



Hypopharyngeal Skin Cancer Following Total Laryngectomy and Pectoralis Flap Reconstruction: Case Report and Literature Review

Shaunak N. Amin¹ · Justin R. Shinn² · Alice Tang³ · James S. Lewis Jr.^{2,4} · Kyle Mannion^{2,5}

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Abstract

Although early complications of microvascular free flaps and regional pedicled flaps of the head and neck are well described in the literature, there is relatively limited knowledge regarding their long-term complications. We describe the case of a 62-year-old gentleman who underwent primary resection and adjuvant radiation therapy for supraglottic squamous cell carcinoma who subsequently underwent salvage total laryngectomy with pectoralis major muscle flap reconstruction. During a later esophageal dilation for complaints of dysphagia, a new exophytic lesion of the hypopharynx was biopsied on endoscopy. The lesion was excised via transoral robotic surgery with final pathology revealing squamous cell carcinoma completely confined to the skin paddle of the pectoralis flap and arising from the epidermis of the skin flap. No further therapy was undertaken and there has been no evidence of recurrence 2 years after resection. Synchronous cutaneous malignancy is a rare complication of free and pedicled flap reconstruction, however its diagnosis is increasing. Given the concern for recurrent mucosal tumors arising in the upper aerodigestive tract which may require extensive resection with or without adjuvant therapy, it is important to determine the etiology of the underlying malignancy to guide appropriate treatment.

Keywords Squamous cell carcinoma · Second primary · Free flap · Pedicled flap · Mucosalization

Introduction

Over the last several decades, tissue transfer and flap reconstruction have become the standard management for deficits of the head and neck, allowing for improved cosmetic outcomes and functional rehabilitation following surgical

treatment of cancers. The most commonly utilized methods of reconstruction include pedicled flaps, which maintain their original vasculature through simple flap transposition, and microvascular free flaps, in which the transferred tissue is completely detached from its vascular supply at the donor site. Although free tissue transfer provides a host of advantages over regional reconstruction of the head and neck region, pedicled flaps are still utilized for select indications.

Common complications of flap reconstruction are well described and include flap failure, fistula formation, infection, and hematoma [1, 2]. Although still rare, there has been an increasing number of reports of squamous cell carcinoma (SCC) arising from the cutaneous portion of the flaps [3–8]. These malignancies do not represent recurrence of mucosally-based cancer—rather they are distinct primary cutaneous cancers that have been inadvertently surgically transferred and, presumably, are of separate etiology.

We present the case of a patient with a primary SCC arising from the cutaneous epithelium of a pectoralis major myocutaneous flap (PMMF) 2 years following pharyngeal reconstruction for SCC of the larynx and summarize the current literature regarding primary cancers in flaps.

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✉ Shaunak N. Amin
shaunak.n.amin@vanderbilt.edu

- ¹ Vanderbilt University School of Medicine, 2209 Garland Avenue, Nashville, TN 37240, USA
- ² Department of Otolaryngology – Head and Neck Surgery, Vanderbilt University Medical Center, Nashville, TN, USA
- ³ Department of Otolaryngology – Head and Neck Surgery, University of Cincinnati, Cincinnati, OH, USA
- ⁴ Department of Pathology, Microbiology, and Immunology, Vanderbilt University Medical Center, Nashville, TN, USA
- ⁵ Division of Head and Neck Surgery, Vanderbilt University Medical Center, Nashville, TN, USA

Case Report

A 62-year-old man with a history of SCC of the right floor of mouth, treated 12 years prior with primary resection and adjuvant radiation therapy, presented to our institution with new-onset hoarseness and odynophagia. Direct laryngoscopy revealed a tumor involving the epiglottis, vallecula, and left aryepiglottic fold. Transoral supraglottic laryngectomy and base of tongue resection confirmed a 2.7 cm tumor, presumed to be a separate primary cancer from his original SCC, that involved the epiglottis, tongue base, and pre-epiglottic space with negative surgical margins (Fig. 1). The patient's post-operative course was complicated by recurrent episodes of aspiration pneumonia and feeding difficulty. Given his compromised quality of life, he then underwent salvage total laryngectomy with PMMF reconstruction for a non-functioning larynx 6 months following his cancer resection. Final pathology was negative for carcinoma.

