

Successful application of platelet rich fibrin; a novel technique for reconstruction of onco-surgical partial glossectomy

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Introduction

Tongue cancer is one of the commonest carcinoma of the oral cavity which needs extensive wide surgical resections in order to minimize post-operative recurrences. Reconstruction of these ablative onco-surgical partial glossectomy defects is essential to minimize post-operative speech and swallowing difficulties. Microvascular free flaps, local flaps, distant flaps and regional flaps are the main reconstructive armamentarium for these surgical defects; however it results additional surgical procedure at another donor site.

Oral & maxillofacial (OMF) region is unique for personal identification and self-esteem as it comprises precise, self-identifiable and self-specific important tissue architectural characters. Since it is an area of highly compact aesthetically and functionally important structures, reconstruction of the OMF region is a challenge and has a high demand. Oropharyngeal cancer is the highest prevalent carcinoma among the Sri Lankan males' and the tongue is the second most common individual site of occurrence [1]. Reconstruction of the partial glossectomy surgical defect after the tumor ablation is an extreme necessity to re-gain the speech and swallowing functions of the individual to maintain the social acceptance and personality.

Platelet rich fibrin is known to be used in many surgical interventions in oral and maxillofacial region with successful outcome. This non-invasive therapeutic option would overlook the necessity of additional reconstructive flap procedures. Use of platelet rich fibrin for human tongue onco-surgical reconstruction is not yet reported in the medical literature. Herein, we describe successful application of platelet rich fibrin for reconstruction of series of onco-surgical partial glossectomy defects.

Platelet rich fibrin

Platelet rich fibrin (PRF) is an autologous second generation platelet concentrate, an improved product over platelet rich plasma (PRP). This was first developed for specific use in OMF surgeries. PRF is considered as a novel non-surgical reconstructive option and it is an ideal biological product to facilitate the regeneration of similar textured anatomical structures of the OMF region. Currently, PRF is widely practiced in OMF reconstructive surgeries as a supportive therapy.

a. Mechanism of action

PRF is recovered from the centrifugation of autologous peripheral blood of the patient in a glass tube which initiates the coagulation cascade. Resulting PRF consists of fibrin matrix polymerized in a tetra molecular structure, with incorporation of platelets, leucocytes, plasma proteins, and circulating stem cells [2]. The matrix of the PRF is an ideal media for cell migration and it serves as a reservoir of numerous bioactive molecules such as growth factors, cytokines, fibrinogen, adhesive proteins, and coagulation factors [3],[4]. Once applied to a surgical site, they are responsible for initiating cellular proliferation and differentiation, angiogenesis and regulating inflammatory reactions. Furthermore, it has been suggested that PRF can protect growth factors from proteolysis leading to sustain their activity for a long time duration [5] resulting rapid wound healing [6].

b. Applications of PRF

PRF is known to use in many surgical interventions in OMF region with satisfactory outcome. There are evidences of successful usage of PRF in bone augmentation, socket preservation, sinus lifts and periodontics for correction of intra bony defects, gingival recession, periapical lesions, guided bone regeneration, pulpotomies, periapical surgeries etc [7]. The use of PRF for the reconstruction of human glossectomy defect is not yet reported in the medical literature although PRP has been tried on murine models following partial glossectomy [8].

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Herein, we describe the application of PRF for reconstruction of partial glossectomy onco-surgical defects done at District General Hospital, Ampara. In the first case, PRF was grafted instead of another reconstructive flap procedure following a regional nasolabial flap failure. It was used as a regenerative agent directly on the partial glossectomy site in the other three cases.

Method and materials

PRF was prepared at the blood establishment of the hospital using the following method.

a. Preparation of PRF

After cleaning the phlebotomy site, 10 ml of patient's venous blood was collected into a sterile tube of 10 ml capacity without anticoagulant and immediately centrifuged at 3000 rpm for 10 minutes using the Heraeus Labofuge 400 bench-top tube centrifuge. Centrifugation at a high spin separates whole blood into layers; the fibrin clot lies just above the red cell layer. The fibrin clot was recovered using a tissue forceps with catch under the sterile condition. A piece of sterile gauze was used to remove the thin layer of red cells remained at the bottom of the clot. Finally, fibrin clot was placed in a sterile container and sent to the theater for application.

b. Application of PRF to the surgical site

PRF was stitched in place by 3-0 vicryl sutures and primary closure was obtained wherever possible. Daily Povidone iodine gentle irrigation was done to minimize the infection risk.

