

Case Report

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Application of concentrated growth factor and immediate auto transplantation on the treatment of mandibular cyst: A case report**Ling Wang^{1*}; Ailimaierdan Ainiwaer²; Dilinuer Keranmu²; Nijiati Nuermuhanmode²**¹Department of Oral and Maxillofacial Surgery, The First Affiliated Hospital of Xinjiang Medical University, China.²Outpatient Department of Oral Surgery, The First Affiliated Hospital of Xinjiang Medical University (Affiliated Stomatological Hospital), Research Institute of Stomatology of Xinjiang Uygur Autonomous Region, Urumqi, 830054, China.***Corresponding Author: Ling Wang**

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Abstract

Introduction and importance: Jaw cyst often results in varying degrees of jaw bone defects as a common disease. The presented case is a pioneering attempt to reconstruct and repair mandibular bone defect with Concentrated Growth Factor (CGF) and immediate tooth transplantation, so as to avoid the use of synthetic bone substitutes and secondary surgical procedures.

Case presentation: A 24-year-old female patient presented to the Department of Oral Surgery of our hospital with pain and swelling of bilateral mandibular posterior teeth. Autogenous Tooth Transplantation (ATT) was performed immediately after the removal of the mandibular bone cyst and the bone defect was filled with CGF. Healing conditions were monitored by radiological techniques.

Conclusion: CGF combined with tooth transplantation can be used as one of the most up-to-date methods to reconstruction of bone defect and restoration of partial edentulism after cyst surgery.

Keywords: Case report; Jaw cysts; Concentrated Growth Factor (CGF); Autogenous Tooth Transplantation (ATT).

Abbreviations: CGF: Concentrated Growth Factor; ATT: Autogenous Tooth Transplantation; PRP: Platelet Rich Plasma; PRF: Platelet Rich Fibrin; CBCT: Cone Beam Computed Tomography; GBR: Guided Bone Regeneration; PDL: Periodontal Ligament; RCT: Root Canal Therapy; PDGF: Platelet-Derived Growth Factors; TGF-B1: Transforming Growth Factor-B1; VEGF: Vascular Endothelial Growth Factor; FGF: Fibroblast Growth Factor; IGF: Insulin Like Growth Factor.

Introduction and importance

Odontogenic jaw cyst is one of the common diseases in the field of oral and maxillofacial surgery. It is often caused by periapical granuloma and chronic inflammatory stimulation, resulting in residual hyperplasia of periodontal ligament epithelium. Degeneration and liquefaction occurred in the center of the

proliferative epithelial mass, and the surrounding tissue fluid continuously exudes, gradually forming a cyst, which can occur in any part of the jaw [1]. Modern surgical protocols imply complete removal of cystic lesion, filling the resulting bony defect and primary wound closure. The complete healing time of bone defect of small jaw cyst is about 1 year while the larger is about

2-5 years [2]. Therefore, the treatment of postoperative bone cavity and reconstruction of bone defect is very important. Numerous grafting materials are used to reduce the course of treatment and maintain the space integrity during the healing period. The materials include autogenous, allogeneic, xenogeneic, and alloplastic bone grafts [3,4]. In recent years, because of the shortcomings of graft materials and limited regenerative outcomes, attention has been focused on growth factors such as platelet concentrate, to increase the clinical success of bone grafts, improve bone healing, and obtain more reliable alternative bone products.

The development of platelet concentrate has been divided into three stages, including Platelet Rich Plasma (PRP), Platelet Rich Fibrin (PRF) and CGF. As the latest generation, CGF was first proposed by Sacco in 2006. CGF is made from autologous venous blood with no addition of any biological agents, non-toxic, no immunogenicity, and separated by special centrifugation, it was claimed to have strong tissue regeneration ability and biodiversity, stable fibrin matrix and high tensile strength [5]. Since the introduction of platelet concentrate into dentistry, CGF has been extensively used in various situations, ranging from the filling of extraction sockets to peri-implant bone defects [6], sinus augmentation procedures [7], simple GBR procedures or as a membrane support in recession coverage [8]. Studies have confirmed that CGF could promote initial cell stretching, proliferation, and osteoblastic differentiation of rat bone marrow cells *in vitro*, and bone regeneration was also presented *in vivo* in rat calvarial bone defects [9]. Recent studies have borne out claims that CGF can be used as a socket filling material following posterior tooth extraction in order to achieve ridge preservation over a 3-3.5 months observation period [10]. Collectively, CGF is a powerful biological scaffold and growth factor library, and the use of autologous CGF does not cause any side effect and is a safe and simple procedure for a specialist, and it is inexpensive and efficacious for the patients.

