Eruptive keratoacanthomatous atypical squamous proliferations (KASPs) arising in skin graft sites

Melanie A. Clark, MD, Joan Guitart, MD, Pedram Gerami, MD, Benjamin R. Marks, MD, PhD, Sapna Amin, MD, and Simon S. Yoo, MD
Chicago, Illinois

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Keratoacanthomas (KAs) and squamous cell carcinomas (SCCs) are common epidermal neoplasms, particularly in sun-exposed areas of fair-skinned individuals. Although surgical excision is the standard of care, eruptive KAs and SCCs provide a therapeutic challenge. We present an unusual case of a patient who developed eruptive low-grade keratoacanthomatous atypical squamous proliferations (KASPs) in split-thickness skin graft (STSG) donor and recipient sites after SCC excision.

Abbreviations used:

KA:	keratoacanthoma
KASP:	keratoacanthomatous atypical squamous proliferation
SCC:	squamous cell carcinoma
STSG:	split-thickness skin graft

CASE REPORT

A 73-year-old Caucasian woman with a history of basal cell carcinoma, SCC, and no known chemical or occupational exposures presented in November 2013 with multiple large well-differentiated SCCs of the bilateral lower extremities. She underwent wide local excision of 3 SCCs on the right leg and 1 SCC of the left leg. All excision sites were repaired with a STSG from a donor site on the proximal aspect of her right thigh.

One month after surgery, the graft donor site on the proximal aspect of her right thigh and the SCC excision site on the right shin that had been repaired with the STSG developed numerous erythematous firm papules (Figs 1 and 2). Histopathology of 2 papules biopsied on the STSG donor site on the proximal aspect of her right thigh showed epidermal hyperkeratosis and infiltration into the papillary dermis by irregular strands of large cells with abundant eosinophilic cytoplasm and pleomorphic nuclei, consistent with low-grade KASPs (Fig 3). A biopsy specimen of a papule on the SCC excision site on the front of her right shin that had been repaired by the graft showed similar pathology. Therapy with acitretin (25 mg) by mouth daily was initiated and the KASPs on the right thigh STSG donor site promptly resolved. Acitretin therapy was complicated by a significant transaminitis and subsequently discontinued without recurrence of these neoplasms on the right thigh. The patient required repeated wide local excision of the right shin for multiple KASPs that were persistent despite acitretin therapy and the defect was repaired with a STSG from a donor site on the proximal aspect of her left thigh.

After surgery, the left thigh graft donor site developed multiple firm papules similar to those that had developed in the right thigh donor site. A biopsy specimen of 2 papules on the left thigh graft donor site showed keratin-filled plugs with epithelial collarettes and large and glassy-appearing keratinocytes without significant atypia, consistent with KAs (Fig 4). Therapy with oral acitretin was restarted with

From the Department of Dermatology, Feinberg School of Medicine, Northwestern University.

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Correspondence to: Simon S. Yoo, MD, Department of Dermatology, Feinberg School of Medicine, Northwestern University, 676 N St Clair St, Suite 1600, Chicago, IL 60611. E-mail: simyoo@yahoo.com.

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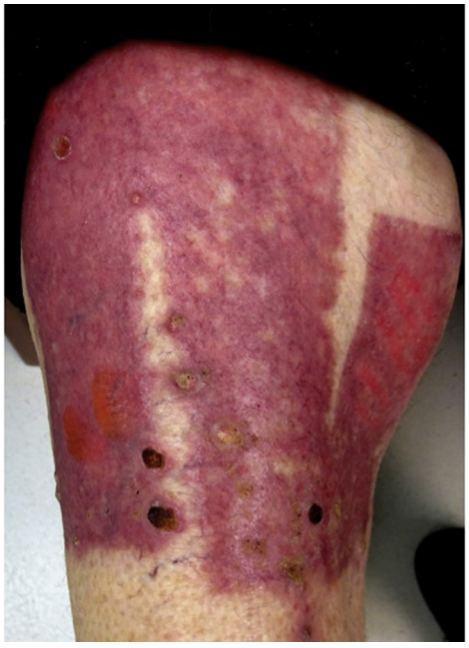

Fig 1. Right thigh split-thickness skin graft donor site.

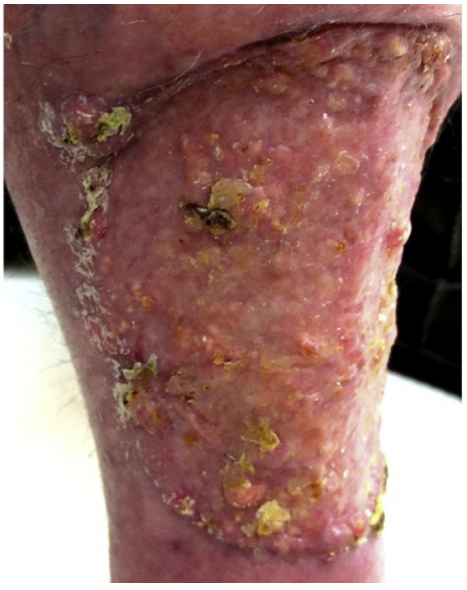

Fig 2. Right shin split-thickness skin graft recipient site.

resolution of the papules on the proximal aspect of her left thigh. Because of a recurrent transaminitis that was persistent even on a lower dose of acitretin (10 mg) by mouth daily, acitretin was discontinued.

