Squamous cell carcinoma arising in a skin flap: case report and review on malignant transformations in skin grafts and microvascular cutaneous flaps

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Objectives. Sufficient closure of intraoral defects can be challenging. Various methods of tissue transfer have been presented in the literature. From skin grafts to microvascular flaps, most techniques used for intraoral reconstruction use skin to line out the oral cavity to guarantee an epithelial surface. Native mucosa tolerates the moist environment of the oral cavity, whereas skin flaps do to just a certain extent. This may lead to chronic inflammation of the flap-skin. Under rare circumstances, these histologic changes can enhance the risk for malignant transformation of the skin graft.

Case report. We present a case of a patient who derived a squamous cell carcinoma in the skin island of a jump flap raised from the abdominal wall 30 years earlier. The flap was used to close a very wide palatal cleft. The patient had no history of malignancy, smoking, drinking, or other risk factors.

Discussion. To the authors’ knowledge, this is the first report on carcinoma in a skin flap in a patient without any history of intraoral malignancy. Although malignant transformations of skin grafts are very rare and usually appear years after the reconstruction, one should be aware that the moist environment can lead to chronic inflammation of the dermis of flap. This fact may increase the risk of malignant transformation in a skin graft. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:e54-e58)

The closure of intraoral defects can be challenging. Although palatal defects may be covered by surgical methods or anaplastologically, other intraoral regions definitely require surgical reconstruction. In the past, jumping skin flaps and local flaps, such as temporalis muscle flaps or pectoralis major flaps, have been used. Since the early 1980s, several microvascular flaps have been described for intraoral reconstruction. Indications for the intraoral use of microvascular flaps are reconstructive procedures after tumor surgery, trauma, or wide palatal clefts and oronasal fistulas after the failure of conventional techniques. Missing intraoral mucosa is commonly reconstructed by skin to guarantee an epithelial lining. The main disadvantage of fascio-cutaneous and myocutaneous flaps in intraoral reconstructions is the different texture of the surface compared with the local mucosa. Skin flap adaption to the oral environment has been reported in several articles. Badran et al. described a gross appearance of the flap skin similar to the native oral mucosa. Furthermore, a gradual “mucosalization” with loss of the stratum corneum and shrinkage of pilosebaceous units has been suggested. However, these changes in appearance are reported to be caused by a chronic inflammation of the dermis. Histologic evaluations of intraoral skin grafts indicate that the different phenotypes of intraoral mucosa and flap skin are maintained. This continued distinction between transferred and native tissues has been explained by the underlying stroma that influences the phenotype of the overlying epithelium. All the described adaptive and inflammatory processes should normally be of minor clinical interest, but could be a cofactor in malignant transformation of the skin graft. We present a case of squamous cell carcinoma arising in a skin flap. Furthermore, a critical review of malignant transformations of skin grafts used for intraoral reconstruction is presented.

DESCRIPTION OF CASE

A 62-year-old woman presented with a painless swelling of the palate. Anamnestically, the patient had a history of cleft palate. The palatoplasty had been performed at another facility when she was a young girl. According to the patient’s files, the palatal artery was injured during the surgery, resulting in necrosis of

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the palatal flap. Further trials to close the cleft failed, so the wide palatal defect was left open until the patient’s adulthood. At the age of 32, a jump skin flap (pedicled tube flap) from the abdominal wall was used to cover the cleft. Using this technique, the palate could be closed sufficiently. After an uneventful period of 30 years, the patient observed a painless swelling of the palate. Clinical investigation showed a tumor of about 4×5 cm that was highly suspicious for malignancy (Fig. 1). A biopsy revealed the diagnosis of squamous cell carcinoma (Fig. 2). Furthermore, a Candida infection was diagnosed. A histologic examination showed that the carcinoma had not arisen from the palatal mucosa but in the skin portion of the jump flap. The patient had no risk factors: there was no history of smoking or drinking alcohol, and the oral hygiene was acceptable. A human papilloma virus (HPV) infection was excluded by immunohistochemistry. A preoperatively performed magnetic resonance imaging scan did not show any hint of lymph node metastasis. A surgical resection was performed with the removal of almost the entire hard palate (Fig. 3). The defect was reconstructed using a prelaminated radial free forearm flap (Fig. 4). The mucosa for prelamination had been harvested from the inner buccal plane. Ten years after reconstruction, the patient has no signs of recurrence, and there are no functional limitations concerning speech and swallowing.

**DISCUSSION**

Reports on carcinoma arising in the skin of flaps and skin grafts are rare. A literature review revealed 8 patients, as presented in Table I. To the authors’ knowledge, this is the first report on the malignant transformation of a skin flap in a patient without any history of malignancy, and no common risk factors, such as smoking, drinking alcohol, HPV infection, or bad oral hygiene. Sa’do et al.9 report on a case of carcinoma deriving from a skin graft 19 years after reconstruction. Ho et al.10 present a patient with a second primary

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**Fig. 1.** Squamous cell carcinoma arising in a skin flap 30 years after palatal reconstruction.

