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CASE REPORT

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Tongue Carcinoma in Immunosuppressed Patients After Liver and Kidney Transplantation: A Case Series

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Background: Solid organ transplant recipients carry an elevated risk of de novo malignancies under chronic immunosuppression, including aggressive squamous cell carcinoma (SCC) of the oral cavity and oropharynx. Practical, evidence-based guidance for maxillofacial management in this population remains limited.

Case Reports: Case 1 involved a 44-year-old man who developed T1N0 SCC of the lateral tongue 23 months after orthotopic liver transplantation for alcoholic cirrhosis. He was treated with partial glossectomy and selective neck dissection, followed by re-excision for a positive deep margin; he remains disease-free at 2 years, with mild residual tongue hypomobility. Case 2 involved a 59-year-old man who developed T2N1M0 SCC of the tongue 8 months after kidney transplantation. He underwent extended hemiglossectomy with neck dissection, anterolateral thigh free flap reconstruction, and adjuvant chemoradiotherapy; suspected locoregional recurrence required limited resection, and he remains disease-free at 5 years. Case 3 involved a 62-year-old woman who developed T1N0M0 SCC of the floor of the mouth 12 years after liver transplantation. She was treated via local excision followed by block neck dissection without adjuvant therapy and remains disease-free at 1 year, with preserved function.

Conclusions: Oral SCC in transplant recipients can arise early or late after transplantation and requires meticulous surgical clearance, judicious use of adjuvant therapy, and vigilant surveillance. Close multidisciplinary coordination with transplant teams to optimize and, when feasible, de-escalate immunosuppression is essential, along with routine oral cancer screening and risk factor modification. Larger multicenter studies are needed to refine screening intervals and peri-oncologic immunosuppressive strategies.

Keywords: Carcinoma, Squamous Cell • Case Reports • Immunosuppression Therapy • Organ Transplantation

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Introduction

De novo malignancies represent a serious complication of solid organ transplantation, particularly liver and kidney transplantation. Transplant recipients face an increased risk of developing new cancers due to chronic immunosuppressive therapy, which weakens immune surveillance and reduces the body's ability to eliminate precancerous and cancerous cells [1,2]. This risk is further compounded by pre-existing factors such as alcohol consumption, smoking, and chronic infections with oncogenic viruses, including human papillomavirus and Epstein-Barr virus. Among de novo malignancies, oropharyngeal squamous cell carcinoma (SCC) is of particular concern due to its aggressive nature, rapid progression, and high mortality rate. A retrospective study of esophageal SCC in 313 patients suggested that immunosuppression associated with liver transplantation can enhance the oncogenic effects of pre-transplant alcohol and tobacco use [3]. Similar acceleration of neoplastic progression has been described for Barrett's esophagus in liver transplant recipients [4].

Liver transplant recipients exhibit an incidence of de novo malignancies ranging from 6% to 18%, with SCC representing a major concern [5,6]. Alcohol-induced cirrhosis is a substantial risk factor for SCC, increasing the likelihood of cancer development by up to 8-fold relative to the general population [7,8]. Moreover, human-papillomavirus-related SCC has emerged as a distinct entity in this population due to the immunosuppressive milieu and pre-existing mucosal damage caused by alcohol and tobacco use [9].

The incidence of de novo malignancies after kidney transplantation ranges from 10% to 24%, exceeding the proportion observed in liver transplant recipients [10]. The risk of de novo malignancies after kidney transplantation is also well documented [11]. In kidney transplant recipients, the most frequent tumors are B-cell lymphoproliferative disorders, which often arise within the first year after transplantation; cancers of the skin, lips, and perineum increase in incidence over time [12]. Among these malignancies, oropharyngeal SCC is prevalent due to the combined effects of chronic immunosuppression, viral infections, and tobacco use [13]. Calcineurin inhibitors, a cornerstone of kidney transplant immunosuppressive regimens, have been implicated in accelerating carcinogenesis by promoting angiogenesis and inhibiting DNA repair [14,15].

De novo SCC lesions in transplant recipients are often aggressive, and rapid progression is attributed to immunosuppressive therapy [16]. Such therapy reduces immune-mediated tumor surveillance and enhances the oncogenic potential of pre-transplant carcinogenic exposures [17,18]. Studies have demonstrated the need for early and regular screening to detect lesions at an early stage [19,20].

