



## Application of concentrated growth factors in reconstruction of bone defects after removal of large jaw cysts – The two cases report

Upotreba koncentrovanih faktora rasta u rekonstrukciji koštanih defekata nakon uklanjanja velikih viličnih cista

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### Abstract

**Introduction.** Coagulation and blood clot formation in bone defects is sometimes followed by retraction of a blood clot and serum extrusion, thus producing peripheral serum-filled spaces between bony wall and coagulum. This can result in a higher incidence of postoperative complications. Stabilization of blood coagulum, which enables successful primary healing, may be accomplished by autotransplantation, allotransplantation, xenotransplantation, or application of autologous platelet concentrate and concentrated growth factors (CGF). **Case report.** Two patients with large cystic lesions in the upper and lower jaw were presented. In both patients postoperative bony defects were filled with autologous fibrin rich blocks containing CGF. Postoperative course passed uneventfully. **Conclusion.** Application of fibrin rich blocks containing CGF is one of the possible methods for reconstruction of bone defects. CGF can be applied alone or mixed with a bone graft. The method is relatively simple, without risk of transmissible and allergic diseases and economically feasible.

### Key words:

jaw cysts; oral surgical procedures; platelet-derived growth factor; transplantation, autologous.

### Apstrakt

**Uvod.** Koagulacija i stvaranje krvnog koaguluma u koštanim defektima posle uklanjanja cističnog sakusa i zatvaranja operativnog polja nekad može biti praćena istiskivanjem seruma, čime se stvaraju periferni, serumom ispunjeni prostori između zidova kosti i površine koaguluma. Ovo može izazvati češću pojavu postoperativnih komplikacija. Radi stabilizacije krvnog koaguluma i očuvanja primarnog zarastanja primenjuje se autotransplantacija, alotransplantacija, ksenotransplantacija, kao i autologni koncentrat trombocita i koncentrovani faktori rasta (KFR). **Prikaz bolesnika.** Prikazana su dva bolesnika sa velikim cističnim lezijama u gornjoj i donjoj vilici. Kod oba bolesnika koštani postoperativni defekt bili su ispunjeni autognim fibrinskim blokovima bogatim KFR. Postoperativni period protekao je bez komplikacija. **Zaključak.** Upotreba fibrinskih blokova bogatih KFR jedna je od mogućnosti rekonstrukcije koštanih defekata. KFR mogu se koristiti samostalno ili u kombinaciji se nekim od veštačkih zamenika kosti. Metoda je relativno jednostavna, bez opasnosti izazivanja transmisionih i alergijskih bolesti, a ekonomski je isplativa.

### Ključne reči:

vilice, ciste; hirurgija, oralna, procedure; faktori rasta, trombociti; transplantacija, autologna.

### Introduction

Bone regeneration processes are highly dependent on the range and extent of the defect, provided that coagulum formation process is not impaired<sup>1</sup>. The average healing time of small cystic defects is usually up to one year, while healing time extends with the size of a defect, ranging from two to five years for medium-size and large cysts<sup>2</sup>. After removal of cystic sac and closing the wound primarily, a bo-

ne defect is filled entirely. However, the initial blood clot formation is followed by clot retraction and serum extrusion, thus producing peripheral serum-filled spaces between bony wall and coagulum surface<sup>1,2</sup>. This significantly interferes with protrusion of vascular epithelium and the healing process. On the other hand, the space formed by the removal of dental cysts usually provides favorable conditions for microbial growth and a risk of infection. Therefore, stabilization of blood coagulum and preservation of primary healing has be-

en accomplished by several methods, such as autotransplantation, allotransplantation, xenotransplantation, or application of autologous platelet concentrate (APC) and concentrated growth factor (CGF) procedures<sup>3</sup>.

