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CASE STUDY

Late onset fibula free flap failure due to osteoradionecrosis in the era of intensity--modulated radiotherapy: a case report

Późna niewydolność wolnego płata strzałkowego spowodowana osteoradionekrozą w erze radioterapii z modulacją intensywności wiązki: opis przypadku

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
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G – Funds Collection

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ABSTRACT:

Introduction: Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity and often requires extensive resection with reconstruction. Fibula free flap (FFF) is the preferred bony reconstructive option in head and neck oncology, as failure rates are the lowest of all free flaps. Late FFF failure in the era of intensity-modulated radiotherapy (IMRT) is rare.

Case report: Fourty-four-year-old male smoker, diagnosed with G2 OSCC. He underwent tumour resection, partial glossectomy, mandibular reconstruction with an osteomyocutaneous FFF and adjuvant IMRT. After 4 years, he experienced total flap failure due to mandibular osteoradionecrosis (ORN), necessitating a salvage pectoralis major myocutaneous (PMMC) flap.

Discussion: Late FFF failure in IMRT is sporadic. This case highlights the synergistic effects of smoking-related vascular compromise and radiotherapy-induced hypoxia and hypocellularity as the pathophysiology behind flap failure. The choice of PMMC for salvage procedure is discussed in the context of its clinical implications, along with the importance of adhering to long-term follow-ups and mitigating risk factors for high-risk patients to improve patient quality of life.

Conclusions: In modern medicine with advanced radiation therapy techniques, every case of FFF failure is a learning opportunity to improve patient care. The importance of long-term surveillance and structured smoking cessation support is crucial to optimise health care outcomes and preserve quality of life for head and neck cancer patients.

KEYWORDS: case report, fibula free flap failure, intensity-modulated radiotherapy, oral squamous cell carcinoma, osteoradionecrosis

STRESZCZENIE:

Wstęp: Rak płaskonabłonkowy jamy ustnej (OSCC) jest najczęstszym nowotworem złośliwym tej okolicy i często wymaga rozległej resekcji z jednoczasową rekonstrukcją. Wolny płat strzałkowy (FFF) jest preferowaną metodą rekonstrukcji kości w onkologii głowy i szyi, ponieważ charakteryzuje się najniższym odsetkiem niepowodzeń spośród wszystkich wolnych płatów. Późna niewydolność FFF w erze radioterapii z modulacją intensywności wiązki (IMRT) występuje rzadko.

Opis przypadku: Czterdziestoczteroletni mężczyzna z rozpoznaniem raka płaskonabłonkowego G2 jamy ustnej został zakwalifikowany do leczenia chirurgicznego. Przeprowadzono resekcję guza, częściową glosektomię, rekonstrukcję żuchwy wolnym płatem strzałkowym kostno-skórno-mięśniowym. Pacjent został poddany uzupełniającej radioterapii IMRT. Po 4 latach obserwacji doszło do całkowitej niewydolności płata z powodu osteoradionekrozy żuchwy, co wymagało wykonania zabiegu ratującego z wykorzystaniem płata piersiowego większego skórno-mięśniowego (PMMC).

Dyskusja: Późna niewydolność FFF w czasach IMRT jest zjawiskiem sporadycznym. Opisywany przypadek podkreśla synergistyczne działanie uszkodzeń naczyniowych związanych z paleniem tytoniu oraz hipoksji i hipokomórkowości indukowanych radioterapią jako podłoże patofizjologiczne niewydolności płata. Omówiono wybór PMMC jako procedury ratującej w kontekście jej implikacji klinicznych, a także znaczenie przestrzegania długoterminowych wizyt kontrolnych i modyfikacji czynników ryzyka u pacjentów wysokiego ryzyka w celu poprawy jakości życia chorych.

Wnioski: Współczesna medycyna, mimo zaawansowanych technik radioterapii, traktuje każdy przypadek niewydolności FFF jako okazję do doskonalenia opieki nad pacjentem. Kluczowe znaczenie ma prowadzenie długoterminowej obserwacji oraz

wdrażanie zorganizowanego wsparcia w zaprzestaniu palenia tytoniu, aby zoptymalizować wyniki leczenia i zachować jakość życia pacjentów z nowotworami głowy i szyi.

SŁOWA KLUCZOWE: niewydolność wolnego płata strzałkowego, opis przypadku, osteoradionekroza, radioterapia z modulacją intensywności (IMRT), rak płaskonabłonkowy jamy ustnej

ABBREVIATIONS

ASCO – American Society of Clinical Oncology
ENT – ear, nose, and throat
FFF – fibula free flap
G2 SCC – moderately differentiated squamous cell carcinoma
IMRT – intensity-modulated radiotherapy
ISOO-MASCC – International Society of Oral Oncology – Multinational Association of Supportive Care in Cancer
MORN – mandibular osteoradionecrosis
ORN – osteoradionecrosis
OSCC – oral squamous cell carcinoma
PMMC – pectoralis major myocutaneous (flap)