Although de novo oral SCC after solid organ transplantation is relatively uncommon, several case reports and small series have described tongue or oral cavity carcinomas in kidney transplant recipients with long-term immunosuppression. Malleshappa et al reported a 30-year-old renal transplant recipient who developed lateral tongue SCC 9 years after transplantation in the context of calcineurin-inhibitor-based therapy, without other major risk factors beyond immunosuppression [21]. Nascimento et al also described tongue SCC arising 15 years after living-donor kidney transplantation in a 57-year-old man receiving a chronic triple-drug regimen [22,23]. In a larger single-center cohort, Narayan et al identified 5 renal transplant recipients who developed carcinoma of the tongue after more than 10 years of latency; these patients were younger at cancer diagnosis and had better survival than kidney recipients who developed non-oral de novo malignancies, suggesting a relatively favorable prognosis when oral lesions are recognized early [23]. Collectively, these observations support recognition of the oral cavity – particularly the tongue – as a target site for de novo SCC in chronically immunosuppressed transplant recipients and provide important clinical context for the present case series. Despite the existing literature, detailed descriptions of tongue SCC arising in liver and kidney transplant recipients, along with practical maxillofacial surgical considerations, remain limited.

This report describes SCC arising in the tongue in 3 patients after liver and kidney transplantation; it discusses implications for surveillance, diagnosis, surgical management, and modification of immunosuppressive therapy in this high-risk population.

Case Reports

This case series was derived from a retrospective review of patients with head and neck malignancies who underwent surgical treatment at the Department of Maxillofacial Surgery in Banská Bystrica, Slovakia, between January 2019 and January 2025. A key strength of our institution is its collaboration with the Transplant Center for liver and kidney transplantation in Slovakia, located in Banská Bystrica. During this 6-year period, 335 patients underwent oncologic resection with microvascular free flap reconstruction. Among these patients, 3 had a history of solid organ transplantation (2 liver and 1 kidney transplant) and developed de novo SCC of the tongue or floor of the mouth.

All procedures involving human participants were conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Because this study comprised a retrospective analysis of existing patient data, it was considered exempt from formal ethical review. The reported clinical and research activities were

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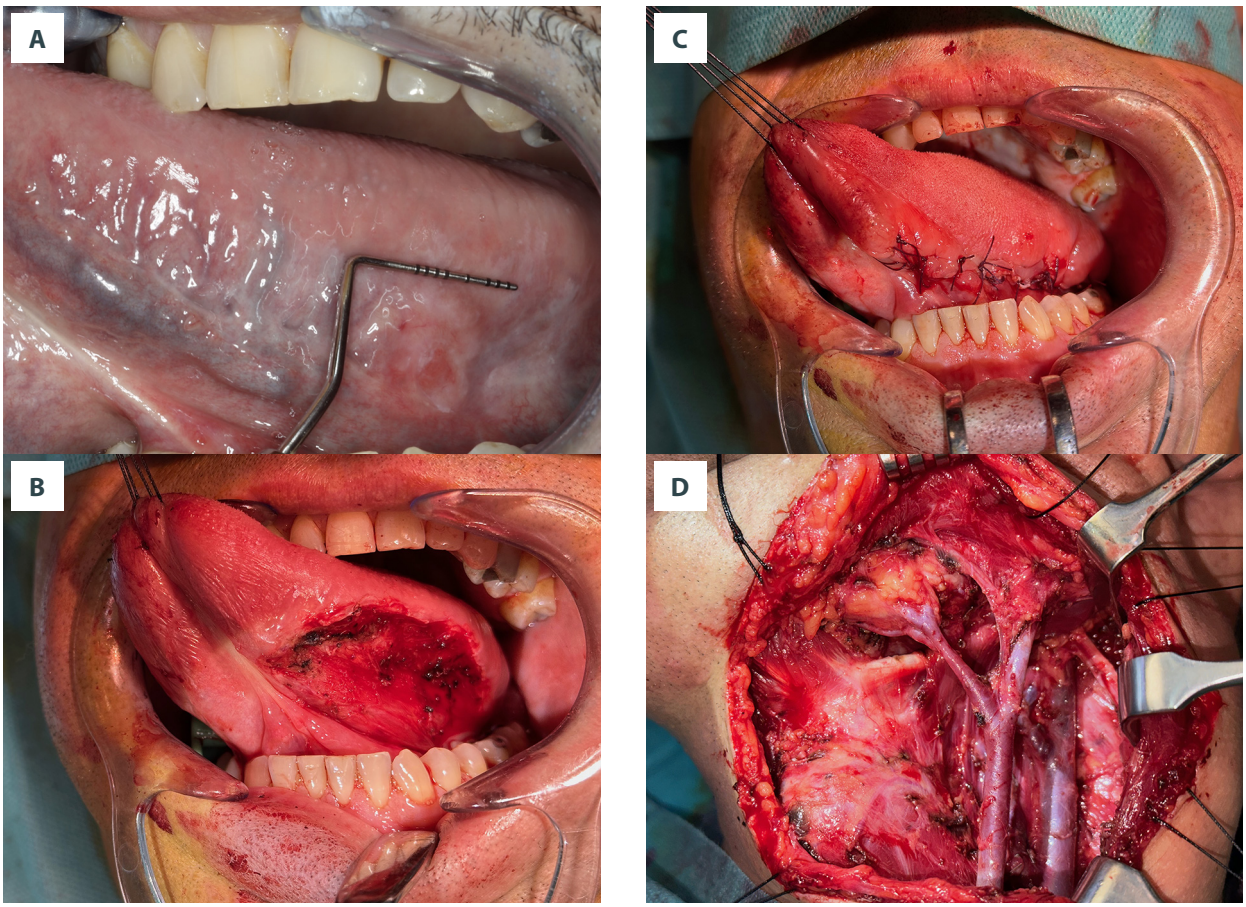
consistent with the Principles of the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