Growth factors are proteins, which regulate complex processes during wound healing. Growth factors are mainly located in blood plasma and platelets and play an important role in cell migration, cell proliferation and angiogenesis during regeneration<sup>4</sup>. Most important and representative growth factors are: platelet derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF) and insulin like growth factor 1 (IGF 1)<sup>5, 6</sup>. First generation of platelet concentrates, platelet-rich plasma (PRP)<sup>7</sup> was introduced in 1998 and the second, platelet rich fibrin (PRF)<sup>8</sup>, in 2000. PRF is a fibrin-rich gel produced with fresh venous blood taken from a patient's vein<sup>8-10</sup>. CGF were first developed by Sacco. CGF show a higher tensile strength, more growth factors, higher viscosity and higher adhesive strength than PRF<sup>11</sup>. The use of autologous fibrin does not cause any side effect and it is a safe and simple procedure for a specialist, and inexpensive and efficacious for the patients<sup>11, 12</sup>.

The aim of this report was to describe two patients with large cystic lesions in the upper and lower jaw, respectively, whose bone defects after cystectomy were filled with by autologous fibrin rich blocks containing CGF.

## Case report

### Case 1

Male patient, aged 54, was presented to the Department of Oral Surgery, Clinic for Dentistry of Vojvodina, with pain and swelling in the anterior lower jaw region. Clinical examination revealed swelling in the lower vestibule, painful and fluctuant to palpation. Mild luxation of the central and lateral incisors was observed (Figure 1). Subsequent to the clinical examination, orthopantomography (OPT) and cone-beam computed tomography (CBCT) scans were taken, showing a 5 cm clearly demarcated oval radiolucency, localized in the anterior region of the lower jaw (Figure 2), and indicating massive bone destruction on the vestibular side of the mandible, with the preserved lingual bony structures.



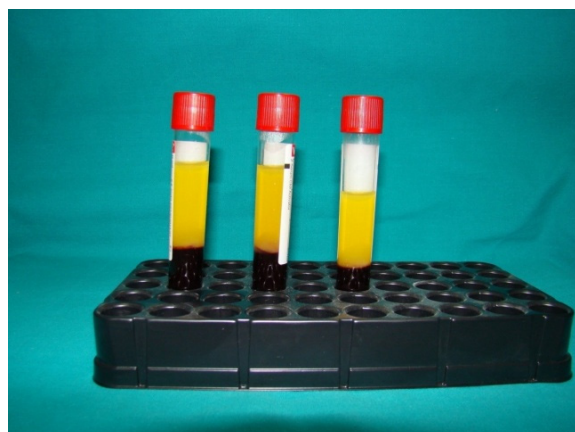
**Fig. 1 – Intraoral finding (mild luxation of the central and lateral incisors).**



**Fig. 2 – Cone-beam computed tomography scan with 3D projection of the mandible.**

The planned surgical treatment included immobilization of the affected teeth by orthodontic splint, complete removal of pathological process, resection of the affected teeth and filling the defect with fibrin rich blocs containing CGF.

Fibrin blocks with CGF were made immediately before the surgical procedure from patient's blood sample (total volume 60 mL), which was distributed into six sterile 10 ccm tubes without chemical additives. The tubes were immediately centrifuged for 14 min at 2,500 rpm (Figure 3). After centrifugation, the tubes were left for 20 min until further processing. 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. Isolated CGF were obtained by pouring off the serum and careful harvesting the middle and lower coagulated layers. In a sterile Petridish, the fibrin block was separated from blood corpuscles with scissors to obtain the pure CGF block, which was ready to be used<sup>12</sup>.



**Fig. 3 – Tubes after centrifugation (fibrin blocks with concentrated growth factors).**

Subsequent to preparing the CGF block, surgical procedure was performed under local anesthesia. After creating a sulcular flap between both lower second premolars, alternating blunt and sharp dissection was applied to separate and remove the cystic lesion from bone. Following cystectomy, root resection of the affected teeth was done. The resulting bone defect was restored by placing six fibrin-rich blocks with CGF, which completely filled the bone cavity (Figure 4). Finally, the flap was sutured in place with silk sutures.



