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Case Report

Use of collagen matrix to improve wound repair after mucosal biopsy: a multicenter case series

Luigi Laino[1], Giuseppe Troiano[2], Dardo Menditti[1], Alan Scott Herford[3], Alberta Lucchese[1], Gabriele Cervino[4], Floriana Lauritano[4], Rosario Serpico[1], Marco Cicciù[4]

[1]Multidisciplinary Department of Medical-Surgical and Odontostomatological Specialties, Second University of Naples, Naples, Italy; [2]Department of Clinical and Experimental Medicine, Foggia University, Foggia, Italy; [3]Department of Oral and Maxillofacial Surgery, Loma Linda University, Loma Linda, CA, USA; [4]Department of Biomedical and Dental Sciences, Morphological and Functional Images, School of Dentistry, University of Messina, Messina, Italy

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Abstract: Oral soft tissue lesions are commonly seen in the daily dental practice. The quick diagnosis of oral potentially malignant disorders and oral precancer disease is of highest clinical importance given the mortality rate of late stage disease. Since the oral cavity is more accessible to complete examination, it could be used in early detection of precancerous and cancerous lesions. But either due to ignorance or inaccessibility of medical care, the disease gets detected in the later stages. Thus, there is a need for improvement in early detection of oral disease, because in the initial stages, treatment is more effective and the morbidity is minimal. Aim of this report is to highlight how collagen membrane graft application seems to offer a perfect healing of the soft tissue after the lesion removal. Some reports and the microstructure of the collagen used have been recorded. The healing of the soft tissue, the bleeding control and the management of postoperative discomfort seem to be more favorable by avoiding a intraoral soft tissue graft and applying a collagen membrane.

Keywords: Collagen matrix, porcine matrix, soft tissues regeneration, oral biopsy, excisional biopsy

Introduction

Despite advances in non surgical diagnostic techniques, a partial or total excision of oral benign, premalignant and malignant disorders is needed to obtain a final histological diagnosis [1]. Harvesting of a proper amount of tissue from the lesion allows the pathologist an easier and safer histological examination [2]. For some disease, total excision of the lesion should be obtained in order to decrease the possibility of relapse [3]. Scalpel biopsy of widespread lesions, results in a big amount of collected tissues and expose the wound to the possibility of healing by secondary intention [4]. Epithelial cells need of some days to migrate from the surrounding tissues to the wound site, and in this period the connective donor tissues are exposed to the oral cavity environment [5]. This is associated to higher morbidity for patients, if compared to the healing by first intention [6]. It has been recently reported in literature that the use of Mucograft® (Geistlich Biomaterials, Wolhusen, Switzerland) as a wound dressing: it has improved the healing during the first week, it reduced the post-operative wound sensitive and it determined a better healing of the wound [7]. Mucograft® has a bilateral structure made of two layers. A compact layer made of compact collagen fibers that should protect against bacterial infiltration, and a second layer consists of a spongious collagen structure [8]. It is known, thanks to their compact structure, collagen matrices work as scaffold and thus accelerate the migration of epithelial cells in the wound tissues [9]. Mucograft® is a porcine collagen matrix and, its use has been reported for the treatment of gingival recession and to improve keratinized tissues around teeth or implants [10]. In these procedures, the use of a matrix may avoid the levy of a graft from the hard palate decreasing the time for intervention and morbidity for the patient. In fact,

Table 1. Summary of the features related to patients and clinical information

Patients	Age	Sex	Systemic disorders	Location	Clinic feature	Intervention	Outcomes	Complication	Follow-up
Case 1	54	M	None	Alveolar crest	Painless, hard, white appearance	Surgical excision and matrix positioning	Disappearance of the lesion and healing with keratinized gengiva	None	18 months
Case 2	83	F	Mild hypertension	Cheek	Painless, hard, white and desquamative	Surgical excision and positioning of 3 matrices	Disappearance of the lesion, faster healing of the site, absence of scars	None	24 months
Case 3	28	F	None	Hard palate	Painful, white and ulcerative	Bioptical excision and matrix positioning	Disappearance of the lesion, faster healing of the site	None	24 months

an additional local anesthesia and a second surgical trauma is required to harvest a graft from a donor site, leading to another wound in the mouth [11]. In this paper, a new clinical use of Mucograft®, to improve the wound healing repair after biopsy of oral lesions is reported. In the three cases reported in this paper the use of Mucograft has been tested to reduce the postoperative sequelae and to improve the wound healing in different subsytes of the oral cavity, for this reason a careful follow-up has been performed.

