SKIN

BRIEF ARTICLE

The Persistent Wound: A Complex Case of Recurrent Cutaneous Squamous Cell Carcinoma Following Mohs Surgery and its Management with Placental Allografts

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ABSTRACT

Introduction: Cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer in the United States, with over 1 million new cases each year. cSCC is categorized as low-risk or high-risk based on features including tumor size, depth, differentiation, and perineural invasion. High-risk cSCC has increased recurrence and poor prognosis, necessitating precise treatment. While Mohs micrographic surgery (MMS) offers higher cure rates for cSCC compared to conventional excision (CE), recurrence and challenges with defect healing remain. Emerging cellular and tissue-based products (CTPs), including placental allografts, provide innovative solutions for MSS defects and chronic wound healing.
Clinical Case: This paper explores the rare case of an 86-year-old woman with significant comorbidities (diabetes, obesity, and lymphedema) who presented to the clinic with chronic nonhealing pretibial ulcers harboring both invasive and in situ cSCC. Following MMS, the patient underwent treatment with EpiEffect and EpiFix placental allografts, which facilitated remarkable wound healing. Despite initial success, recurrence occurred after 12 months, necessitating a second Mohs procedure and subsequent application of CTPs, which again achieved complete wound closure.
Conclusion: This case highlights the challenges of managing recurrent cSCC in a high-risk patient with chronic wounds. It emphasizes the diagnostic complexity of malignancy in nonhealing ulcers, recurrence after Mohs surgery, and the innovative role of placental allografts in achieving rapid wound healing. By integrating oncologic and reconstructive approaches, this report underscores the importance of sustained vigilance in monitoring treated sites and provides valuable insights into optimizing care for complex, recurrent cSCC lesions.

INTRODUCTION

Cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer in the United States, with an estimated annual incidence of over 1 million new cases. [1] Despite the lack of inclusion in national cancer registries, cSCC rates continue to rise and remain a significant public health concern. [1, 2] cSCC generally appears as a single, rough papule or plaque with central ulceration, commonly described by patients as nonhealing and prone to bleeding easily. [3] Most of these lesions originate from precancerous actinic keratoses which

eventually undergo malignant transformation driven by UV radiation.[1-3] cSCC lesions can be broadly categorized into low-risk and high-risk subgroups, with the latter displaying features associated with higher chances of recurrence, metastasis, and poor prognosis.[2, 4] High-risk cSCC is often distinguished by characteristics such as tumor diameter greater than 2 cm, depth over 2 mm, poor histological differentiation, and the presence of perineural invasion.[2-4] Additionally, lesions arising from chronic wounds and scars, or those occurring in immunosuppressed individuals, are more likely to exhibit aggressive behavior. [2] These defining features underscore the importance of accurate risk stratification to guide appropriate management and treatment options.

In general, surgical excision is the mainstay for cSCC treatment.[5] Two surgical approaches include conventional excision (CE), where 5 to 10 mm margins of uninvolved skin surrounding the tumor are excised and evaluated by pathology postoperatively, and Mohs micrographic surgery (MMS), a tissue-sparing technique that uses fresh frozen horizontal sections to microscopically assess the tumor's deep and peripheral margins, ensuring precise excision and conservation of healthy tissue.[1, 5, 6] Comparing these methods, MMS is the more costly option, yet it is safer, more effective for high-risk cSCC subtypes, and gives the highest cure rates.[3, 5] Regardless of these advantages, cSCC recurrence after MMS is still possible. As noted in the retrospective cohort analysis of 882 high-risk cSCC patients treated with MMS, 2.5% had local recurrence.[7] Recent studies have investigated factors such as tumor size (p=0.025) and biomarker expression (AXIN2 p=0.001; SNAIL p=0.001) to be predictive of cSCC recurrence after MMS.[8] In addition to potential recurrence, another challenge occurring after MSS involves healing of the Mohs defect.

Surgical wounds, such as those derived from MSS, may be expensive to treat and can require advanced reconstruction depending on wound size and severity.[9] Local flaps and full-thickness skin grafts (FTSG) are traditionally used after MSS, however patient age and prior surgeries complicate their use.[10] Emerging research on cellular and tissue-based products (CTPs), including human placental-derived allografts like EpiEffect or EpiFix, highlights their potential as promising alternatives for managing complex wounds.[9-11] Placental allografts retain a collagen-rich extracellular matrix and growth factors essential for wound healing, providing anti-inflammatory and antimicrobial properties.[10] These skin substitutes are particularly beneficial for patients with limited donor tissue availability, advanced age, or comorbidities that hinder autologous grafting.[10, 11]

CASE REPORT

An 86-year-old female with a history of type 2 diabetes, obesity, lymphedema, hypertension, atrial fibrillation, and prior excisions for basal and squamous cell carcinomas presented to the wound clinic with a chronic right pretibial ulcer present for over one year. Initial examination revealed two distinct lesions: a 1 × 1.5 cm pedunculated growth with a thick yellow slough layer and a 3.5 × 3 cm ulcer with a cobblestone-like granular wound bed and slightly raised edges. Biopsies confirmed invasive squamous cell carcinoma in one lesion and squamous cell carcinoma in situ in the other.

