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Initial experience with ovine forestomach matrix graft for glossectomy defect reconstruction: A case series

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ABSTRACT

Soft tissue reconstruction of oral cavity defects, such as glossectomy defects secondary to malignancy, pose a challenge for head and neck, oral, and maxillofacial surgeons. Reconstruction options for mucosal defects include primary closure, healing by secondary intention, full mucosal and split-thickness skin grafts, pedicled flaps, and microvascular free flaps. Biological grafts have become an integral part of the modern reconstructive ladder and are widely used for the regeneration of various soft tissue defects, including oral defects. This case series describes our initial experience using ovine forestomach matrix grafts in tongue and oral cavity reconstruction. Oral reconstruction using ovine forestomach matrix grafts was undertaken on three patients post wide excision and resulted in good functional and cosmetic outcomes. The rate of tissue formation provided by the graft and the grafts' relative resistance to the hostile environment of the oral cavity support further clinical research to validate the use of these devices in oral reconstruction.

1. Introduction

Malignancies of the oral cavity affecting the tongue can be a challenge to manage given the unique anatomy and functions of the tongue and mucosal surfaces. Resections of the oral cavity, such as the floor of the mouth (FOM), may also be complicated by osseous involvement such as osteoradionecrosis and osteomyelitis [1]. Adhesions, loss of re-establishing muscle bulk to the tongue, surgical site infection, scarring, and poor functional outcomes have been associated with primary closure, healing by secondary intention, and skin grafts [2]. Further, limited tissue mobility may preclude reconstruction via primary closure, mucosal and split-thickness skin grafts, pedicle flaps, and advanced microsurgical free flaps. While autologous grafts and flaps have higher rates of success and better functional and cosmetic outcomes, these are inherently more difficult procedures and have notable disadvantages associated with donor site morbidity and higher overall healthcare costs.

The use of biological grafts (e.g. acellular dermal matrices (ADM) and decellularized extracellular matrix (dECM)) as an alternative to free tissue transfer procedures has been previously reported for non-mobile areas of the oral cavity [1,3,4]. Biological graft-based reconstruction negates risks associated with donor site morbidity, and unlike a split-thickness skin graft, a biological graft regenerates a mucosal epithelium rather than a keratinized epithelium [5]. Within oral cavity reconstruction, biological grafts are now more widely utilized and have been reported to lead to reduced scarring and reduced cost of care compared to free tissue transfer approaches [6].

While many biological grafts are commercially available, the products differ by the tissue raw material and the manufacturing process used to convert the tissue to an acellular matrix. One challenge for these technologies in the oral cavity is the relatively hostile environment created by bacteria, salivary enzymes (e.g. amylases, proteases, lipases), and tissue movement [7]. Ovine forestomach matrix (OFM) grafts have been developed for surgical applications in complex soft tissue reconstruction and have been shown to be

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particularly robust in the presence of contamination or local tissue inflammation [8,9]. Studies have shown that the acellular matrix retains many known ECM-associated proteins, including growth factors and cytokines, that are known to perform critical functions during tissue regeneration [10–12]. This current report presents our initial clinical observations using OFM grafts as an alternative to free tissue transfer based reconstruction of partial glossectomy and oral cavity defects and has been reported in line with the SCARE Criteria [13].

2. Case 1

A 75-Year-old male with no significant medical history presented with early-stage squamous cell carcinoma involving the left lateral tongue which required partial glossectomy (Fig. 1). Using the TNM staging system, the tumor was designated as T2. Following a left-side selective neck dissection, tumor resection was performed following standard practice with dissection and ligation of the lingual artery to control hemorrhage and ensure adequate visibility. Excision of the surgical mucosal margins were negative (Fig. 1A). Micronized OFM (Myriad Morcells™, Aroa Biosurgery Limited, New Zealand; 500 mg) was placed into the ~7 cm × 4.5 cm defect to contact the underlying muscular wound bed of the intrinsic muscles of the tongue surface. Then, OFM graft (Myriad Matrix™, Aroa Biosurgery Limited, New Zealand; 5-layer), was trimmed to size, hydrated with normal saline solution and secured with resorbable sutures in both an interrupted and running continuous fashion (Fig. 1B). The tongue was dressed with a contact layer (Adaptic™) to protect the OFM graft and a petroleum-based dressing (Xeroform™, Cardinal Health, Dublin, OH) to bolster the graft to the defect and to protect against movement. Margins were confirmed to be negative. Post-operatively, the patient had a Dobhoff nasogastric tube placed for the first 2 weeks and had a hospital length of stay of 3 nights. The healing defect was left undisturbed, then at 3 weeks, the bolster dressing was removed. At post-operative week 3, the graft was completely integrated, and the mucosal surface had re-epithelized over the graft (Fig. 1C). Additionally, a significant reduction in the depth of the glossectomy defect was noted. After an additional ~3–4 weeks, the patient underwent adjuvant chemoradiotherapy (>55 Gy). At week 13 follow-up, examination revealed good cosmesis of the tongue with complete resurfacing of the mucosal epithelium giving the tongue a smooth contour (Fig. 1D). No scarring was noted, and the patient had good range of tongue motion and minimal speech dysfunction, no dysphagia, and tolerated a regular diet. The patient continued to have good cosmesis and function of the tongue at 12-month follow-up (not shown). No surgical site infections or post-operative complications were noted.