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity [1]. Historically, OSCC primarily affected men in their 5th and 6th decades of life, but it is now increasingly seen in younger men, largely due to smoking. Globally, an estimated 7 million people are affected by OSCC in this younger demographic group [2]. More than 50% of head and neck cancer patients continue to smoke after diagnosis, and 27% continue during radiotherapy [3]. The risk of osteoradionecrosis (ORN) has declined due to contemporary radiotherapy techniques like Intensity-Modulated Radiotherapy (IMRT). However, OSCC patients remain at a higher risk of ORN than those with other head and neck cancers [4]. ORN results from radiation-induced damage to bone and vasculature. According to Marx's theory, radiation induces endarteritis, resulting in hypoxia, hypovascularity, and hypocellularity [5]. The fibula free flap (FFF) is the preferred bony reconstructive option for head and neck oncological patients because, in most cases, the FFF does not fail. When failure does occur, it usually occurs in the early postoperative period due to anastomosis complications. Late failure is sporadic [6].

The article describes the case of a middle-aged patient diagnosed with moderately differentiated squamous cell carcinoma of the head and neck. Despite his diagnosis and treatment, the man didn't stop smoking. We illustrate through this patient's treatment course the challenges we encountered and explore therapeutic and prophylactic strategies for managing radiotherapy-induced osteoradionecrosis in head and neck cancer.

CASE REPORT

Initial diagnosis

A 44-year-old patient presented to the Accident and Emergency Department of the University Clinical Centre of the Medical University of Warsaw in 2017 with a tumour in the oral cavity. On history, he reported no chronic conditions. During his hospitalisation in the Department of Otorhinolaryngology, Head and Neck Surgery, biopsies were taken from the tumour on his tongue for histopathological examination. Microscopic examination of the biopsies revealed the presence of stratified squamous epithelium covering the tongue mucosa with slight fibrosis of the soft tissues and skeletal muscles, together with an infiltration of moderately differentiated G2 squamous cell carcinoma (G2 SCC).

Treatment

During the patient's hospitalisation at the Department of Otorhinolaryngology, Head and Neck Surgery at the Medical University of Warsaw, a surgical treatment plan was drawn up, which involved resection of the cancer of the floor of the mouth and tongue, as well as the left mandibular ramus, together with bilateral level I–III lymphadenectomy (Fig. 1). Simultaneous tissue reconstruction was performed using a microvascular free fibular osteocutaneous-muscle flap. The flap was harvested from the non-weight-bearing fibula, 8 cm in length, together with a musculocutaneous island. A titanium plate was used to fix the bone segment to the remaining mandibular fragment. To ensure adequate blood supply to the flap, an arterial anastomosis was performed with the carotid artery and the external carotid artery, and a venous anastomosis with the internal jugular vein. The postoperative period was uneventful. Histopathological examination of the tissues removed during the operation revealed squamous cell carcinoma and a marked desmoplastic reaction along the posterior margin of the incision within the mandible, as isolated clusters of oncogenic changes were beginning to form in the trabeculae. No vascular invasion or metastases to the cervical lymph nodes were found.

Follow-up

After discharge, he received IMRT. During the 4-year oncological follow-up, no recurrence of the malignant tumour was observed.

Complications

In 2021, the patient was readmitted to the clinic with suspected recurrence. The man was referred for surgical treatment. Histopathological examination showed necrosis and inflammation of the fibula bone graft. The soft palate and submental mucosa exhibited acanthotic growth without dysplasia. The dermis exhibited chronic inflammatory infiltrates, fatty tissue hyperplasia, haemorrhages, and hemosiderin deposits. No microscopic evidence of malignancy was observed, consistent with ORN diagnosis criteria. The heavily compromised graft warranted an immediate secondary salvage procedure.

Salvage surgery

The skin on the chin and right cheek was incised, extending above the plate connecting the fibula to the mandible. The exophytic tumours on the chin were excised and sent for intraoperative examination. Intraoperative analysis confirmed no cancerous infiltration in excised tumours or lymph nodes, confirming mandibular osteoradionecrosis (MORN). The fusion plate and the altered bone tissue of the mandible and fibular graft were removed. A wide orocutaneous mouth fistula was noted, and a pectoralis major myocutaneous flap (PMMC) procedure was used for closure. A musculocutaneous island measuring 7 x 5 cm was harvested from the right pectoralis major muscle and pedicled with axial vessels through a tunnel in the anterior neck triangle (Fig. 2.). The skin edges from the free flap were sutured, and the oral fistula was closed. The post-operative period was uneventful, and following completion of his life-saving treatment, the patient was discharged home. He remains under regular outpatient care and continues to smoke. This rare sequence of clinical events laid the foundation to explore interactions between smoking and radiation in flap survival, discussed below.

