CASE REPORT

The effect of plasma rich in growth factors in bone augmentation after sinus lift complications: a case report

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Abstract

The case report describes a sinus membrane elevation procedure, where the augmentation was performed exclusively with plasma rich in growth factors (PRGF) and fibrin clot, followed by osseous regeneration at eight months. The patient exhibited a marked osseous atrophy in the premolar–molar area of the left superior alveolar process. Initially, we performed a sinus membrane elevation, with autologous bone on the sinus floor and bovine bone, followed by horizontal augmentation with autologous bone harvested from the mandibular ramus. The fragments were covered with PRGF and fibrin clot. Implants were inserted six months post-intervention, but due to the insertion high speed, a vestibular abscess occurred three months later. The implants and sinus graft were removed; after curettage, the sinus was filled with PRGF and fibrin clot. Eight months later, we observed the bone regeneration and the implants were reinserted. Along with implant insertion, bone was harvested for histological examination. Microscopically, the bone formation was revealed in the sinus, with differences between crestal and apical zones. The bone remodeling process was more advanced in the crestal zone compared with the apical zone. Bone regeneration was complete, and the bone density allowed the implant insertion with appropriate primary stability. Four months after implant insertion, the panoramic radiography and cone-beam computed tomography (CBCT) confirmed the implant osseointegration. Results obtained after using PRGF and fibrin clot alone as osseous addition materials in sinus lifting are highly promising, but in order to draw scientifically reasoned conclusions, further clinical studies are required.

Keywords: growth factors, sinus elevation, alveolar ridge augmentation, osseointegration.

Introduction

Progressive atrophy of the alveolar bone begins shortly after extraction, leading to a reduction in volume and density of the alveolar bone, along with soft tissue atrophy [1, 2]. Tooth loss in the posterior area of the maxilla is initially followed by a reduction in bone thickness [2]. The reduced height of bone, in the posterior maxilla, is caused not only by osseous crest atrophy but also by maxillary sinus pneumatization [2–5]. Through transversal atrophy of the bone, the osseous crest will have a medial position in relation to the central fossa of the mandibular teeth, which prevents the insertion of the implant in a correct position, concerning the interocclusal relationship [2, 5]. Various classifications aimed to describe bone resorption in the posterior maxilla and consequently the therapeutic options. However, when horizontal and/or vertical bone loss is present, sinus lift alone is not enough to avoid restorations which overload posterior implants and produce high tension in the bone. Osseous expansion, directed bone regeneration, horizontal and/or vertical augmentation with autologous bone blocks are surgical techniques utilized in these situations [2, 4–8]. Grafting materials used in sinus lift can range from autologous bone to allograft, xenograft and alloplastic, each with their advantages and disadvantages [2, 4, 5, 7, 9]. Nevertheless, even if it is a debatable subject, sinus lift with lateral approach can be performed without any grafting material [4, 10–12]. On the other hand, clinical studies accompanied by histological examination showed that the use of platelet-rich plasma (PRP) in sinus lift, where autologous bone, allografts, xenografts and alloplastic were used as grafts, determined an increased rate of bone formation and the amount of bone formed into the sinus [4, 5, 7, 13, 14].

The objective of the study was to assess the regeneration processes in bone augmentation using plasma rich in growth factors (PRGF) and fibrin clot after the dental implants explantation and sinus lift. These aspects were studied and exposed on the basis of a case report. The particularities of the case were represented by: (i) the infectious complication (vestibular abscess) that occurred after implants insertion and sinus lift, and consequently the surgical stage was compromised; (ii) although it would have been necessary to perform the explantation of the
dental implants and removal of previously inserted bone
graft materials, the use of autologous PRGF and fibrin clot
for bone regeneration proved to be beneficial for the
primary stability of dental implants (subsequently reinserted
after the regenerative processes were stabilized). The
novelty of the presented case resides in the success of
the therapy applied in the conditions of a site that had
experienced local inflammatory and infectious processes.

Case presentation

The patient, E.F., a 54-years-old female, non-smoker,
presented in private surgery, in April 2015, with a high
bone atrophy in the posterior area of the superior left
maxilla, accompanied by sinus pneumatization and bone
width reduction due to an old edentation (Figure 1).

Patient’s informed consent was obtained for the
following medical procedures.