3. Case 2

A 76-Year-old female with no significant medical history presented with early-stage squamous cell carcinoma involving the right lateral tongue, TNM Stage T2, requiring a partial glossectomy (Fig. 2). The lingual artery was ligated, and the tumor was resected

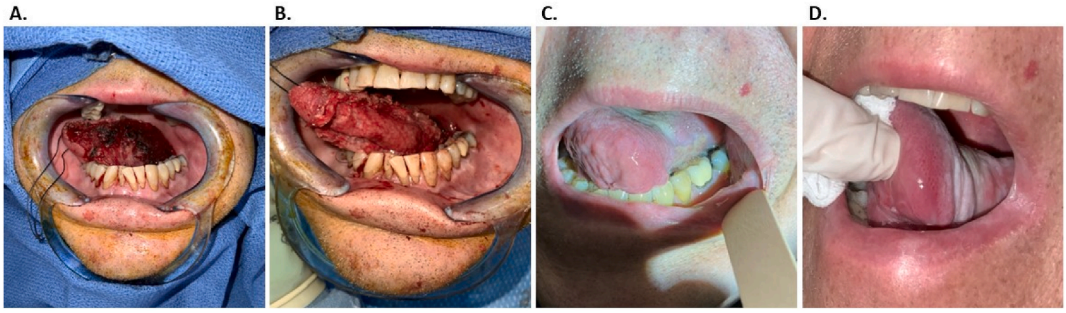

Fig. 1. Case 1, partial glossectomy. **A.** Left lateral tongue post SCC excision. **B.** OFM graft placement. **C.** Post operative week 3, following removal of the bolster dressing. **D.** Post operative week 13.

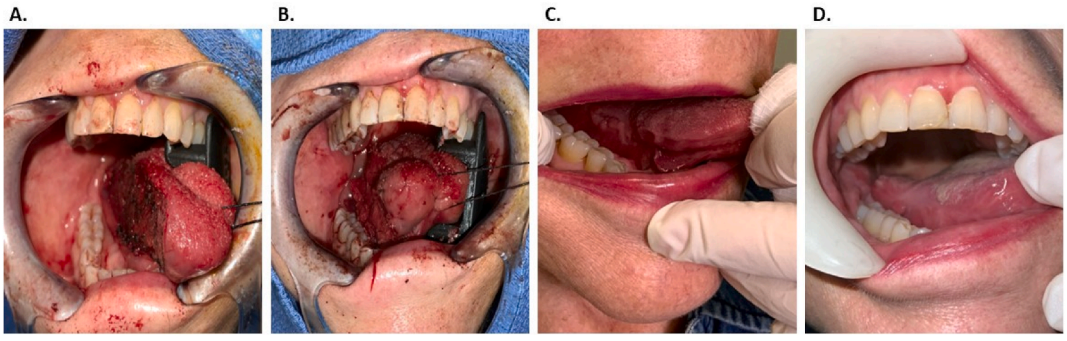

Fig. 2. Case 2, partial glossectomy, right lateral tongue. **A.** Post SCC excision. **B.** Application of OFM graft. **C.** Post-operative week 10. **D.** Long term follow-up at 7 months.

(Fig. 2A). OFM grafts (micronized OFM (500 mg), and 5-layer OFM graft) were placed into the resulting defect (~6 cm × 2 cm) (Fig. 2B) and dressed, as described above. Post-operative care proceeded as described above, with the bolster dressing remaining undisturbed until post-operative week 3 (Fig. 2C). Similarly, a Dobhoff nasogastric tube was placed for 2 weeks, and the patient stayed three nights in the hospital. Of note, all margins were confirmed to be negative. The patient did not require post-operative adjuvant therapy at any time. At post-operative week 10, the tongue defect was resurfaced with mucosal epithelium, depth had been restored, and the patient's speech was minimally affected (Fig. 2D). After one year (not shown), the patient maintained a good cosmetic and functional outcome of the tongue with no appreciable scarring or impairment, and no post-operative complications were noted.