Material and methods

Selection criteria

The IRB of University of Foggia Dental Clinic approved this study, and all participants signed an informed consent agreement. All the patients affected by non-malignant oral mucosal disease, when dubious the lesion type had to be ascertained through a previous incisional biopsy were involved in the surgical procedure of excisional biopsy and then soft tissue reconstruction with the collagene membrane. The exclusion criteria were as follows: documented allergy to collagen, mepivacaine or other local anaesthetics. The porcine matrix Mucograft®, was used for replacing the lesion removal and to improve the wound healing of soft tissues. The healing effectiveness was evaluated by the "restitution ad integrum" of the soft tissues involved in the study. The presence/absence of bleeding, swelling, or color alterations have been recorded in the postoperative up to 6 months follow-up in all the reported cases (**Table 1**).

Surgical procedures

After the bioptical excision of the lesion, carried out in order to remove the same one and perform a histological examination, a piece of collagen matrix was sutured in close contact to the cleavage site of the biopsy. When necessary, in relation to the size of the lesion multiple matrices have been placed in the healing site. The matrix of Mucograft was stabilized through the use of multiple interrupted sutures, all patients were treated under local anaesthesia. In the postoperative period, all patients received antibiotics prior to the surgery. Anti-microbial prophylaxis was obtained with the use of 1 gr of Amoxicillin + Clavulanic acid (Augmentin, GlaxoSmithKline, Brentford, Middlesex, United Kingdom) (or erythromycin 500 mg if allergic to penicillin), starting one day before surgery and for the following 5 days. Patients were instructed to use of 1% clorexidine gel twice a day for 2 weeks and then 0.2 chlorhexidine mouthwashes twice a day for up to the second month, to avoid brushing and trauma on the surgical sites.

Case series

Case-1: A 54 years-old-man was referred to the Department of Clinical and experimental medicine, University of Foggia, for the presence of a white keratinized lesion on the edentulous alveolar ridge. The patient didn't declare the presence of other systemic diseases. He seemed to be very anxious regarding the presence of the lesion and asked for a final histologic diagnosis and, if possible, the restore of the lost tooth with an implant-supported fixed single crown. We decided to perform an excisional biopsy of the lesion in order to obtain a histologic diagnosis. In addition, to accelerate healing and avoid a healing by secondary intention, we covered the wound site with Mucograft® in order to obtain a suitable amount of keratinized gingiva for a possible implant insert in a second step (**Figure 1**). Histological examination reve-

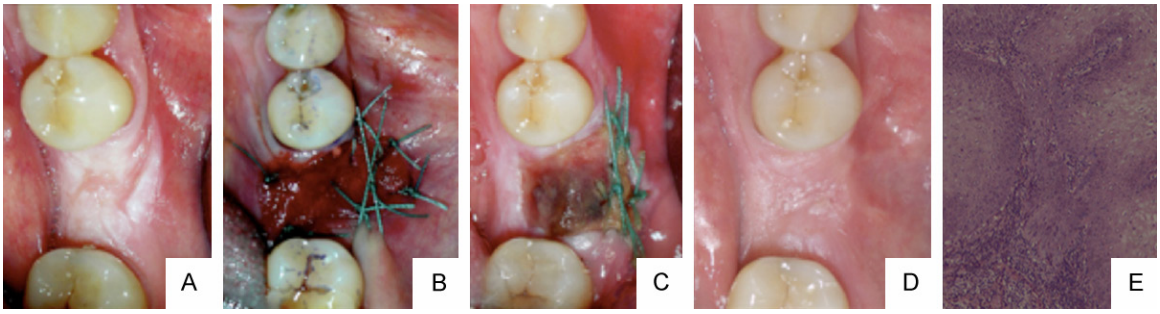

Figure 1. A. A white keratinized lesion localized on the alveolar ridge. B. Removal of the lesion and placement of the matrix. C. Wound healing after one week. D. The healing of the soft tissue shows no more presence of white keratinized lesion after one month. E. Histopathology investigation revealed the corrected diagnosis of cell differentiation typical of keratosis alveolar ridege.