Immediate auto transplantation is a feasible choice to reconstruct the wound surface and repair the dentition defect when there are available donor teeth. The history of tooth transplantation can be traced back to the 1950s. ATT refers to the transplantation of physically intact tooth without biological function, such as impacted, dislocated or ectopic tooth, from one position to another to support the masticatory function of the affected tooth. ATT is most commonly used in the third molar to replace the damaged first or second molar [11]. Studies have shown that the shorter the extra-oral time, the less likely the PDL was to be damaged. Compared with traditional methods, oral Cone Beam Computed Tomography (CBCT) guided method is extremely helpful during the preparation of the recipient socket as it minimized the trauma to the Periodontal Ligament (PDL) and Hertwig's root sheath, reduced the extra-oral time of the donor tooth, and improved the predictability of surgery [12]. Increasingly studies have shown that 3D printing model based on CBCT data is an economical and effective method, which can reduce the operation time and the potential iatrogenic damage to the donor tooth [13].

However, the reconstruction of cystic defects with CGF and simultaneous ATT has not been reported. A previous study showed that the application of CGF in recipient site with a small area of chronic periapical lesions can accelerate the regenera-

tion of alveolar bone and the healing of inflammation, greatly shorten the healing period. Additionally, the use of CBCT based 3D printing model can greatly reduce the extra-oral time of donor teeth [14]. Therefore, the presented case is a pioneering attempt to reconstruct and repair mandibular bone defect with CGF and immediate tooth transplantation, so as to avoid the use of synthetic bone substitutes and secondary surgical procedures. The purpose of this report is to describe a patient who underwent immediate ATT after the removal of a mandibular cyst, and filling the bone defect with CGF. The treatment results of the case followed up for 12 months are reported as follows.

Case presentation

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. All applicable rules regarding the ethics of experimentation and research integrity were followed. This work has been reported in line with the SCARE 2020 criteria [15]. Female patient, 24 years old, with good health, no history of drug use or any relevant family or genetic disease information, was presented to the department of oral surgery of our Hospital, with pain and swelling in the bilateral mandibular posterior teeth area of the lower jaw. The affected teeth were repaired with a porcelain crown in the outer hospital 5 years ago. Clinical examination showed that there was a fistula in the left posterior tooth area, with slight swelling and palpation pain and overflow of pus. Preoperative examination results of routine blood test and electrocardiogram showed no obvious abnormalities. The X-ray and CBCT, showing a clearly demarcated (16*10) mm and (13*7) mm oval radiolucency, respectively, localized in the region of bilateral mandibular first molars.

Because the scope of the cyst on the right side of the patient is larger than the left side, the surgical procedure of the patient is to curette the cyst on the right side, transplant the right impacted tooth (#48) to the right mandibular first molar (#46) first, and then the left side after 3 months. After 5 days of anti-inflammatory treatment, the operation was performed when there were no signs of infection. This case was conducted by an experienced oral surgeon and the patient demonstrated good adherence and tolerability to treatment throughout the process.

The data obtained by the CBCT was converted into DICOM format, and then imported into MIMICS software and 3D printer to replicate and print the resin tooth model. Acrylic models were sterilized by ethylene oxide before surgery, aseptically packed and ready for use.

CGF was prepared according to Sacco's protocol before operation. The blood sample was distributed into four 10.0 mL sterile test tubes without anticoagulants, followed by centrifugation at the program of 30-second acceleration, 2 minutes 2700 rpm, 4 minutes 2400 rpm, 4 minutes 2700 rpm, 3 minutes 3000 rpm, and 36 seconds deceleration by a specific centrifuge (Silfradent, Italy). After centrifugation, the upper layer contained the separated serum, fibrin-rich block with CGF was in the middle of the tube, whereas blood corpuscles were precipitated in the bottom layer. The fibrin block was separated from blood corpuscles with scissors to obtain the pure CGF block, which was ready to be used.