4. Case 3

A 65-Year-old female with no significant medical history presented with high-grade dysplasia of the anterior FOM and ventral tongue (Fig. 3), designated T2 using the TNM staging system. The patient required extensive resection wide local excision of the affected portion of the FOM and ventral tongue (Fig. 3A), and ligation of the lingual artery. Following resection of the affected tissue, the margins were confirmed to be negative and the defect (~4 cm × 3 cm) was reconstructed with OFM grafts (micronized OFM (500 mg), and 5-layer OFM graft) (Fig. 3B) and dressed with a contact layer, as previously described. However, in this instance, due to the location of the defect, a bolster dressing was not employed. A Dobhoff nasogastric tube was placed for 2 weeks. The patient was discharged on the day of surgery and was placed on a clear liquid diet for 2 weeks. The contact layer was removed at 3 weeks and the OFM graft was fully integrated at both the ventral tongue and FOM, with evidence of epithelial mucosa across both areas (Fig. 3C). At one month, the patient had good muscle function and minimal to no speech dysfunction (not shown). There were no post-operative complications observed.

5. Discussion

Surgical reconstruction of the oral cavity and tongue offers the best functional and cosmetic outcomes for earlier-stage oral malignancies, although the optimal method for reconstruction is still debated [14]. The use of biological grafts in oral cavity reconstructions is an emerging surgical option. For example, one study reported five cases of glossectomy reconstructions performed with a collagen scaffold following partial glossectomy, and the results after 6 weeks were deemed satisfactory in terms of restoration of function and healing [7]. A study by Terai et al. reported 13 patients who underwent tongue reconstruction with an artificial bilayer membrane and reported uneventful healing and improved speech function compared to the control group [15]. Interestingly, one study utilizing a biological graft comprised of urinary bladder matrix (UBM) for reconstruction of oral cavity defects reported acceptable outcomes (64 % success rate) but also reported notable graft-related complications such as detachment of the graft, hematoma, and surgical site infection [1].

In this case series, we report our initial outcomes following tongue reconstruction using an OFM-based graft. Contracture and fibrosis of the tongue is a potential concern following glossectomy and reconstruction using any surgical technique. In these three cases, OFM was able to scaffold the regeneration of glossal tissue including mucosa, with minimal fibrosis and contracture observed at post-operative follow-up (Fig. 1D, 2D and 3C). Along with good cosmetic and functional outcomes, OFM also demonstrated advantageous handling characteristics such as durability, pliability, and conformability to reconstruct the uniquely dynamic structure of the tongue and anatomy of the oral cavity. Prior studies have demonstrated that components of OFM are inhibitory towards tissue proteases, suggesting there may be a natural protection from proteolysis that would make these devices ideally suited to the oral cavity [16]. Studies have shown that OFM can facilitate volumetric soft tissue regeneration with restored anatomic depth and contour in a variety of wound etiologies such as, acute traumatic defects, neoplasm excisions, and chronic non-healing diabetic foot ulcers [8,9,17–19]. Several biological grafts have been explored in oral reconstruction and have widely varying costs, including allogeneic acellular dermal matrix ($USD30-50/cm^2), artificial bilayer membrane ($USD 49/cm^2), bovine dermal matrix ($USD 39/cm^2), and urinary bladder matrix ($USD 19/cm^2) [20]. Comparatively, OFM graft ($USD9–11/cm^2) is an affordable alternative, which together with documented clinical performance, supports continued adoption into oral reconstruction procedures.

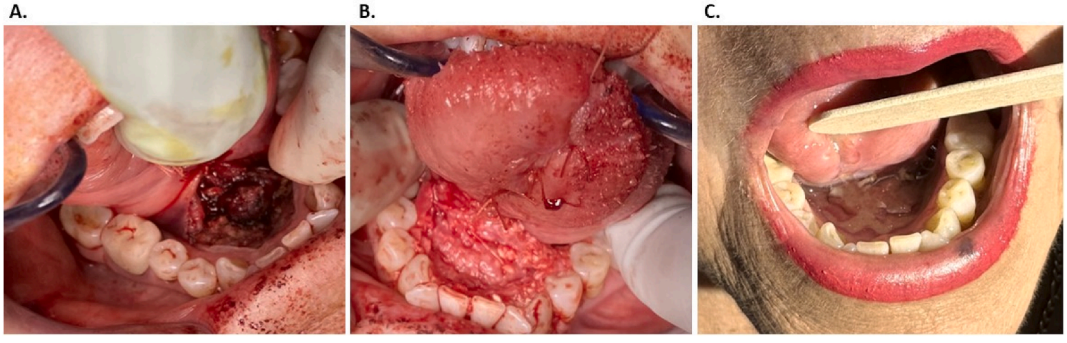

Fig. 3. Case 3, dysplasia of the FOM and ventral tongue. **A.** Post excision. **B.** OFM graft placement. **C.** Post-operative week 3 following removal of the dressing.

This study is comprised of observations from a single center with all the limitations of a retrospective case series. The promising outcomes observed warrant future studies involving an appropriately powered controlled prospective study design.

Consent

Patients voluntarily provided consent for use of medical information provided in this manuscript.

Consent

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CRediT authorship contribution statement

Terry Su: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

There are no financial disclosures or conflicts of interest to report.

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