Case 1

A 44-year-old man developed T1N0 SCC of the lateral tongue 23 months after orthotopic liver transplantation for alcoholic cirrhosis. The patient had a history of alcoholic hepatitis in the context of liver cirrhosis and acute decompensation; he had undergone orthotopic liver transplantation in 2021. Risk factors included chronic alcohol abuse and long-term tobacco use. Since transplantation, the patient has maintained complete alcohol abstinence and reports being a former smoker. The initial immunosuppressive regimen included 500 mg of intravenous methylprednisolone administered during the anhepatic phase of surgery, followed by mycophenolate mofetil 500 mg twice daily beginning on postoperative day 1. Tacrolimus was administered at a titrated dose of 0.1 mg/kg/day, with target trough levels of up to 10 µg/L during the immediate post-transplant period. Corticosteroid therapy continued postoperatively with 20 mg intravenous methylprednisolone, which was later transitioned to oral dosing and gradually tapered. After orthotopic liver transplantation, the patient experienced an episode of acute cellular rejection requiring high-dose corticosteroid pulse therapy, which consisted of 1000 mg intravenous methylprednisolone administered every other day for a total dose of 3 g. Over time, the immunosuppressive regimen was adjusted. Despite fluctuating transaminase levels, which responded well to increased corticosteroid dosing, the patient declined to resume regular mycophenolate mofetil therapy. He is currently maintained on tacrolimus 6 mg once daily, with a trough level of 5.10 µg/L.

Twenty-three months post-transplantation, the patient was referred to the Department of Maxillofacial Surgery after excision of a lesion on the left lateral border of the tongue at a private dental clinic (**Figure 1A**). The referral was prompted by histopathological confirmation of invasive SCC with positive deep resection margins and a recommendation for further radical surgical intervention. In our department, the patient underwent radical resection of a clinically staged T1N0 SCC of the left lateral tongue, along with selective neck dissection (levels IA-III) on the left side (**Figure 1B-1D**). Intraoperative frozen section analysis confirmed negative margins, and the defect was closed primarily. However, definitive histopathology based on paraffin-embedded sections revealed residual carcinoma at the deep margin (**Figure 1E-1G**). A multidisciplinary tumor board recommended re-excision, which achieved clear