Two years later, a new exophytic lesion of hypopharynx was discovered incidentally during an upper gastrointestinal endoscopic exam performed due to complaints of dysphagia (Fig. 2). A biopsy was positive for keratinizing-type SCC in situ with foci suspicious for invasion. The lesion was transorally resected with partial resection of the skin paddle and negative surgical margins. Pathological examination revealed a 2.2 cm, p16-negative SCC that was not mucosally-based but, rather, was completely confined to the skin paddle of the PMMF (Fig. 3). The postsurgical course was complicated by continued dysphagia secondary to neopharyngeal stenosis which later required resection of the stenotic segment. No adjuvant therapy was indicated. There has not been evidence of tumor recurrence 2 years following resection of the cutaneous malignancy.

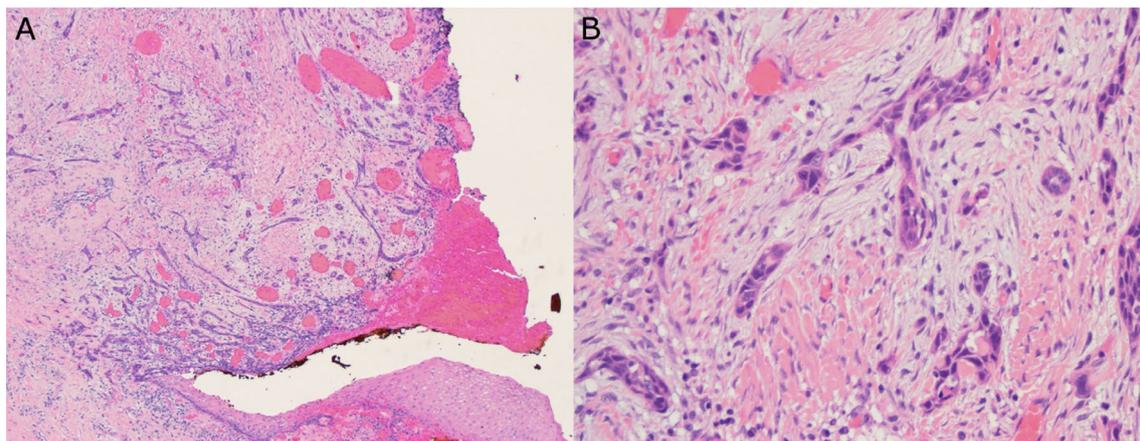


Fig. 1 Pathologic features of the resected, post-treatment, supraglottic SCC. **a** Low power view showing a highly infiltrative, cord-like, poorly differentiated, keratinizing type, SCC with an ulcerated

surface ($\times 4$ magnification). **b** High power view showing the small, cord-like nests of infiltrating tumor in a densely fibrotic, desmoplastic stroma ($\times 20$ magnification)



Fig. 2 Esophagogastroduodenoscopy for esophageal stenosis revealed a fungating mass (asterisk) arising from the myocutaneous flap surface