Case scenario

Case 1: A 28-year-old lady with a gradually expanding ulcerative exophytic growth on left tongue, measuring 4 cm x 2 cm with everted and indurated margins was seen at the OMF clinic. It had started as a pin point lesion and expanded to this level during the last three months with no pain, however gradual reduction of the tongue mobility affected the speech and swallowing greatly. The lesion extended to ventral aspect of the tongue however the floor of the mouth was not involved. She was otherwise healthy and was not on any medication. Multiple-incisional biopsies histo-pathologically confirmed the lesion as squamous cell carcinoma. In addition, 2 cm single ipsilateral submandibular lymph node with no clinical evidence for distant metastasis suggested the lesion as T2N1M0.

Wide local surgical resection of the primary tumor was done

and ipsilateral pedicled naso-labial flap was used for the reconstruction of the partial glossectomy defect, which was more than 6 cm x 4 cm in size. Naso-labial flap was harvested, preserving the underneath facial vascular pedicle with elliptical skin paddle to match the surgical deficiency. Reconstructive flap was mobilized to the neck and delivered to the glossectomy site by creating a surgical tunnel through the mylohyoid muscle. Ipsilateral extended supra-omohyoid selective neck dissection was done to control the local metastasis of the disease.

The reconstructive flap was functioning well initially, however looked dry, shrunken and gradually separating with time, indicating failure. The cause would be compromised vascularity in the level Ib submandibular region and post-operative tissue oedema. Therefore, the flap was removed, indicating an additional reconstructive option for the surgical defect. The surgical options available were another local, regional or distant pedicled myo-mucosal flap or a radial forearm or anterior lateral thigh free flap. By this time, we could obtain the histopathology results of the excised primary lesion. It reported, complete resection of the tongue lesion with more than 10 mm margins in all directions and no neck nodal involvement in the selective neck dissection. As she was a young girl, instead of an additional reconstructive flap procedure with another donor site wound and a post-operative surgical scar, we preferred PRF grafting as a non-invasive reconstructive option for the surgical defect.

PRF graft, prepared from autologous whole blood, was applied to the glossectomy defect and secured by 3-0 vicryl sutures (Figure 2- a & b). Nasogastric feeding was done to minimize disturbances during meal. Supportive oral care, good hydration and initial antibiotic cover to minimize risk of infections were facilitated.



Figure 1: a- Squamous cell carcinoma tongue, b-wide local resection of the primary lesion, c-Naso-labial flap reconstruction, d-failure of the regional flap



Figure 2: a & b- PRF grafted and secured with 3/0 vicryl suture, c-regeneration after three weeks

With the above evidences of successful partial glossectomy regeneration, we used PRF for reconstruction of partial onco-surgical glossectomy defects in patients fulfilling following specific inclusion criteria. Patients' informed consent was taken before each application.

1. The lesion should be proved as a cancer with an incisional biopsy.
2. The lesion should be less than 4 cm in size (Up to T2 - TNM 8 Oro-pharyngeal cancer classification).
3. There should not have clinically or radiologically suspected cervical lymph nodes.
4. Additional 10mm cuff of normal healthy tissues need to be incorporated to the excisional biopsy from all directions including the deeper margins in order to minimize the recurrence.
5. For inclusion, the lower limit of platelet count was taken as $150 \times 10^9/L$.

Meantime patients with below mentioned conditions were excluded.