The oral was cleaned with compound chlorhexidine, and the injection site of anesthesia and operation area were disinfected with iodophor cotton balls. After local anesthesia was performed with 2% lignocaine in 1:200000 adrenaline, the compromised molar was extracted atraumatically. A (16*10) mm cyst was then carefully enucleated by using bone curettes. The tissue specimen was dipped in 10% buffered formalin and sent to the histopathology lab for further examination. The 3D model of the donor tooth was used to guide the modification of the alveolar socket until it was completely in place. Then the CGF membrane with certain elasticity and adhesion was placed in the alveolar fossa of the recipient site to make the CGF membrane completely cover the bone defect. After minimally invasive extraction, the impacted tooth was immediately transplanted into the recipient socket to check whether they reached the ideal position. When further adjustment was needed, the donor tooth was placed in the sterile saline. The donor tooth was put in place by using finger pressing without touching the root. After transplantation, the tooth were fixed with 8-shaped cross suture and periapical radiograph was taken immediately after the surgery as a baseline reference.

All the post-surgical instructions were given to the patient and analgesics along with cefdinir were prescribed. Sutures were removed 7 days later. All the transplanted teeth in our study were required to receive RCT within 2-4 weeks after transplantation when they showed physiological mobility. The patient felt no obvious pain and swelling after operation. The histological manifestation of the lesion was stratified squamous epithelium in the capsule wall, with chronic inflammatory cell infiltration. During the following 12 months, the wound healed uneventfully without any signs of inflammation and nerve injury. The periapical radiograph taken after transplantation showed a more radiopaque image compared with the previous radiographs. The increased radiopacity over the cystic lesion in the radiographs was observed with time. During the follow-up period, the patients expressed that she could use the masticatory function of the transplanted teeth normally and were satisfied with the treatment results.

The boundary between the bone defect area and normal jaw tissue was blurred 3 months after surgery. 6 months after the operation, the bone density of the bone defect area was similar to the surrounding normal bone, and the new bone and the surrounding bone tissue grew well. During the 1-year follow-up, the patient showed acceptable chewing function, and there was no pathological radiation. The transplanted teeth showed no remarkable findings such as tooth mobility, periodontal pocket, gingival swelling, root resorption, ankylosis and any other adverse event.

Clinical discussion

The recurrence rate of odontogenic jaw cysts is reported to be as high as 58.3%, with the highest recurrence rate occurring in the posterior region of the mandible [16]. What is more, it was reported that the fastest recurrence observed about 7 months postoperatively, 74.3% occurred within 5 years after the first operation [17]. Therefore, we decided to repair the crown when the cyst showed no signs of recurrence.

An increasing number of studies have shown that ATT is an alternative method for the repair of missing teeth, which can provide immediate and permanent restoration [18]. The success rate of ATT was affected by several factors, such as the degree of root development, age, overall periodontal condition,

extra-oral time of the donor tooth and the volume of alveolar bone in the recipient area [19]. ATT can achieve ideal effect when the root of donor tooth was developed to 1/2-3/4 of its length. The third molar with complete root formation, even the supernumerary tooth, can also be used as donor. Later treatments such as Root Canal Therapy (RCT), resin filling and crown restoration are also helpful to achieve good functional and aesthetic effects without affecting the success rate of ATT [20]. However, the existence of cystic lesion at the recipient site restricts the selection of indications and the application of ATT. At 6 and 12 months after operation, the osteogenic rate of jaw cyst after curettage was basically maintained at 50% and 80% [21], and the larger the range of bone defect, the longer the osteogenic time. In the current case, the cysts were curettled and the tooth transplantation was performed with CGF, the patient could continue to exercise masticatory function during the recovery period while the density of the inflammatory area gradually improved.

At present, bone transplantation and biomaterial implantation are often used to promote the restoration of bone defect to its original physiological structure and appearance. Although autologous bone transplantation is recognized as the gold standard of materials used in bone augmentation techniques due to their osteogenic potential, optimal adaptation, and the fact that they do not elicit an immune response [22]. However, autologous bone grafting has other disadvantages, such as rapid absorption, secondary surgery, more trauma formation and high donor site incidence. Therefore, researchers are committed to finding a better biomaterial to promote the repair of alveolar bone.