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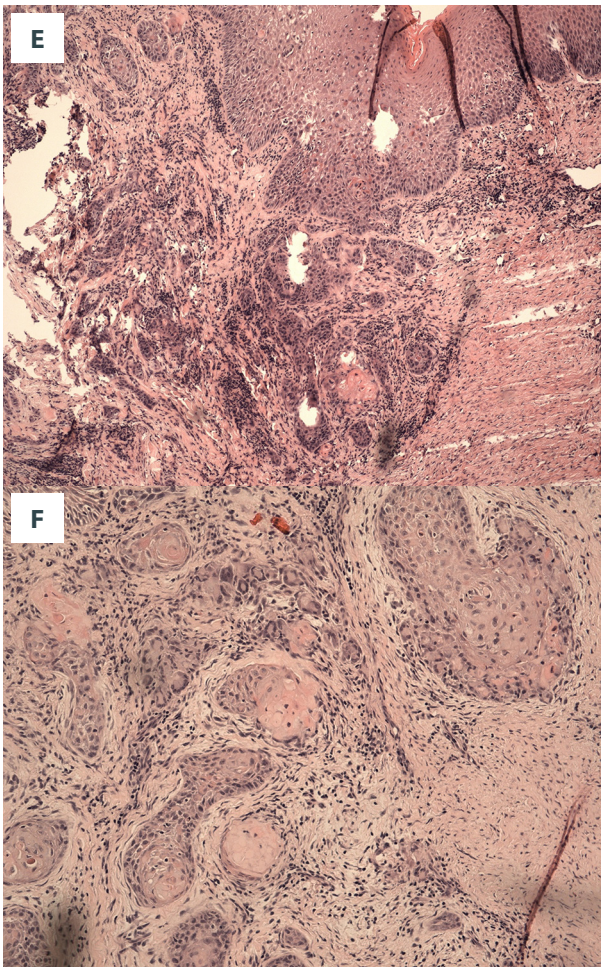

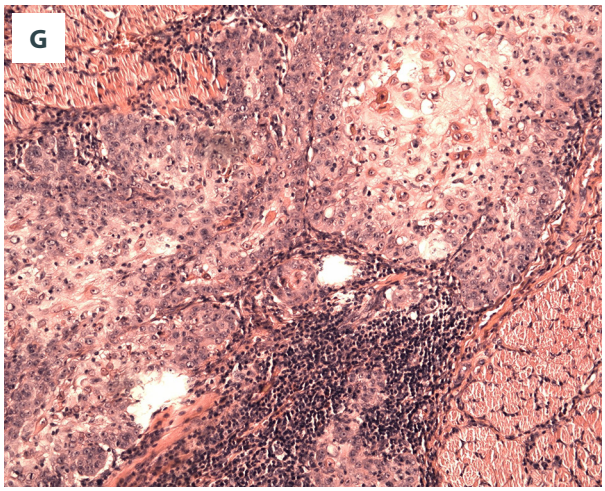

Figure 1. Case 1: Tongue squamous cell carcinoma after liver transplantation. (**A**) Non-homogeneous lesion with underlying invasive SCC on the left lateral border and ventral surface of the tongue. (**B**) Surgical defect after partial glossectomy. (**C**) Primary closure of the tongue defect. (**D**) Left selective neck dissection (levels IA-III). (**E**) Low-power hematoxylin-and-eosin-stained section showing dysplastic squamous epithelium with irregular proliferation and invasion of tumor nests into the lamina propria and underlying stroma, accompanied by a dense chronic inflammatory infiltrate (original magnification ×100). (**F**) Medium-power view demonstrating infiltrating nests of atypical squamous cells with abundant eosinophilic cytoplasm and keratin pearl formation in a desmoplastic stroma, consistent with well- to moderately differentiated SCC (original magnification ×200). (**G**) Medium-power view highlighting pronounced nuclear pleomorphism, prominent nucleoli, frequent mitotic figures, and keratinized tumor nests (original magnification ×200). SCC – squamous cell carcinoma.

surgical margins (R0 status). The patient was subsequently referred for oncologic follow-up. No adjuvant therapy was indicated. Two years after the final surgery, the patient reports reduced tongue mobility; however, articulation remains good and speech is intelligible. There is currently no evidence of locoregional recurrence.