**Fig. 4 – Bone defect filled with concentrated growth factors.**

After surgery, the patient was instructed about appropriate hygienic-dietary regimen. A combination of clindamycin and metronidazole was prescribed. Postoperative course passed without complications and sutures were removed 7 days later. During the following six months, a uniform and steady filling of the defect by newly formed bone was recorded.

## Case 2

A female patient, aged 42, was referred to the Department of Oral Surgery, Clinic of Dentistry of Vojvodina by her polyvalent dentist, for surgical treatment before prosthodontic rehabilitation. Although the patient did not have subjective problems, OPT scan revealed large round radiolucency 4 cm in diameter, extending distally towards the right maxillary sinus and cranially towards hard palate. Clinical examination revealed mild swelling in the anterior upper labial sulcus, insensitive to palpation. The mucosa above the swelling was regular in color and moisture. The teeth 11 to 13 were non-vital. A 3D CBCT scan revealed massive destruction of the upper jaw in the aforementioned region and interrupted communication towards the right maxillary sinus and nasal cavity (Figure 5).

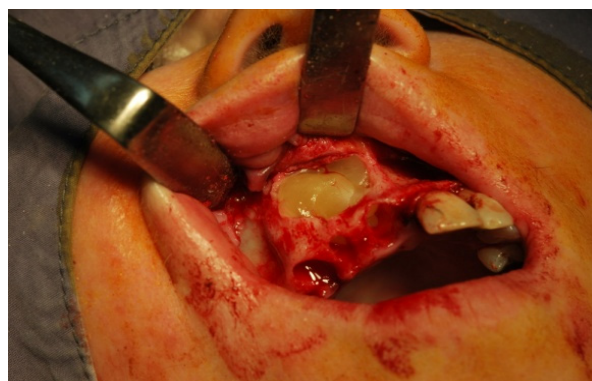


**Fig. 5 – Cone-beam computed tomography scan and 3D projection of the maxilla.**

After discussing the options of surgical treatment with the patient, who worried a lot about the pathological process and treatment outcome, we decided to extract the affected te-

eth, completely remove the pathological process applying closed surgery and restore the defect with fibrin-rich blocs with CGF. Fibrin-rich blocks with CGFs were made immediately before surgery as previously described, using five 10 ccm tubes. A full-thickness sulcular mucoperiosteal flap was made from teeth 23–17 on contralateral side in order to ensure better visibility of the operative field. After lifting the mucoperiosteal flap, osteotomy was performed on the frontal side of the maxilla above the pathological change. The pathological change was entirely removed with caution, applying blunt and sharp dissection, completely preserving sinus and nasal mucosa. The resulting bone defect was entirely filled out with CGF blocks and the flap sutured back in place (Figure 6).

The patient was prescribed a combination of clindamycin and metronidazole as the previous patient, and instructed about appropriate hygienic-dietary regimen. Sutures were removed 7 days later. During the following six months, a complete recovery and almost full reconstruction of bone defect was recorded, and the patient underwent prosthetic restoration (Figure 7).



**Fig. 6 – Bone defect of the maxilla filled with concentrated growth factors.**



**Fig. 7 – The patient after prosthetic rehabilitation.**

## Discussion

Reconstruction of bony defects after removing large cystic lesions in the upper and lower jaw may, at times, be associated with problems. Contraction of the coagulum, serum extrusion, and formation of dead spaces, as well as a possibility of secondary infection, significantly interfere with reparatory and regenerative processes in the jaws. A number of



authors have addressed this issue, and a range of scientific papers and reports resulted from numerous clinical studies. Modern surgical protocols imply complete removal of cystic lesion, filling the resulting bony defect and primary wound closure. The principal dilemma of the surgeon is a way of bone defect reconstruction. According to the available literature, large bony defects are commonly filled and reconstructed with autotransplants obtained from the iliac ridge, ribs or donor sites in the oral cavity. Application of autotransplants enables primary wound healing, preservation of bone contours and its fast regeneration. However, a drawback of this approach is the need for additional surgical procedure, highly specialized personnel, general anesthesia and very high expenses<sup>2</sup>.

