**	**Recipient site**
Lee et al (2017)[a]	93/F	Keratoacanthoma	3 mo	Split- thickness	Donor and **Recipient** sites
Our case (2022)	57/M	Basal cell carcinoma	2 wk	**Full-thickness**	**Recipient site**

Abbreviations: F, female; KA, keratoacanthoma; M, male; SG, skin graft.
Note: Similar cases are bolded.
[a]Case of **multiple** and **recurrent** KA all around the edge of the skin graft site.

regression exists, treatment with bleomycin Intralesional injection administration can be considered, instead of surgical resection.[2,4] This report presents information that may provide guidance to clinicians performing dermatologic surgeries and identify better therapeutic strategies. In addition, the possibility of postoperative KA development should be explained to patients when skin grafts are used in a surgical site of previous oncogenic insult. Since most of the previously reported cases developed KA within 2 months, careful follow-up should be done at least 2 months postoperatively.

Patient Consent

The patient provided written informed consent for the publication and use of their images.

Authors' Contributions

Conceptualization: J.H.K., S.H.L. Data curation: J.H.K., S.H.L. Formal analysis: S.H.L. Investigation: J.H.K., S.H.L. Methodology: J.H.K., S.H.L. Project administration: J.H.K., S.W.K. Visualization: S.H.L., S.P.H. Writing-original draft: J.H.K., S.H.L. Writing-review & editing: S.P.H., J.Y.K., S.W.K. Approval of final manuscript: all authors.

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Conflict of Interest

None declared.

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