1. Lesions with clinically and radiologically suspicious neck nodes or distant metastasis
2. Lesions larger than 4cm in size(lesions beyond T2 –TNM8 oro-pharyngeal cancer classification)
3. Patients on anti-platelet drugs
4. Patients with known platelet function disorders

Case 2: A 65-year gentleman presented with a gradually enlarging irregular, non-tender, hard, whitish patch with indurated margins measuring 1 cm x 1.5 cm on left anterior lateral boarder of the tongue. Incisional biopsy confirmed the lesion as squamous cell carcinoma which was clinically T1N0M0. Wide local resection with adequate margins and PRF grafting was carried out. The defect resolved completely

with similar tongue tissues maintaining the functional and aesthetic outcome in three weeks' duration (Figure 3).



Figure 3: a- primary lesion, b-wide local resection of the primary lesion, c- primary closure with PRF, d- regeneration of the tongue after three weeks

Case 3: A 63 year male patient with exopythic growth on the right anterior tongue measuring 3cm x 3 cm was diagnosed as verrucous carcinoma with the incisional biopsy. Wide local surgical resection and PRF grafting was carried out which gave the expected similar functional and aesthetic results in three weeks' time (Figure 4 & 5).



Figure 4: a-verrucous carcinoma left anterior tongue, b-wide local resection, c-glossectomy defect following surgical excision, d-grafting of PRF

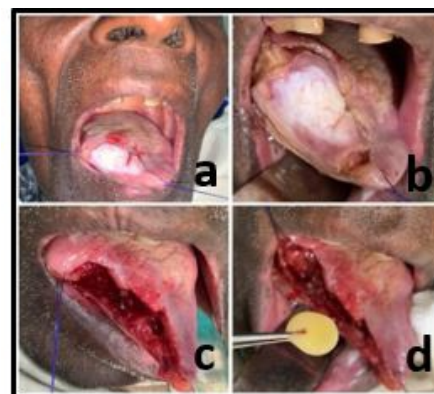


Figure 5: a & b - Verrucous carcinoma c- surgical defect after primary resection d- Incorporation of PRF

Case 4: fifty five year old male patient presented with predominantly whitish irregular lesion measuring 3 cm x 3 cm in size with everted exophytic nature was diagnosed as verrucous carcinoma of the tongue with an incisional biopsy. PRF grafting was done following wide surgical excision of the lesion and near normal regeneration of the tongue was observed in three weeks' time (Figure 6 & 7).



Figure 6: a-left anterior tongue verrucous carcinoma, b-close look of the lesion, c & d- resection of the primary lesion, e-grafting of PRF, f-primary closure of the surgical site



Figure 7: Regeneration of the surgical defect with normal epithelial covering and mobility

Superficial/epithelial and deep incisional biopsies from the regenerated site in all cases were done and confirmed it's the normal tongue tissue with neither residual tumor nor any recurrences.

We could obtain satisfactory results in all cases of PRF grafted regeneration of the partial onco-surgical defects, with neither complications nor any tumor recurrences or any residual tumor. All patients were satisfied about the functional outcome of the implemented non-surgical intervention and are being followed up in the routine OMF clinic.

Discussion

Oral cancer is an emerging dilemma in South Asian region including Indian subcontinent. Squamous cell carcinoma of the oral cavity is the prime cancer among Sri Lankan males, attributed to habits of betel chewing, tobacco and excessive alcohol consumption. Buccal mucosa is the commonest site of occurrence while tongue and floor of the mouth rated subsequently [1]. Wide local resections of these aggressive lesions cause massive aesthetically and functionally unacceptable defects which needs proper reconstruction to maintain the social acceptance, self-esteem and the personality.

Glossectomy defects can be categorized as partial-glossectomy, hemi-glossectomy, sub-total glossectomy and total glossectomy according to the amount of tongue tissue resection. Tumor ablations of the tongue essentially affect the swallowing and quality of speech of the individual. Site, size, type and the nature of the cancer determines the additional resection needed to minimize the recurrence of the disease. Moreover, tongue, floor of the mouth and midline cancers are recommended for excessive resections with additional wider margins, due to high vascularity and bilateral lymphatic drainage, which may disseminate the disease easily and frequently.

