



Squamous cell carcinoma arising on a forearm free flap 21 years after hemiglossectomy

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Squamous cell carcinoma arising on a forearm free flap 21 years after hemiglossectomy

AIM: Free and pedicled flap are methods of choice for reconstruction of post-surgical defects consequent to oral squamous cell carcinomas (SCCs), and missing intraoral mucosa is commonly reconstructed by the cutaneous component of the flap to guarantee an epithelial lining. Even if rare, cases of second tumors arising in the skin flap have been described. We present our experience reporting a clinical case.

CASE REPORT: A squamous cell carcinoma arose on a forearm free flap 21 years after hemiglossectomy in a 72 years old woman. No smoking or alcohol habits were referred, and it was decided to perform surgical resection of the flap.

RESULTS: Resection in free margins of a moderate differentiated (G2) SCC staged as pT2 was achieved and reconstruction with anterolateral thigh free flap was performed.

DISCUSSION: Even if rare, secondary tumors arising in the skin flap in case of oral cavity defects reconstruction are described. It is important to recognize them early in order to perform surgical resection.

CONCLUSION: We think that it is fundamental to perform a prolonged follow-up of skin flap if a white patch or erythema raising clinical suspicion are present. Incisional biopsy has to be performed in order to identify those lesions potentially inclined to a malignant transformation, such as p53 expression and Ki67 index.

KEY WORDS: Free flap, Oral cancer, Squamous cell carcinoma

Introduction

Free and pedicled flap are methods of choice for reconstruction of post-surgical defects consequent to oral squamous cell carcinomas, and missing intraoral mucosa is commonly reconstructed by the cutaneous component of

the flap to guarantee an epithelial lining^{1,2}. Even if rare, cases of second tumors arising in the skin flap have been described³⁻⁵. This phenomenon has been explained by the fact that skin flap undergoes a "mucosalisation" process with the progressive loss of the stratum corneum and shrinkage of pilosebaceous units^{3,6}. Inflammatory process has been recognized as a cofactor in malignant transformation of free flap, while irradiation and common risk factors, such as smoking, drinking alcohol, HPV infection, or bad oral hygiene seem to have only a secondary role⁴.

We present a case of squamous cell carcinoma arising on a radial forearm free flap (RFFF) 21 years after hemiglossectomy in a 72 years old woman.

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Case report

An actually 72 years-old female, with no smoking or alcohol habits, had first come to our attention on 1994 (age: 51) with a squamous cell carcinoma of the left side of the tongue that was treated with a left hemiglossectomy en-bloc with SND (level I-III) with the “pull-through” technique and contemporary reconstruction with a right RFFF. Histological examination confirmed a moderately differentiated squamous cell carcinoma staged as pT2pN0 R0, so that no adjuvant treatment was required. Suddenly, implant-prosthetic rehabilitation of the lower alveolar ridge was performed. After a twenty years follow-up free of disease, the patient referred to our department on February 2015 because of the presence of a white patch developed on the RFFF skin flap (Fig. 1). Incisional biopsy revealed an infiltrating squamous cell carcinoma; according to pre-operative CT scan with contrast the neoplasm was staged as cT2cN0 (Fig. 2), and the patient underwent surgical resection of the skin flap and contemporary reconstruction with an antero-lateral thigh (ALT) free-flap. Histological examination of the specimen showed a moderately differentiated SCC staged as pT2 R0; no signs of candidosis or HPV infection were present, and at immunohistochemistry high expression of p53 was found, and a Ki67 index of 7-8% was detected too (Fig. 3). No post-operative complications were observed. On the basis of histological findings, it was decided to perform the follow-up.



Fig. 1: Pre-operative intraoral view.



Fig. 2: Pre-operative CT scan with contrast (coronal view) showing the lesion arising in the flap (arrow).

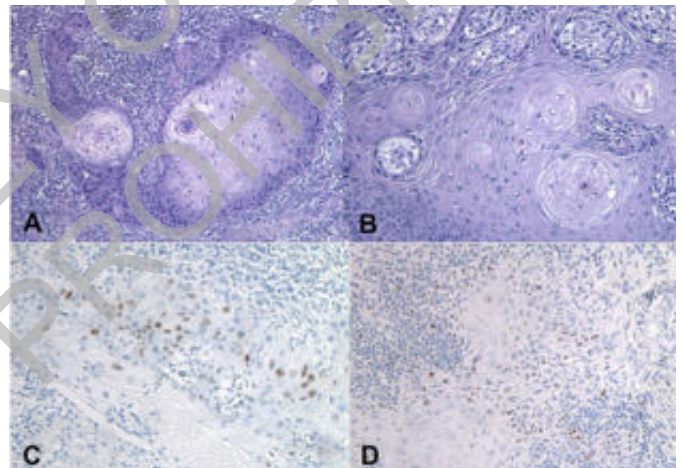


Fig. 3: A) Moderately differentiated SCC. Nests of squamous cells with central keratinization (formation of keratin pearls), inflammatory infiltrate and mitosis (10x); B) Moderately differentiated SCC. Nests of squamous cells with central keratinization (formation of keratin pearls), inflammatory infiltrate and mitosis (10x); C) Photomicrographs demonstrating p53 expression in SCC; D) Photomicrographs demonstrating Ki-67 expression in SCC. Abbreviation: SCC, squamous cell carcinoma.