Case 2

A 59-year-old man developed T2N1M0 SCC of the left lateral tongue 8 months after kidney transplantation. The patient had undergone left nephrectomy in 1999 for a Grawitz tumor (renal cell carcinoma). Following surgery, he required management of chronic tubulointerstitial nephritis in his solitary right kidney. In March 2019, he received a right kidney transplant. Prior to transplantation, he underwent induction immunosuppressive therapy with anti-thymocyte globulin at 1.5 mg/kg (body weight, 95 kg), along with 500 mg of methylprednisolone. In the early post-transplant period, he was treated with tacrolimus (0.1 mg/kg/day; target trough level ≤10 µg/L), mycophenolate sodium 360 mg twice daily (later increased to 720 mg twice daily), and prednisone 20 mg orally once daily.

As part of standard post-transplant monitoring, the patient underwent regular screening assessments, including urological and dermatological evaluations (with emphasis on cutaneous nevi), dental examinations, abdominal ultrasound every 6 months, colonoscopy after the age of 50 [24], and bone densitometry.

Eight months post-transplantation, the patient was referred by an otorhinolaryngologist to the maxillofacial surgery clinic for evaluation of a lesion on the left side of the tongue. Biopsy confirmed SCC, clinically staged as T2N1M0 (**Figure 2A-2C**). He was a chronic smoker, a recognized risk factor for SCC of the oral cavity.

The patient underwent radical surgical treatment, including neck dissection (levels I-V) and extended hemiglossectomy. Reconstruction was performed using an anterolateral thigh free flap (**Figure 2D**). Adjuvant oncologic therapy was administered postoperatively, consisting of external beam radiotherapy to

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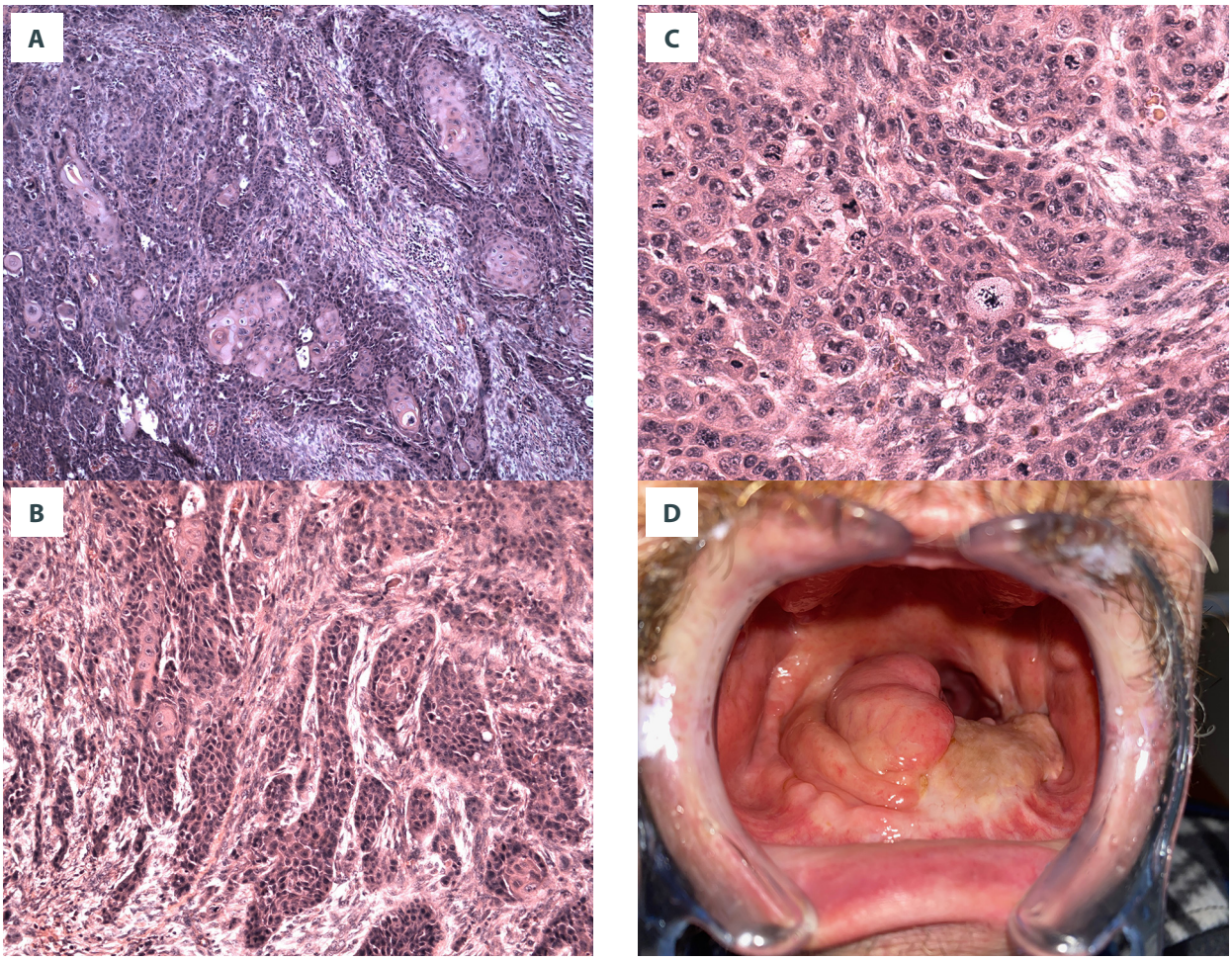