The patient underwent Mohs surgery to excise both lesions, leaving two adjacent

circular defects separated by a small skin bridge, with a total surface area of 24.5 cm². (**Figure 1**). Cellular tissue-based products (CTP), specifically EpiEffect grafts, were applied weekly, resulting in significant wound contraction and epithelialization. By the 10th week, the wound size decreased by 95%, reaching 0.7 cm², and ultimately closed with a thin epithelial layer.

Recurrence was noted 12 months later, this time as a single distal pretibial lesion measuring 1 cm in diameter. Biopsy confirmed squamous cell carcinoma in situ. Following repeat Mohs surgery, which resulted in a defect measuring 1.7 × 1.4 cm, a new series of CTP graft applications, including EpiEffect and EpiFix placental grafts, were initiated. These grafts accelerated healing, reducing the wound from 1.7 × 1.4 cm to complete closure over the course of 6 weeks.

Figure 1. Initial wound surface area (16.8cm^2) after first Mohs micrographic surgery (MMS) measured with Silhouette.

DISCUSSION

This case underscores the diagnostic challenges of identifying malignancy hidden in a chronic, nonhealing wound and highlights the risk of cSCC recurrence within the same anatomical location, even after successful initial management with MSS. The innovative use of placental-derived allografts, such as EpiEffect and EpiFix, demonstrated remarkable efficacy in promoting rapid wound healing and achieving complete epithelialization, despite the complexity of managing recurrent malignancy.

By showcasing this approach in a high-risk patient, this case report emphasizes the importance of integrating oncologic and

reconstructive strategies to optimize care for difficult-to-heal and recurrent cSCC lesions. Additionally, it highlights the critical need for sustained vigilance in monitoring treated sites to promptly address recurrence. This case contributes valuable insights into addressing the challenges of managing advanced cSCC while underscoring the potential of placental allografts as a transformative tool in post-MMS wound care. Further research is warranted to refine these techniques and evaluate their long-term efficacy in similar high-risk populations.

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References:

1. Jiang R, Fritz M, Que SKT. Cutaneous Squamous Cell Carcinoma: An Updated Review. *Cancers (Basel).* 2024;16(10):1800. doi:10.3390/cancers16101800
2. Que SKT, Zwald FO, Schmults CD. Cutaneous squamous cell carcinoma: Incidence, risk factors, diagnosis, and staging. *J Am Acad Dermatol*. 2018;78(2):237-247. doi:10.1016/j.jaad.2017.08.059
3. Firnhaber JM. Basal Cell and Cutaneous Squamous Cell Carcinomas: Diagnosis and Treatment. *Am Fam Physician*. 2020;102(6):339-346.
4. Thompson AK, Kelley BF, Prokop LJ, et. al. Risk Factors for Cutaneous Squamous Cell Carcinoma Recurrence, Metastasis, and Disease-Specific Death: A Systematic Review and Meta-analysis. *JAMA Dermatol*. 2016;152(4):419-428. doi:10.1001/jamadermatol.2015.4994
5. Zürcher S, Martignoni Z, Hunger RE, et. al. Mohs Micrographic Surgery for Cutaneous Squamous Cell Carcinoma. *Cancers (Basel).* 2024;16(13):2394. doi:10.3390/cancers16132394
6. Hunt WTN, Earp E, Brown AC, et. al. A review of Mohs micrographic surgery for skin cancer. Part 3: Squamous cell carcinoma. *Clin Exp Dermatol.* 2022;47(10):1765-1773. doi:10.1111/ced.15187
7. Matsumoto A, Li JN, Matsumoto M, et. al. Factors predicting outcomes of patients with high-risk squamous cell carcinoma treated with Mohs micrographic surgery. *J Am Acad Dermatol*. 2021;85(3):588-595. doi:10.1016/j.jaad.2021.01.063
8. Zhao G, Kim KY, Zheng Z, et al. AXIN2 and SNAIL expression predict the risk of recurrence in cutaneous squamous cell carcinoma after Mohs micrographic surgery. *Oncol Lett*. 2020;19(3):2133-2140. doi:10.3892/ol.2020.11324
9. Lu KW, Khachemoune A. Skin substitutes for the management of Mohs micrographic surgery wounds: a systematic review. *Arch Dermatol Res*. 2023;315(1):17-31. doi:10.1007/s00403-022-02327-1
10. Toman J, Michael GM, Wisco OJ, et. al. Mohs Defect Repair with Dehydrated Human Amnion/Chorion Membrane. *Facial Plast Surg Aesthet Med*. 2022;24(1):48-53. doi:10.1089/fpsam.2021.0167
11. Zhu H, Lewis DJ, Haynes D, et. al. Engineered Skin Substitutes in Dermatologic Surgery: A Systematic Review. *Dermatol Surg.* 2024;50(12):1175-1181. doi:10.1097/DSS.0000000000004375