**Fig. 2.** Squamous cell carcinoma of a skin flap stained with hematoxylin and eosin (magnification ×40).

**Fig. 3.** Intraoral view after resection of the squamous cell carcinoma.

**Fig. 4.** Palatal reconstruction with a prelaminated radial free forearm flap.
<table>
<thead>
<tr>
<th>Anamnestic details</th>
<th>Ex-heavy smoker</th>
<th>Ex-heavy smoker and alcohol abuse</th>
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<th>Alcohol abuse</th>
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<td>27 Years</td>
<td>20 Years</td>
<td>10 Years</td>
<td>19 Years</td>
<td>12 Years</td>
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<tr>
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<td>Oral cavity</td>
<td>Floor of mouth reconstruction</td>
<td>Pharynx reconstruction</td>
<td>Floor of mouth reconstruction</td>
<td>Closure of palatal cleft</td>
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<td>Deltopectoral flap</td>
<td>Radial free forearm flap</td>
<td>Free skin graft</td>
<td>Pectoralis major myocutaneous flap</td>
<td>Deltoperatorial flap</td>
<td>Acromiothoracic tube pedicle</td>
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SCC, squamous cell carcinoma.
squamous cell carcinoma arising in the skin of a pectoralis major mycutaneous flap 12 years after reconstruction of the floor of the mouth. Monnier et al. report 1 carcinoma arising in a forearm flap 3.5 years after surgery and 1 in a deltopectoral flap 10 years after surgery. Sakamoto et al. present the case of a second primary squamous cell carcinoma in a radial forearm flap 10 years after reconstruction. Iseli et al. report on a patient developing a carcinoma in the skin of a deltopectoral flap 27 years after pharyngeal reconstruction.

All reports on carcinomas arising in cutaneous flap reconstructions concern patients with a history of oropharyngeal carcinoma and risk factors, such as heavy smoking and drinking alcohol. The role of radiotherapy is questionable, but it could be a cofactor in the development of malignancies on skin flap. One can speculate regarding the question of whether the tumors occurred after a primary tumor. The late occurrence is evidence against this theory. However, Scott and Klassen discuss a patient who developed a squamous cell carcinoma in a skin graft (acromiothoracic tube pedicle) 43 years after intraoral reconstruction. The primary tumor was an adenocarcinoma, which excludes the possibility of recurrence. In the present report, the patient developed a squamous cell carcinoma in a skin flap 30 years after reconstruction, and there were no risk factors and no history of malignancy, as mentioned previously. The question is whether the tumor originated from the oral mucosa or the skin flap. The differences between the skin flap and the oral mucosa are characteristic. In fact, the junctional zone between the skin flap and oral mucosa can be identified by a sudden loss of the horny and granular layer, a reduction in basal keratinocyte pigmentation, and replacement of dermal appendages by minor salivary glands. Badran et al. described a change in the architecture of the connective tissue between the oral mucosa and flap skin. The behavior of skin flaps transplanted into the oral cavity and histologic changes have been clearly described by several authors. Badran et al. concluded that the change in the appearance of the radial forearm skin flap does not represent a true, permanent change in the epithelial type. These transformations were found to be reactive and reversible depending on the degree of inflammation in the dermis. This is in accordance with the findings of Sinclair et al. Woolgar and Triantyfyllou report that, in cases without active inflammation of the flap surface, cutaneous phenotypes are maintained. However, sweat glands and pilosebaceous units appear to be reduced in number and size. In contrast, Shibahara et al. report the total absence of hair roots, follicles, and sebaceous glands in forearm flaps 32 months after grafting. The authors conclude that the skin flap begins to undergo mucosalike changes caused by inflammatory factors about 10 months after the grafting of a forearm flap. Although native mucosa tolerates constant moist conditions, skin flaps do to just a certain extent. Constant immersion in a watery environment enhances the risk of cutaneous candidiasis, which may lead to cutaneous reactions, such as epidermal hyperplasia, acanthosis, and marked hyperorthokeratosis and epithelial dysplasia in the skin flap. Epithelial dysplasia is a potential risk factor in developing an in situ or invasive squamous cell carcinoma. Woolgar and Triantyfyllou report that around 10% of the skin flap biopsies they analyzed revealed the diagnosis of carcinoma in situ, which seems surprisingly high. On the other hand, their sample size is reported to be small. Still, chronic candidiasis is not uncommon in oral cancer patients even when it is not noted clinically and may be a cofactor for malignant transformation. Candida colonized the carcinoma in the present case as well as the nonaffected areas of the flap (Fig. 1). Smear tests could clarify a Candida infection and indicate to biopsy any lesions that do not respond fully to antifungal therapy. One the other hand, an enormous number of intraoral reconstructions with skin-flaps are performed and the number of reported malignant transformations is negligibly small. However, some authors expect an increasing number of patients, as microvascular procedures are currently state-of-the-art. To eliminate the disadvantages of various surfaces, prelaminated flaps have been introduced. Flaps have been lined with oral mucosa to better withstand the intraoral moist environment. To the authors’ knowledge, there are no reports on the malignant transformation of prelaminated flaps used for intraoral reconstruction. In conclusion, one can state that there is a potential risk of chronic inflammation in intraoral skin grafts caused by the moist environment. Still, a malignant transformation should be a rarity.

REFERENCES

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