Figure 2. Case 2: Surgical reconstruction after extended hemiglossectomy. (**A**) Low-power hematoxylin-and-eosin-stained section demonstrating irregular nests of moderately differentiated SCC infiltrating the fibrous stroma, with multiple keratin pearls and a peritumoral lymphocytic infiltrate (original magnification ×100). (**B**) Medium-power view showing islands of atypical squamous cells with eosinophilic cytoplasm and keratinization within a desmoplastic stroma (original magnification ×200). (**C**) High-power view of the invasive front demonstrating pronounced nuclear atypia, an increased nuclear-to-cytoplasmic ratio, atypical mitotic figures, and focal keratin pearl formation (original magnification ×400). (**D**) Intraoral view showing an anterolateral thigh free flap reconstruction of the left lateral tongue and floor of the mouth after extended hemiglossectomy and neck dissection. SCC – squamous cell carcinoma.

a total dose of 66 Gy combined with 2 cycles of chemotherapy (carboplatin and 5-fluorouracil).

In September 2020, during routine clinical examination, a suspicious ulceration was noted in the left retromolar region. Multiple biopsies were obtained; histological SCC was confirmed, indicating locoregional recurrence. A positron emission tomography-computed tomography scan showed no evidence of distant metastasis. Based on these findings, surgical intervention was planned with anticipated reconstruction using a free fibular flap. Intraoperatively, however, all perioperative biopsy samples did not exhibit malignancy. Consequently, a less extensive resection was performed, and flap reconstruction was not required.

After oncologic surgery, mycophenolate sodium was permanently discontinued from the immunosuppressive regimen. The current regimen consists of tacrolimus 1 mg/day (trough level, 4.4 µg/L) and prednisone 10 mg orally once daily. The patient continues to be followed regularly. At the most recent follow-up 5 years after surgery, he showed no clinical or radiological evidence of locoregional recurrence.

Case 3

A 62-year-old woman developed T1N0M0 SCC of the left floor of the mouth 12 years after liver transplantation. She had undergone orthotopic liver transplantation in 2011 for liver cirrhosis secondary to alcoholic liver disease. Her medical history included alcohol abuse until the development of

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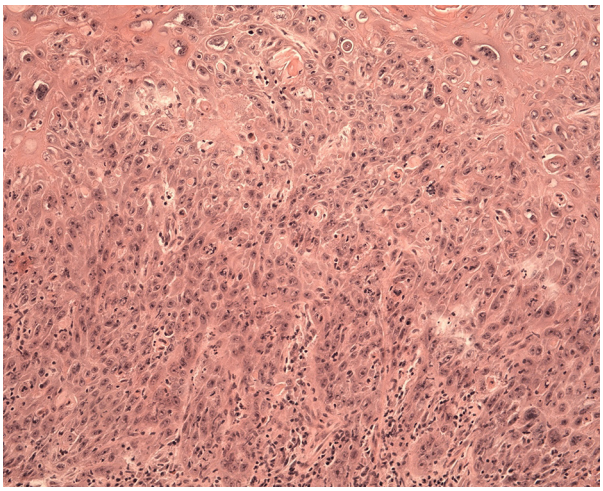

Figure 3. Case 3: Squamous cell carcinoma of the floor of the mouth after liver transplantation. Hematoxylin-and-eosin-stained section showing infiltrative proliferation of atypical squamous cells extending into the submucosal connective tissue. Tumor cells display pleomorphic, hyperchromatic nuclei, prominent nucleoli, and focal keratinization (original magnification ×200).

decompensated cirrhosis, as well as prior tobacco use. Since autumn 2010, the patient has remained abstinent from alcohol and has not smoked.