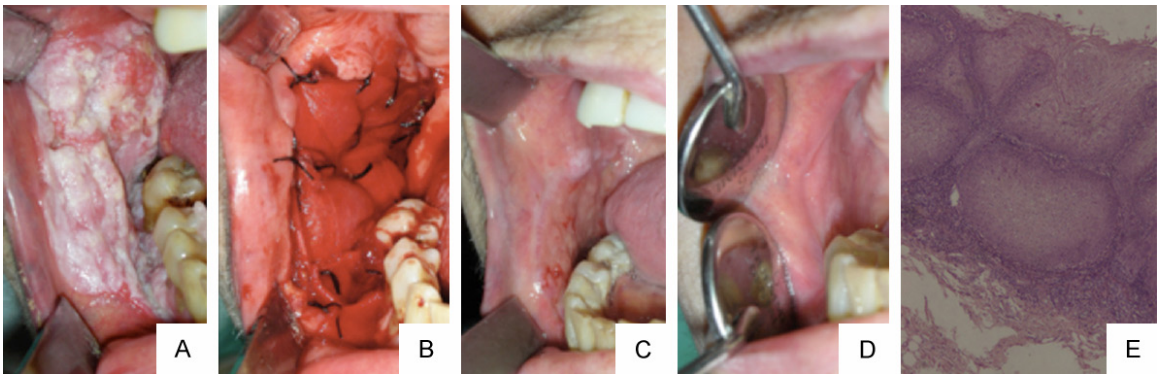

Figure 2. A. Presence of a wide keratinized white lesion on the cheek mucosa. B. Bioptical excision of the lesion and placement of three matrices of Mucograft®. C. Wound healing after two weeks from the biopsy. D. After one month the healing of the cheek mucosa was obtained. E. Histopathology investigation revealed the corrected diagnosis of cell differentiation Proliferative verrucous leukoplakia.

aled the presence of a benign alveolar ridge keratosis (BARK) of the alveolar ridge A correct surgical healing with a good amount of keratinized tissue was seen at 1-months after the surgical biopsy. However, the patient decided to postpone the time of implant insertion for personal motivations.

Case-2: A 83-year-old-woman was referred to the Multidisciplinary Department of Medical-Surgical and Odontostomatological Specialties, Second University of Naples. The patient complaints the presence of a wide hyperkeratotic lesion on the mucosa of the cheek. To exclude the malignancy of the lesion a multiple randomized incisional biopsy of the lesion was performed. The histological examination revealed the presence of a proliferative verrucous leukoplakia (PVL) with areas of moderate grade dysplasia. After a healing period, of two weeks it has been decided for a total excision of the lesion. In the pre surgical decision-making, it has been decided to improve the cheek mucosal healing through the use of three matrices of Mucograft®. This decision has been taken in order to avoid the reconstruction through the levy of grafts from intra or extraoral donor sites. The excision of the lesion has been performed with a surgical scalpel bard parker n°15C, and the three matrices have been stabilized with multiple interrupted sutures. At 2 weeks follow-up, a partial re-epithelization of the lesion and the absence of colour alterations were seen. In addition, the patient was able to resume a normal diet. Patient was checked routinely with a 6 months follow-up (**Figure 2**).

Case-3: A 28-year-old woman presented to the Department of Clinical and experimental medicine, section of oral pathology, University of Foggia, complaints the presence of a white, painful ulcerative lesion on the border between hard and soft palate. The patient declared to not suffer for other systemic pathologies and to

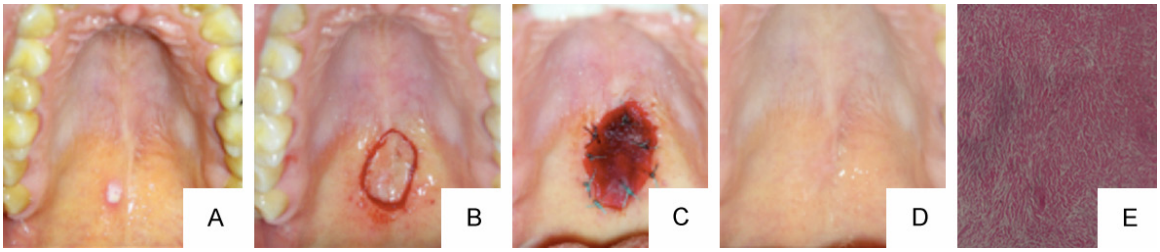

Figure 3. A. A white spot lesion is evidenced in the soft palate. B. The lesion is removed. C. The porcine matrix is placed. D. The perfect healing of the soft tissue at one month follow-up. E. Histopathology investigation revealed the corrected diagnosis of cell differentiation and moderate-grade dysplasia.

have never smoked or drink alcohol. The lesion arose about one month before and had never regressed. No presence of gingivitis, caries or probing depth > 3 mm was recorded during the dental clinic examination. We decided to perform an excisional biopsy of the lesion to obtain a final histologic diagnosis, also we decided to cover the surgical site with Mucograft® to decrease the postoperative discomfort. The histological examination revealed the presence of a moderate dysplasia involving the margin of the specimen. The lesion relapsed after a month from the first biopsy, so given the young age of the patient we decided to intervene to widen the margins of excision. During the second surgical operation again we decided to cover the wound site with Mucograft® membrane. The second histological report confirmed the presence of a moderate-grade dysplasia that was not present, however, on the margins of the lesion. After a month, a perfect wound tissues repair was obtained, and the patient was controlled routinely with a 6 months follow-up (**Figure 3**).