Application of growth factors in guided bone regeneration procedure has been well-known for long time. This procedure is of particular relevance to implantology, especially regarding diverse augmentation procedures, unfavorable anatomic conditions (horizontal and vertical augmentation, sinus lift etc.)<sup>5</sup>. CGF can be applied alone or mixed with bone autotransplants or other bone graft substitutes. The aforementioned indications represent small bony defects that can be easily reconstructed. The application of CGF alone in the reconstruction of large cystic defects has not yet been reported. The presented cases are a pioneering attempt of reconstructing and restoring bone defects of the upper and lower jaws thereby avoiding application of synthetic bone substitutes, secondary surgical procedures and chemical additi-

ves. The only method that is somewhat comparable with the presented cases is a lateral sinus lift procedure with filling dead spaces between the sinus mucosa and bony palate with pure CGF blocks. The published papers addressing this topic indicate that new bone tissue of satisfactory quality (density) and quantity is formed within 3–6 months, and is associated with minimum postoperative complications. Moreover, the procedure is economically acceptable to the patient<sup>11,12</sup>.

### Conclusion

Application of fibrin-rich block with concentrated growth factors is one of the most up-to-date methods for reconstruction of bone defects in the dentoalveolar region. Concentrated growth factors are applicable alone or mixed with a bone graft. The two cases presented in this paper, demonstrate their efficiency in significant shortening of bone-healing time, particularly in massive bone defects, reducing the incidence of postoperative relapse, alleviating the postoperative course and enabling better restitution of surrounding soft tissue structures. Apart from the aforementioned cases, concentrated growth factors are applicable in implantology and periodontology, with the aim of preventing disturbance of the bone and soft tissue architecture. The method is relatively simple, without risk of transmissible and allergic diseases, and economically feasible.

### R E F E R E N C E S

1. *Archer WH*. Oral maxillofacial surgery. 5th ed. Philadelphia: W.B. Saunders Co; 1975.
2. *Donoff B*. Manual of oral and maxillofacial surgery. St.Lois: Mosby Co; 1987.
3. *Vitezslav Z, Jindrich P, Vladislav M*. Bone defect of the facial skeleton-replacement with biomaterials. Biomed Papers 2003; 147(1): 51–6.
4. *Clark RA*. Fibrin and wound healing. Ann N Y Acad Sci 2001; 936: 355–67.
5. *Lazić Z, Bubalo M, Petković-Curvin A, Dukat M, Mibajlović B*. Therapeutic use of platelet-rich plasma in oral surgery. Vojnosanit Pregl 2009; 66(10): 821–5. (Serbian)
6. *Plachokova AS, Nikolidakis D, Mulder J, Jansen JA, Creugers NH*. Effect of platelet-rich plasma on bone regeneration in dentistry: a systematic review. Clin Oral Implants Res 2008; 19(6): 539–45.
7. *Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR*. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 85(6): 638–46.
8. *Choukroun J, Adda F, Schoeffler C, Vervelle A*. Une opportunité en parodontologie: le PRF. Implantodontie 2000; 42: 55–62.
9. *Choukroun J, Diss A, Simonpieri A, Girard M, 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.
10. *Choukroun J, Diss A, Simonpieri A, Girard M, Schoeffler C, Dohan SL, et al*. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006; 101(3): 299–303.
11. *Sohn DS, Moon JW, Moon YS, Park JS, Jung HS*. The use of concentrated growth(CGF) for sinus augmentation. J Oral Implant 2009; 38: 25–38.
12. *Mirković S, Đurđević-Mirković T, Petrović L, Božić D*. The use of concentrate growth factors in guided bone regeneration after lateral sinus lift procedure (case report). HealthMED 2013; 7(2): 700–4.

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