The transplantation was complicated by delayed graft function and bleeding, which required surgical intervention. During the anhepatic phase of transplantation, she received 500 mg of methylprednisolone. Post-transplant immunosuppressive therapy was initiated on postoperative day 1 with mycophenolate mofetil 500 mg twice daily, tacrolimus dosed at 0.1 mg/kg/day (target trough level up to 10 µg/L in the early post-transplant period), and corticosteroids beginning with 20 mg intravenous methylprednisolone, followed by a gradual transition to oral administration with tapering doses.

At the time of SCC diagnosis in June 2023, the patient's immunosuppressive regimen consisted solely of tacrolimus 3 mg once daily, with a trough level of 3.2 µg/L.

In June 2023, the patient was referred by her attending dentist to the maxillofacial surgery clinic for evaluation of an exophytic tumor on the left floor of the oral cavity. She had first noticed a small mass beneath her tongue approximately 9 months earlier and reported weight loss of 4 kg during the preceding 6 months. Clinical evaluation was followed by complete tumor resection under local anesthesia. Histopathological analysis and staging investigations confirmed SCC of the left floor of the oral cavity, staged as T1N0M0 (**Figure 3**).

Although clear margins were initially achieved, further radical surgery was performed, consisting of resection of the left floor of the oral cavity and block neck dissection (levels I-III). This approach was implemented to ensure adequate oncologic clearance because the initial procedure was a local excision, rather than a formal oncologic resection; moreover, floor-of-mouth SCC carries a risk of occult cervical metastasis. Postoperative histology showed no residual malignancy. After multidisciplinary tumor board review, adjuvant therapy was considered unnecessary. Postoperatively, the patient maintained good functional outcomes without difficulty eating or speaking. At the 1-year follow-up, there was no evidence of locoregional recurrence.

The patient underwent standard post-transplant screening, which for women includes gynecological examinations, mammography, dermatological evaluation with emphasis on cutaneous nevi, dental examinations, abdominal ultrasound every 6 months, and colonoscopy after age 50. Additional investigations are performed as indicated and were not required in this case, including imaging such as 4-phase computed tomography of the liver; colonoscopy based on gastroenterological indication or in cases of inflammatory bowel disease; and magnetic resonance cholangiopancreatography for patients with transplantation due to primary sclerosing cholangitis.

Discussion

These 3 cases highlight multiple practical considerations for the maxillofacial management of oral SCC in solid organ transplant recipients. First, SCC may develop early after transplantation, as in the kidney transplant recipient, or many years later, as in the liver transplant recipients, underscoring the need for lifelong oral surveillance. Second, tongue and floor-of-mouth SCC in this population can behave aggressively and may require re-excision or salvage procedures to achieve durable oncologic control. Third, successful management depends on coordinated multidisciplinary care involving maxillofacial surgeons, oncologists, and transplant physicians to balance oncologic clearance, functional reconstruction, and individualized adjustment of immunosuppression.

De novo SCC after solid organ transplantation, particularly liver and kidney transplantation, represents a key clinical challenge. The incidence of de novo malignancies among transplant recipients is substantially higher than in the general population, ranging from 6% to 24% [5,10]. Among these malignancies, SCC of the oral cavity and oropharynx is particularly concerning due to its aggressive behavior and high mortality. In liver transplant recipients, the incidence of de novo malignancies has been reported to range from 6% to 18%; alcohol-induced cirrhosis represents a major risk factor for SCC.

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The first case illustrates the challenges of achieving negative surgical margins in oral cavity SCC. Despite radical resection and neck dissection, positive margins persisted, requiring additional surgical intervention. This persistence underscores the importance of intraoperative histopathological assessment to ensure complete tumor removal. The patient achieved favorable oncologic and functional outcomes, although mild tongue mobility impairment was observed. These findings are consistent with existing literature that emphasizes the importance of precise surgical technique and rigorous postoperative follow-up to reduce recurrence risk [6,7].