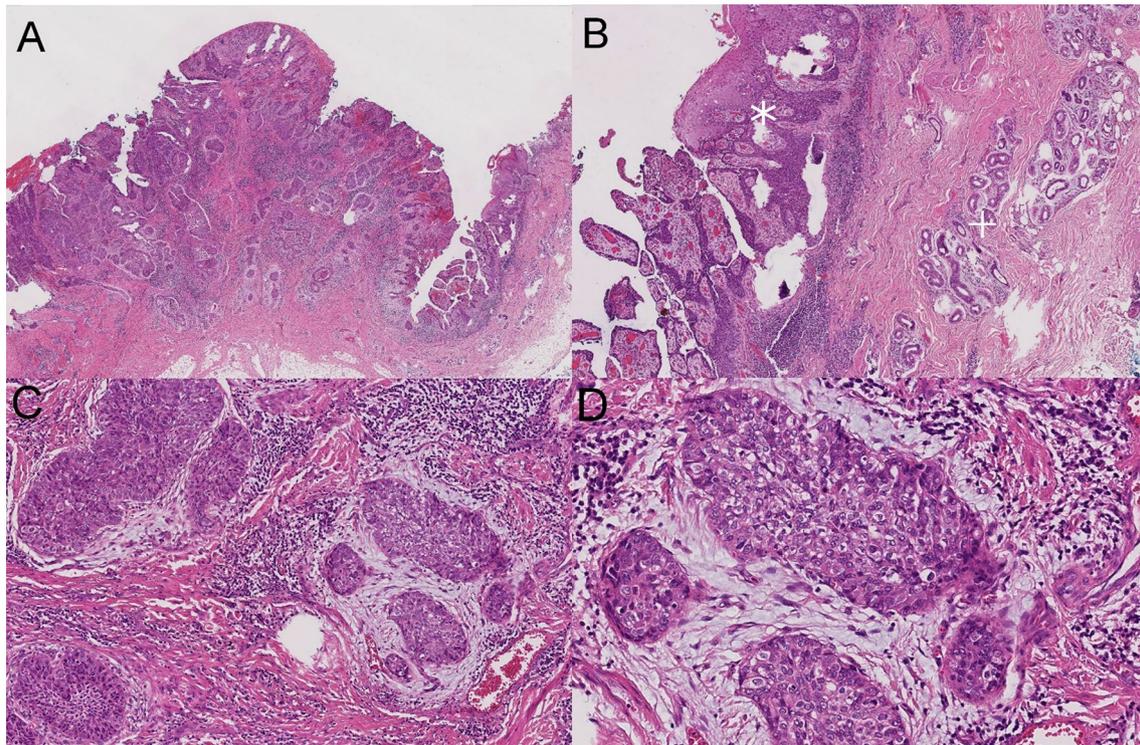


Fig. 3 Pathologic features of the resected pectoralis flap tumor. **a** Low power view showing an exophytic and somewhat papillary tumor ($\times 1$ magnification). **b** Medium power showing that the tumor arises from squamous carcinoma in situ of the adjacent skin (white asterisk) and with dermis containing eccrine sweat glands confirming

this as skin with dermal adnexal structures (white + sign) ($\times 4$ magnification). **c, d** Medium and high power views showing the invasive SCC component with associated basophilic, desmoplastic stroma reactive to the invasive tumor ($\times 8$ and $\times 20$ magnification, respectively)

Discussion

We describe a case of a separate primary SCC arising within the skin paddle of a PMMF 2 years following pharyngeal reconstruction. Although the etiology of cutaneous tumors in head and neck skin flaps is often unclear, several potential mechanisms have been proposed in the literature: (1) colonization of the flap by residual malignant cells from the primary lesion at the time of surgery, (2) colonization of the skin flap by a secondary tumor arising in the adjacent mucosa, (3) introduction of a pre-existing tumor in the skin flap at the time of reconstruction, and (4) induction of a second primary tumor through exposure of the skin flap to new environmental conditions [4, 6].

In the presented case, it is unlikely that there was implantation of the supraglottic SCC into the pectoralis flap during the initial tumor resection and pharyngeal reconstruction. At that time, the surgical margins of the resected tissue were negative for malignancy. Additionally, 2 years had passed between the resection and the incidental discovery of the secondary SCC with no evidence of disease in between, making it more likely that the tumor was a result of a new process. It is also not likely that the skin flap malignancy

originated in adjacent tissue and spread to the flap as final histopathology showed that the new carcinoma was completely confined to the skin flap and the patient has shown no evidence of disease in the intervening years. Although possible, it is unlikely that the tumor already existed in the flap before it was raised. The patient did have a history of radiation exposure to the neck when he received adjuvant therapy for his initial floor of mouth SCC years prior, increasing his risk for the development of a second primary, however, the dose of radiation to the portion of the chest used for the flap was likely minimal. He additionally did not endorse a history of extensive ultraviolet light exposure nor any family history of cutaneous SCC. Furthermore, gross examination of the flap at the time of reconstruction did not reveal any worrisome lesions.