As the third generation platelet concentrate, CGF has two core structures, including three-dimensional fibrin scaffold and a variety of endogenous growth factors. Compared with PRF and PRP, CGF separates various components in blood more completely through variable speed centrifugation, forms a more resilient fibrin network and provides a three-dimensional space for cell adhesion and proliferation [23]. In addition, its protein network contains a large number of leukocytes, which can not only regulate host defense mechanism, but also inhibit the occurrence of inflammation. Variable speed centrifugation can also release higher concentrations of CD34+cells (hematopoietic stem cells, involved in vascular maintenance, neovascularization and angiogenesis) and growth factors, and more stably polymerize leukocytes and platelets in CGF, thus possessing stronger regeneration ability. Furthermore, CGF can release a variety of bioactive substances, including a variety of growth factors, such as Platelet-Derived Growth Factors (PDGF), transforming growth factor- β 1(TGF- β 1), Vascular Endothelial Growth Factor (VEGF), basic Fibroblast Growth Factor (FGF), Insulin like Growth Factor (IGF), etc. These growth factors can promote the proliferation, differentiation and angiogenesis of fibroblasts and osteoblasts, so as to promote the healing of wound [24]. Moreover, CGF has good plasticity and compatibility, and can be prepared into extract, lyophilized material, CGF membrane and CGF medium.

Due to the good biological properties, the application of CGF in the oral and maxillofacial region has been extensively studied. A previous study found that the application of CGF in the recipient site with chronic periapical lesions could accelerate inflammatory healing and alveolar bone regeneration [14] similarly, in one case report [25], two patients with extensive periapical lesions were treated with CGF, after 6 months of follow-up, ideal

bone healing was found Huang et al [26]. Evaluated the effect of CGF in alveolar cleft and concluded that the bone resorption rate and the bone density improvement with better results in CGF group than in Acellular Dermal Matrix (ADM) group. Two patients with large cystic lesions in the upper and lower jaw were presented in one case report, and the postoperative bony defects were filled with autologous fibrin rich blocks containing CGF. The results showed that CGF can significantly shorten the bone-healing time, particularly in massive bone defects, reduce the incidence of postoperative relapse, alleviate the postoperative course and enable better restitution of surrounding soft tissue structures [27]. It can be seen that CGF has a good clinical effect in bone augmentation in the oral and maxillofacial region. In our study, the patient showed no signs of infection 12 months after operation, the hard tissue of the bone defect area healed well and the transplanted teeth could exercise normal chewing function with high patient satisfaction.

In order to preserve the vitality of periodontal ligament stem cells on the root surface and ensure the success rate of ATT, the extra-oral time of the transplanted teeth should be controlled within 5 min [28]. In the present study, both of the donor teeth were transplanted into the recipient site within 60s after extraction, and such a short time was due to the auxiliary application of 3D printing model. It is worth mentioning that during the 9-month recovery period, #36 underwent occlusal reconstruction and a good occlusal relationship has been achieved. This may benefit from stimulating periodontal ligament healing during bone remodeling and thereby promoting tooth movement. In addition, strict and standardized aseptic operation in the process of surgery is a powerful guarantee to reduce the risk of postoperative infection, and it is also the key to the successful application of CGF combined with ATT technology in the repair of jaw cyst bone defect.

Conclusion

In this study, CGF combined with ATT achieved predictable clinical effects in the treatment of bone defects after jaw cyst surgery. The method is relatively simple and effective, without risk of transmissible and allergic diseases, and its success was confirmed by the lack of postsurgical alterations and no recurrence of the lesion. CGF combined with tooth transplantation can be used as one of the most up-to-date methods to reconstruction of bone defect and restoration of partial edentulism after cyst surgery. However, longer period of follow-up and in-depth study are needed to confirm long term effect of ATT and the exact mechanism of the regenerated bone during wound recovery in the later stage.

Declarations

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Consent and ethics: Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions:

Ailimaierdan Ainiwaer: Study design; operator of surgeries; review of manuscript.

Dilinuer Keranmu: Study design; data curation; writing & review of manuscript.

Nijiati Nuermuhanmode: Formal analysis; data curation; review of manuscript.

Ling Wang: Study design: review of manuscript.

Research registration: This case report does not include any 'first in man' studies, so, registration was not required.

Guarantor: A.Prof. Ling Wang, director of the outpatient department of oral and maxillofacial surgery of the First Affiliated Hospital of Xinjiang Medical University.

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