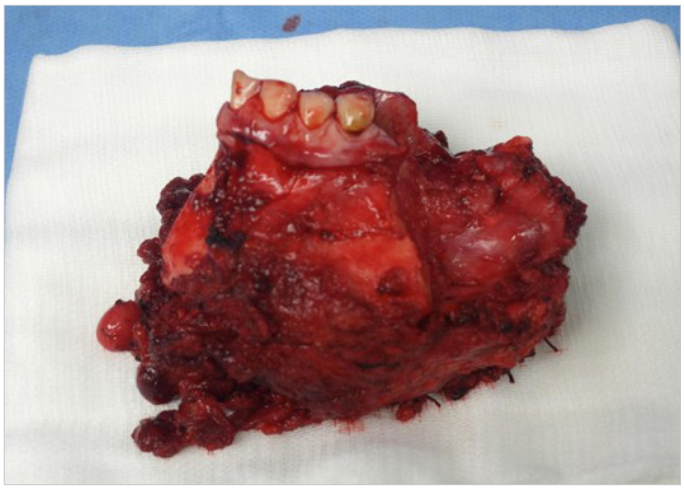


Fig. 1. Resected specimen for intraoperative pathology analysis.



Fig. 2. Intraoperative image showing the harvest of the pectoralis major flap along with its rich vasculature.

DISCUSSION

Rarity of flap failure

The novelty of this case presentation lies in the late-onset total FFF failure due to ORN in the IMRT era and the unique characteristics of the patient, a middle-aged male smoker. The sequelae of events are extremely rare, as contemporary radiotherapy employs IMRT, a technique that enables contouring of radiation beams to target affected tissue precisely. As a result, rates of ORN have declined significantly [7]. The mean onset of MORN is 3.9 years post radiotherapy [8], historically ranging between 2 and 5 years [9]. Long-term studies of MORN report a lower incidence of ORN in patients treated with IMRT but emphasise that younger patients remain at higher risk [8]. Illustrating this, our patient was only 48 years old when his ORN progressed enough to compromise his FFF. Studies have reported near-perfect success rates, in some cases reaching 100% for this microsurgical procedure [10]. Late free flap failure, such as 4 years after successful treatment, is exceptionally uncommon.

Pathophysiology of flap failure

The combined impact of radiotherapy-induced damage and the deleterious effect of tobacco likely explains the pathophysiology behind this rare total FFF failure. Smoking is a risk factor that exacerbates radiation injury and impairs wound healing by compromising blood flow through vasoconstriction and endothelial dysfunction [11]. Interestingly, to date, both large-scale and small-centre studies have not demonstrated increased flap failure rates in smokers compared to non-smokers [12–15]. However, the combination of smoking-related injury and radiotherapy-induced hypoxic and hypocellular damage has been proven to increase osseous flap failure rates [16].

Reconstructive options

Given that the patient had already undergone FFF reconstruction surgery and radiotherapy to the neck, further surgical treatment using a free flap would have carried a high risk of failure. It was decided to use PMMC to close the extensive defect resulting from the resection of necrotic tissue. Historically, PMMC has been a mainstay of facial reconstructive procedures in head and neck cancer patients due to its rich vascular supply and shorter operative time. However, it has drawbacks, including low patient satisfaction. The absence of an osseous structure contributes to an obvious facial deformity and reduced quality of life. It is also associated with higher rates of flap failure [17]. On the other hand, the estimated quality of life plays an important role in the evaluation of the treatment plan. Patients who underwent FFF reported greater satisfaction, mainly due to preserved physiological function and normal facial anatomy, as described consistently in both international and Polish literature [18]. This underscores the need to preserve the longevity of the FFF procedure, as it highlights the benefits for both patients and clinicians striving for the best possible outcome.

Clinical implications

The treatment outcome of our patient might have improved with longer, well-coordinated multidisciplinary follow-up. Patient`s smoking history increased his vulnerability to develop ORN, a factor that should have been considered to safeguard the long--term success of the treatment plan from 2017. Head and neck cancer patients show higher dependence on tobacco. While 76% of these patients report motivation to quit smoking, only 39% of ENT specialists felt adequately trained to counsel them in Poland [3]. Meanwhile, Poland has introduced several successful anti-smoking campaigns, such as the "Great Smoke-Out", which have reduced smoking prevalence [19]. However, studies consistently show that no organised system of smoking cessation support exists for cancer patients in Poland [20, 21].

We stress the importance of long-term follow-up, extending up to 5 years, with 17 patient visits for patients classified as high risk. This includes younger patients, those with a history of smoking, and those who consume alcohol, in line with new follow-up regulations published by the Polish ENT Society Board and Head and Neck Experts [22]. International guidelines from International Society of Oral Oncology – Multinational Association of Supportive Care in Cancer (ISOO-MASC) and American Society of Clinical Oncology (ASCO) recommend optimising modifiable risk factors to reduce the ORN risk. They emphasise patient education, including smoking cessation campaigns, counselling, and reinforcement of the importance of follow-ups to improve health outcomes [23].

CONCLUSIONS

With many Polish oncological centres having adopted IMRT [23], and ORN rates at historic lows, each case of flap failure offers critical insight, highlighting areas that still require close attention and improvement. At the time the patient's treatment resumed in 2021, there were no "gold standards" for the treatment of ORN. The subsequent development of these guidelines and expansion of research in head and neck oncology underscore the significance of this case. Patients like ours existed before the IMRT era and represent a growing cohort, underrepresented in the literature even today. Their ongoing presence demands adaptation from hospitals, clinicians, and policymakers to optimise resource allocation and improve quality of life for patients in Poland.

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