Wei et al. [9] described a tendency for PMMF to undergo metaplasia when exposed to new mucosal environments in head and neck reconstruction. Common histologic changes include progressive epidermal desquamation and partial loss of epidermal appendages [9]. This process is thought to be triggered by chronic inflammation secondary to exposure of the skin to abnormal external stimuli such as saliva, food, and oral flora [3, 4]. Chronic inflammation is a known

risk factor for SCC in other regions of the body, notably in degenerating burn ulcers [10]. Similarly, metaplastic transformation secondary to environmental stimuli has been implicated in oncogenesis in other clinical situations such as the development of esophageal adenocarcinoma from Barrett's esophagus [5].

It is possible that the cutaneous malignancy developed from exposure of normal squamous epithelium to a new mucosal environment, resulting in "mucosalization" and inflammation of the skin paddle and subsequent carcinogenesis, which has been previously reported in the literature [3–7]. Alcohol and tobacco abuse, HPV infection, and prior radiation may also exacerbate the environmental hostility [4]. In the reported case, the patient had no history of alcohol abuse and, although he had a 60 pack-year history of tobacco abuse, he had quit smoking 4 years prior to his flap reconstruction. The epidermal-derived SCC was p16-negative, essentially excluding it being driven by transcriptionally-active high risk HPV and cutaneous SCC is almost never associated with high-risk HPV carcinogenesis.

In patients with a history of upper aerodigestive tract malignancies, it is critical to monitor for recurrence and distinguish whether the tumor is a second primary cancer or whether it is locoregional recurrence. Tokita et al. [4] defined a list of diagnostic criteria for primary SCC arising in skin flaps: (1) the tumor is limited to the skin flap and is far from the oral mucosa, (2) there is no tumor remnant after the initial treatment, (3) some years have elapsed since the end of initial treatment, (4) skin SCC is confirmed by histopathologic examination, and (5) there are no skin malignancies elsewhere on the body. The patient presented in this case satisfied all five criteria.

It is important to determine the etiology of a new mass as this has significant implications for treatment. Recurrent cancer, particularly greater than 2 years from treatment, represents a highly aggressive process and the surgeon likewise must act aggressively if the tumor is safely resectable, necessitating wide surgical margins at the expense of significant patient morbidity. Recurrent disease also often incorporates consideration of elective treatment of the neck, whether with surgery or radiation. However, if the flap lesion presents as a primary cutaneous malignancy which can be difficult to determine pre-operatively, partial or total resection of the skin flap is reasonable and often does not necessitate prophylactic treatment of the neck or adjuvant therapy.

It is difficult to determine if partial resection of the skin flap for cutaneous malignancies is suitable rather than complete resection, and it remains controversial within the literature. To our knowledge, there is only one reported case of local recurrence of a cutaneous malignancy after partial flap resection, and no cases following total resection [8]. In the reported case, our patient had a partial resection with negative surgical margins and he remains disease-free after

2 years. Even so, it has been noted that after complete resection of the skin flap, there are often multiple isolated foci of chronic inflammation in benign regions of a flap with a single focus of primary cutaneous malignancy [4]. This finding suggests that partial resection of the skin paddle may not be sufficient in susceptible patients, however, further investigation is needed.

Our paper has several limitations including limited access to the patient's medical information prior to his presentation at our institution. We were unable to obtain details of his adjuvant radiation therapy for the initial floor of mouth cancer 12 years prior to presentation and are therefore uncertain if the chest wall from which the PMMF was derived was within the treatment field. As with all case reports, associations do not imply cause-effect relationships. Future controlled studies should be performed to examine any causal relationship between "mucosalization" of head and neck free flaps and oncogenesis.

Conclusion

The use of pedicled and free flaps to reconstruct the upper aerodigestive tract is expanding worldwide as it has become the standard for management of head and neck defects. Although uncommon, primary cutaneous malignancy arising within flaps is a complication that should be considered by all reconstructive surgeons. When introduced to an unfamiliar mucosal environment, the squamous epithelium of the flap is susceptible to metaplasia which may contribute to carcinogenesis. It is important to maintain follow up of these patients with serial examination of the mucosal surface of the upper aerodigestive tract and cutaneous surface of the skin paddle. If a new tumor is discovered, it is critical to distinguish whether it is a new primary cancer or a local recurrence as this difference has significant implications regarding appropriate treatment.

Compliance with ethical standards

Conflict of interest All authors declared that they have no conflict of interest.

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