The STSG donor sites on the bilateral thighs remained clear of KASPs and KAs, however the patient again went on to develop recurrent low-grade KASPs on the front of her right shin. She was treated with a combination of cryosurgery and topical 5-fluorouracil under occlusion with partial involution of these neoplasms. Radiation therapy is planned for future recurrences not responsive to topical treatments and cryotherapy.

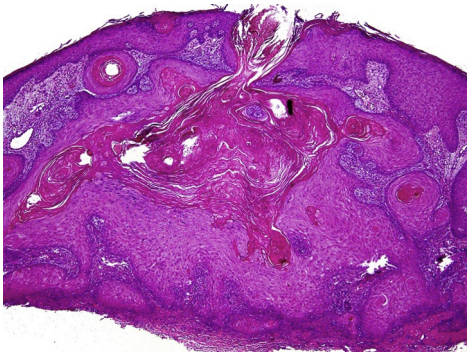

Fig 3. Right thigh, keratoacanthomatous atypical squamous proliferation. (Hematoxylin-eosin stain; original magnification: ×10.)

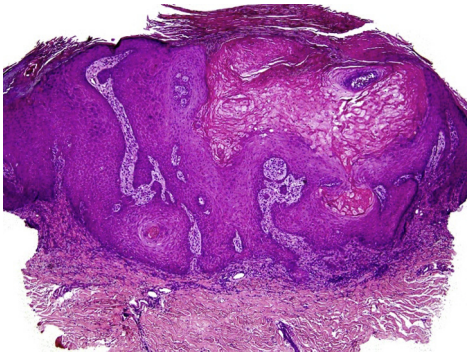

Fig 4. Left thigh, keratoacanthomatous atypical squamous proliferation. (Hematoxylin-eosin stain; original magnification: ×10.)

DISCUSSION

KAs and KASPs are rapidly proliferating epidermal tumors that are considered a variant of SCC and thought to be follicular in origin. These neoplasms most commonly occur on sun-exposed areas of light-skinned middle-aged and older individuals as single lesions. Multiple KAs have been described in the Ferguson-Smith, Grzybowski, and Witten and Zak subtypes and in genetic syndromes with defects in DNA repair systems such as Muir-Torre and xeroderma pigmentosum. The pathogenesis of KAs and SCCs is not fully understood but these entities have been associated with chemical carcinogen exposure, immunosuppression, human papillomavirus, and trauma.

The presentation of multiple eruptive KASPs occurring within a surgical site and STSG donor site is rare. Few case reports describe a similar presentation to our patient in which multiple KAs or SCCs developed at a surgical wound after SCC excision.[1,2] Approximately 10 cases of a single KA or well-

differentiated SCC arising within a STSG donor site have been reported since this entity was first described over 60 years ago. However, only 1 case of numerous KAs occurring in a STSG donor and recipient site was identified.[3] Eruptive KAs within sites of diffuse trauma caused by fractional photothermolysis, medium-depth chemical peels, tattoos, and photodynamic therapy with microdermabrasion have been reported suggesting a role of pathergy triggering these neoplasms.[4-8] Pathergy has also been described as a precipitant of KAs in the Grzybowski subtype. It is unclear to what degree pathergy may have triggered atypical squamous proliferation development in our patient or if trauma may have caused chronic inflammation that promoted the growth of these neoplasms within vulnerable sites in an already predisposed individual. On review of our patient's pathology from her initial excisions and subsequent biopsy specimens of eruptive neoplasms postoperatively, all appeared histologically similar and within the spectrum of low-grade KASPs. These atypical squamous proliferations (which may otherwise be identified as either well-differentiated SCCs or KAs) are all believed to be part of the same entity in this patient. In an otherwise healthy individual who has continued to do well clinically, it is unclear to what degree these are truly neoplastic with metastatic potential or if they are a manifestation of chronic inflammation.

The clinical presentation of eruptive KASPs presents a therapeutic challenge. Surgical options include excision, Mohs micrographic surgery, and cryosurgery. When lesions are multiple, large, or surgery is contraindicated, treatment with an oral retinoid may be successful, however systemic toxicity may limit the use of these agents as was the case in our patient. Topical and intralesional therapies that have anecdotally been reported as beneficial include topical 5-fluorouracil, intralesional 5-fluorouracil, intralesional methotrexate, intralesional bleomycin, intralesional interferon alfa-2b, and intralesional corticosteroids.[9,10] Radiation therapy may also be considered to control localized disease.

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