Local, regional and distant flaps are recommended for the post-ablative glossectomy defect reconstruction, besides radial forearm and anterior lateral thigh free flaps, the gold standards in developed world [1]. Even smaller glossectomy defects could seal-off with primary closure, for moderate to severe defects (more than 2-3cm) need reconstruction armamentarium beyond primary closure and secondary intension to minimize post operative speech and swallowing deformities [1]. Pedicled naso-labial regional flap was used for the extensive partial glossectomy defect closure of the first case, however it was not successful. Since she was a young lady, considering the donor site morbidity of another local or regional surgical reconstruction, PRF grafting was preferred, and this paved the pathway to initiate this non-surgical intervention.

With the successful outcome of the first case, we considered the effectiveness and safety of implementing this method to onco-surgical partial glossectomy defects, with inclusion and exclusion criteria. Malignant tumors more than 4 cm in size were excluded, as they have higher tendency of local and distant metastasis [1]. Any patient with clinically or radiologically suspicious cervical nodes were left out, as they

have higher chance of loco-regional spread of the disease. Normal tissue cuff 5 mm is recommended in oro-pharyngeal cancer primary resections, however, more than 10mm margins were considered in this case series to minimize recurrences [1]. This was taken as an additional measure since there is a possibility of PRF induced cancer recurrence, if any tumor remnants left behind [9]. This was confirmed with excisional biopsy report for the first case and additional wider excision for the other cases as fresh frozen section facility is not yet available in our center. Further evaluation of the regenerated sites with superficial and deep incisional biopsies after six months of complete healing confirmed the presence of normal regional tissue architecture with neither recurrences nor residual tumor.

For hemi-glossectomy and partial-glossectomy defects up to 4cm, PRF grafting would be a better option [7]. Further, this non-invasive option would effectively cut down the long theatre times of cancer surgeries and would reduce the length of ICU care as there is no surgical reconstruction is needed. Since the method of PRF production is simple, non-expensive and cost-benefit wise it is a very useful alternative for invasive surgical options. Minimum scarring of the post ablative glossectomy site with PRF mediated regeneration, decrease the swallowing and speech alterations, which seems a huge privilege of this method.

Conclusion

Precise reformation of ablated tissues is not being completely obtained by any type of reconstructive flap procedure. Because of this, introduction of this novel glossectomy reconstructive option with precise aesthetic and functional correction, is worth exploring to meet the increasing demand.

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Conflicts of Interests

There is no Conflict of Interest to declare.

Learning Points:

- Platelet Rich Fibrin (PRF) is an advanced autologous regenerative therapy that enhances healing and improves outcomes in reconstructive surgery.
- Most prevent cancer among Sri Lankan males is Oral Cancer.
- Reconstructing glossectomy defects is crucial for minimizing post-operative speech and swallowing difficulties.
- PRF can be effectively utilized for reconstructing up to stage 2 (T2) partial glossectomy onco-surgical defects, under controlled conditions, to reduce the need for complex advanced surgical reconstructions.

References

1. National guidelines for management of oral cancer Sri Lanka, National cancer control programme, Ministry of health, Sri Lanka 2020.
2. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: clinical effects on tissue healing. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;101(3):56-60.
3. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;101(3):45-50.
4. Dohan Ehrenfest DM, Pinto NR, Pereda A, Jiménez P, Corso MD, Kang BS et al. The impact of the centrifuge characteristics and centrifugation protocols on the cells, growth factors, and fibrin architecture of a leukocyte- and platelet-rich fibrin (L-PRF) clot and membrane. *Platelets* 2018;29(2):171-184.
5. Saglanmak A, Cinar C, Gultekin A. Platelet Rich Fibrin (PRF) Application in Oral Surgery. In: Kerrigan S W, eds. *Platelets* [Internet]. London: IntechOpen, 2020:1-14. Available from: <https://www.intechopen.com/chapters/72614>
6. Wu CL, Lee SS, Tsai CH, Lu KH, Zhao JH, Chang YC. Platelet-rich fibrin increases cell attachment, proliferation and collagen-related protein expression of human osteoblasts. *Aust Dent J* 2012;57:207-212.