Discussion

Malignant transformation of the skin of flaps used to reconstruct post-oncological defects of the oral cavity is rare. It can develop after a long latency period, and a case in which a squamous cell carcinoma arose on a skin flap 43 years after intraoral reconstruction has been described⁷.

In order to exclude neoplasms secondly involving the skin flap, some conditions are requested: 1) histologi-

cally proved squamous cell carcinoma arising in the skin flap, not involving oral mucosa; 2) no tumor remnant after the initial treatment; 3) some years elapsed since the end of initial treatment; 4) absence of other skin malignancies elsewhere on the body^{4,8}. Since most second primary tumors arise after a long latency period, implantation of the neoplastic cells at the time of reconstruction can be excluded, and it is clear that observation can lead to rule out the presence of a primary tumor on the skin flap present at the time of harvesting⁴. The most likely explanation is the fact that cancerization can be consequent to the new environmental conditions to which the flap is exposed in the oral cavity. Radiation therapy performed after surgery can be considered a cofactor, even if a direct correlation has not been identified since it was not performed in a significant number of cases⁴; HPV infection too seems not to play a role in malignant transformation. Common risk factors for oral cancer, such as smoking, alcohol consumption, poor hygiene and chronic traumatism seem to be unlikely contributors. Although if not always recognized, chronic candidiasis is not uncommon in oral cancer patients and may be a cofactor for malignant transformation⁹. Robinson et Al analyzed 10 incisional biopsy of suspect lesions arising in skin flaps in the oral cavity, finding that p53 staining was present in all strata of the epithelium in the dysplastic grafts and adjacent dysplastic mucosa, in which a significantly higher Ki-67 labelling index was detected too¹⁰.

In our case no signs of candidosis or HPV infection were present, and at immunohistochemistry high expression of p53 was found; a Ki67 index of 7-8% was detected too. Patient did not received post-operative irradiation and denied smoking or alcohol habits. The only factor that can be implicated in malignant transformation in our case is the chronic traumatism due to the presence of a dental prosthesis. Nevertheless, as showed in Fig. 1, it is clear that the leukoplasic lesion is far away from the alveolar ridge, so that we can not affirm surely that it is the cause of malignant transformation. Another possibility is that the epidermis of the skin flap can become colonised by oral epithelial cells by either a "creeping" or "seeding" mechanism, but in most cases histological examination showed a well defined junctional zone between the affected epidermis and the oral epithelium and the lesion is located far away from the junction⁹.

Also considering previous described cases, the most plausible explanation is that the mucosal metaplasia of the skin flap could be a pre-disposing condition to carcinoma, such as for the intestinal metaplasia seen in Barrett's esophagus⁸. The "mucosalisation", characterized by loss of keratinization and the partial loss of dermal structures such as the hair follicles and sweat glands, is determined by prolonged exposition to external stimuli, such as saliva or dietary substances, to which skin is not normally exposed^{8,9}. According to this explanation, surgical treat-

ment should consist in complete removal of the skin flap, as performed in our case. Nevertheless determinant factors leading to malignant transformation are unknown.

Conclusion

Due to these facts, it is fundamental to perform a prolonged follow-up of skin flap put in the oral cavity if a white patch or erythema raising clinical suspicion develop. Incisional biopsy has to be performed in order to identify those lesions having the potential for malignant transformation, such as p53 expression and Ki67 index¹⁰. Nevertheless, other perspective studies are required.

Riassunto

Allo stato attuale i lembi liberi ed i pedunculati rappresentano l'opzione di scelta nella ricostruzione dei difetti del cavo orale derivanti dalla resezione di neoplasie maligne. In questi casi la mucosa viene ricostruita nella maggior parte dei casi dalla porzione cutanea del lembo di modo da garantire il rivestimento epiteliale. In rari casi è stata descritta l'insorgenza di tumori secondari a livello della suddetta porzione cutanea.

CASO CLINICO: Presentiamo un raro caso di carcinoma squamocellulare insorto sul lembo libero di avambraccio 21 anni dopo la ricostruzione effettuata a seguito di un'emiglossoplectomia in una paziente di 72 anni non bevitrice e non fumatrice. In tale caso è stata effettuata l'asportazione chirurgica del lembo e la concomitante ricostruzione con lembo libero fasciocutaneo di anterolaterale di coscia.

RISULTATI: L'esame istologico ha confermato la presenza di un carcinoma squamoso moderatamente differenziato (G2), completamente escisso, stadiato come pT2. Il decorso post-operatorio è stato scevro da complicanze.

Discussione: Sebbene sia rara evenienza, l'insorgenza di un secondo tumore nella porzione cutanea di un lembo utilizzato per la ricostruzione di difetti del cavo orale va prontamente riconosciuta al fine di poter effettuare la resezione chirurgica.

CONCLUSIONI: Sulla base della nostra esperienza e della letteratura, riteniamo che sia necessario effettuare un follow-up prolungato in pazienti che abbiano subito un intervento chirurgico di ricostruzione del cavo orale con lembo fasciocutaneo nel caso in cui si sviluppino a tale livello lesioni leucoplasiche e/o eritematose. In questi casi la biopsia incisionale è obbligatoria al fine di identificare le lesioni a rischio di trasformazione maligna mediante l'identificazione di fattori di rischio quali l'espressione di p53 e l'indice di proliferazione cellulare (Ki67 index).

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