Discussion

The use of a porcine collagen matrix to improve wound healing after oral biopsy has been discussed in this paper. Up today, clinicians have been mainly focused on the use of Mucograft® in periodontal procedures, such as: treatment of recessions on teeth and implants and increment in the amount of keratinized gingiva [12]. The effectiveness of this matrix for the use in the oral wound healing has been validated by in vitro and in vivo studies. Improvements in oral healing seems to be related with the better cytocompatibility of Mucograft® on human mesenchymal stem cells (MSC). Beitzel et al [13] compared five types of matrices by histologic analysis and electron microscopy, they found that Mucograft® showed the best results for cell adhesion and proliferation rate of MSC cells. In addition, the porcine membrane stimulates an increased production of pro inflammatory mediators in the mononuclear cells and a decreasement in cellular proliferation of these last ones [14]. A good proliferative activity of fibroblasts has also been seen in both the layers of the matrix [15]. Ghanaati et al [16], in a study on murine model, found a good integration in host tissues of Mucograft®, this last one showed to remain impermeable to invading cells for the first 30 days after treatment. Its capability in tissue integration has also been studied in a dermal pig model, in which Mucograft® proved a similar behaviour to autogenous dermal grafts regarding: epithelialization, vascularization and degradation [17]. Its biological and mechanical properties have suggested the use in substitution to the gingival graft from the palate for tissue reconstruction. Herford et al [18], were the first to use this matrix in guided bone regeneration (GBR) procedures in a pig-model. They showed a better result in GBR procedure when the graft (autogenous and bovine bone secured with a titanium mesh) was covered with Mucograft®, they also suggested a synergic effect with the use of platelet-derived growth factor (PDGF). In this case series, it has been reported about a further possible use of the porcine matrix to improve oral healing after pathological excision and simultaneously restore of a correct soft tissues architecture. As reported for case 1, Mucograft® may be use to prevent the lack of keratinized tissues following the bioptical levy and prepare the site for a later restoration. In fact, although a direct relationship between bone loss around implants and amount of keratinized tissues has been denied [19], the lack of keratinized mucosa around implants correlated with plaque accumulation and soft

tissues inflammation [20]. Due to the presence of the external compact layer, Mucograft may be easily sutured and provide protection to the underlying tissues in the heal for secondary intention. While the internal non-cross-linked spongious layer stabilizes the blood clot and act as scaffold for the proliferation of the underlying mesenchymal cells [21]. These features have been exploited to improve the amount of soft and hard tissues in the socket preservation techniques, instead of levy a connective graft from a donor site. The use of Mucograft®, in post extraction socket preservation, is supported by randomized clinical trials, in which the porcine membrane revealed similar outcomes than epithelial-connective tissue graft for socket preservation [22, 23].

The excellent of the healing recorded at the time of suture removal and after two months, clearly underlined how this collagen device give the clinicians the opportunity of not harvesting palatal or soft tissue graft for the management of oral disease involving hard and soft palate. The great advantage is not having a double surgical site and this reduce the patient's discomfort. In this study, the features above mentioned have been exploited to improve the healing after the excisional biopsy. The lesions reported in this study occur in three different subsites within the oral cavity. In all the cases, the use of Mucograft® led to a complete healing both regards the color that bleeding at 6 months follow-up. It should be noted as in the case 2, a wide lesion occurred on the cheek mucosa; that area was subject to the displacement action of the cheek muscles, but even so the healing proved to be optimal. Although, the design of the study is poor, it is plausible to think that the use of Mucograft® after biopsy excision should be investigated in further studies.

Conclusions

Mucograft® is a pure porcine collagen matrix composed of two different layers. Its high biocompatibility, together with its excellent mechanical properties, has suggested the use in periodontal surgery until today. In this paper, we suggest a new use of this matrix to improve oral healing after excisional biopsy. The use of Mucograft® is recommended in cases in which both aesthetic and functional features have to be restored.

Disclosure of conflict of interest

None.

Address correspondence to: Marco Cicciù, Department of Biomedical and Dental Sciences, Morphological and Functional Images, School of Dentistry, University of Messina, Policlinico G, Martino, Via Consolare Valeria 98100, Messina, Italy. Tel: +39-0902216920; E-mail: acromarco@yahoo.it; mcicciu@unime.it

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