The second case involved a kidney transplant recipient who developed SCC of the tongue and experienced recurrence despite initial extended hemiglossectomy with free flap reconstruction. Locoregional recurrence required salvage surgery, highlighting the aggressive nature of SCC in immunosuppressed patients. Early detection of recurrence, facilitated by advanced imaging modalities such as positron emission tomography-computed tomography, is critical for timely intervention [13]. This case further underscores the importance of individualized surgical planning in managing recurrent SCC while minimizing morbidity.

The third case emphasizes the challenges of delayed-onset SCC occurring more than a decade after liver transplantation. Early surgical intervention achieved negative margins and obviated the need for adjuvant therapy, resulting in excellent oncologic and functional outcomes. This case highlights the importance of patient education and routine post-transplant screening in facilitating early diagnosis and treatment. It also underscores the value of multidisciplinary tumor boards in guiding optimal, individualized treatment decisions. According to the Delphi consensus statement published in 2021, the development of SCC in post-transplant patients warrants discussion with the transplant team regarding oral chemoprevention and modification of immunosuppression [25].

Compared with previously published case reports, the presentation and clinical course of our 3 cases are broadly consistent but also demonstrate important differences in timing, tumor site, and management. Most reported cases of post-transplant tongue SCC involve middle-aged men who present with painful ulcerative or exophytic lesions after a prolonged post-transplant latency of 7 to 23 years [22,23]. In contrast, our series includes both an early-onset tumor (T2N1 tongue SCC 8 months after kidney transplantation) and intermediate-latency lesions (T1N0 tongue SCC at 23 months and T1N0 floor-of-mouth SCC 12 years after liver transplantation), all arising under calcineurin-inhibitor-based immunosuppression and in the context of substantial pre-transplant exposure to alcohol and/or tobacco.

Whereas earlier reports have focused on lesions of the dorsal or lateral tongue and the lower lip [23], our series also documents de novo SCC of the floor of the mouth detected via routine dental surveillance, underscoring the need for thorough examination of all oral subsites during post-transplant follow-up. Diagnostic pathways were similar to those described by Nascimento et al, in which oral medicine or dental teams played a central role in identifying suspicious lesions and initiating biopsy [22]. Management strategies in published kidney transplant cases have typically involved partial or hemiglossectomy with or without neck dissection, reserving adjuvant radiotherapy for more advanced disease or adverse pathological features; generally favorable local control has been achieved [23]. Our approach is comparable: radical resection with selective or comprehensive neck dissection and microvascular reconstruction – supplemented by adjuvant chemoradiotherapy only in the T2N1 case – led to durable disease control in all 3 patients, who remain disease-free at 1 to 5 years with acceptable functional outcomes.

Finally, immunosuppression management should be explicitly addressed in treatment planning. In our series, immunosuppression was modified after oncologic surgery in the kidney transplant recipient (discontinuation of mycophenolate), and ongoing coordination with transplant physicians was essential to maintain graft function while treating cancer. Prior literature supports multidisciplinary management and – when appropriate – adjustment of immunosuppression after de novo carcinoma in transplant recipients, including the use of mechanistic target of rapamycin (mTOR) inhibitors, which provide immunosuppression and exhibit anticarcinogenic properties by inhibiting angiogenesis and tumor proliferation [7].

Conclusions

Oral SCC in solid organ transplant recipients can arise early or late after transplantation and requires meticulous surgical clearance, selective use of adjuvant therapy, and lifelong surveillance. Close coordination with transplant teams to optimize and (when feasible) reduce immunosuppression, along with routine oral cancer screening and risk factor modification, may reduce morbidity in this high-risk population. Larger multicenter studies are needed to refine surveillance intervals and immunosuppressive strategies.

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Department and Institution Where Work Was Done

F.D. Roosevelt General Hospital of Banská Bystrica, Slovakia.

Ethics Declaration

This study was conducted in accordance with the ethical standards of the relevant committee responsible for clinical trials and the 1964 Declaration of Helsinki, revised in 2000.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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