The bone height value, detected on cone-beam computed
tomography (CBCT), was 4.27 mm in tooth 2.5 area and
4.67 mm in tooth 2.6 area, while its thickness on this sector
(distally from tooth 2.3 area) was between 2.5 mm and
3 mm. The following medication was prescribed to
the patient: antibiotic, Amoxicillin + Clavulanic Acid
(Augmentin 1 g, GlaxoSmithKline Beecham®), one day
prior to and five days after intervention, anti-inflammatory
and analgesic Naproxen and Esomeprazole (Vimovo
500/20 mg, Astra Zeneca®), one hour before surgery
and 3–4 days post-intervention (two tablets/day). Prior
to surgery, 80 mL of blood were withdrawn from the
cephalic median vein using Sodium Citrate as an anti-
coagulant, in order to prepare PRGF. After anesthesia of
the superior and posterior alveolar nerves and anterior
palatine nerve (Ubistesin forte, 3M®), we proceeded to
sinus lift. The surgical approach of the left posterior
maxilla was effectuated through an incision along the
palatine crest, starting from the distal face of the canine
up to the maxillary tuberosity. A releasing incision was
performed distally to the canine and a mucoperiosteal
flap was lifted. After removing the fibrous tissue, we cut
a lateral access window in the sinus, using ultrasound
surgery (VarioSurg, NSK®), while irrigating with sterile
saline solution. The bone was gradually cut up to the
Schneiderian membrane, and then the osseous wall was
carefully detached from the sinus membrane and placed
in PRGF (fraction 2).

The sinus membrane was detached from the osseous
walls and then lifted, highlighting a narrow sinus and a
thin osseous crest. Horizontal augmentation of the osseous
crest was performed with autologous bone harvested from
the mandibular ascending ramus. The two thin bone blocks
were firmly fixed on the vestibular part, each with two
osteosynthesis screws (Stoma®), leaving a space between
them and the vestibular face. The space was filled with
moderately condensed cortical-spongy mixture (mainly
cortical and less cancellous bone) of autologous bone.
The same mixture of cortical-spongy bone was placed on
the bottom of the sinus and then covered with a mixture of
inorganic bovine bone (Bioteck®), maintained in PRGF
throughout the intervention and activated with 10% CaCl2
before usage.

The fibrin membrane was placed on the lifted sinus
membrane and the original osseous window was placed
back to its initial anatomical position, fixed by a 30°
rotation, thus obtaining primary stability. Finally, the
window and the autologous bone used for horizontal
augmentation were covered with autologous fibrin. We
performed the horizontal mattress suture technique, using
a 4-0 resorbable monofilament (Resorba®) thread (Figure 2).

After six months, upon lifting the flap, we noticed an
adequate bone width and autologous graft integration
(the graft presented a reddish color), which allowed bone
drilling for implant insertion. PRGF (activated fraction 2)
was injected into the drilled spaces (Figure 3), using the
same solution to moisten the implants before insertion
(Universal Platform Implants Ø 3.5 mm, length 13 mm

Figure 1 – CBCT: Vertical and horizontal bone loss in the left posterior maxilla. CBCT: Cone-beam computed
tomography.
for tooth 2.4, 10 mm for tooth 2.5 and Universal Plus Implant Ø 5 mm and 10 mm length for tooth 2.6, BTI®). After implants placement, the entire wound was covered with fibrin membrane (Figure 3).

Figure 2 – Steps in the sinus lift procedure: (A) Sinus elevation and narrow crest can be noticed; (B) Grafted bone from the mandibular ascending ramus fixed each with two osteosynthesis screws and adapted to the narrow crest; (C) Filling the gap between the cortical bone and narrow crest with cortical-spongy mixture autologous bone from mandibular ascending ramus; (D) Sinus augmentation with cortical-spongy mixture autologous bone and bovine bone; (E) Sinus laterally window covering the grafted material; (F) Covering the entire graft with fibrin membrane; (G) Mattress suturing of the flap.

Figure 3 – Insertion of Titanium implants: (A) Bone graft integration after six months; (B) Reddish bone after drilling into the grafted bone; (C) PRGF activated fraction 2 filling the implant hole; (D) Implant insertion into the grafted bone; (E) Covering the wound with fibrin membrane; (F) Panoramic X-ray image after three months of implants placement. PRGF: Plasma rich in growth factors.
The new bone was mainly trabecular in the entire specimen, but some differences between the zones could be noticed; in the coronal zone, there was a layer of calcified tissue resembling compact bone in both aspect and density, although it was not yet organized as typical osteons (Figure 6A). Contrarily, in the apical zone, the newly formed bone had the typical aspect of the trabecular osteons (Figure 6A). The lamellar bone exhibited orderly arrangement of the collagen fibers, higher mineral density in the matrix and flattened osteocytes with their short axis parallel to the collagen fibers and the morphology of the osteocytes. The lamellar bone was also observed in the apical zone, but the ratio was approximately 2:1, suggesting that remodeling was less pronounced (Figure 8C). The same tendency to form osteons was seen in the trabecular bone that was continuous with the surface of the alveolar crest and extended into the depth; compared with the periosteal surface, the medullary spaces were larger, and the concentric arrangement of the lamellae was still not well defined (Figure 7, B and C).

Histological examination of the specimen harvested from the intervention area revealed new bone formation and the presence of both woven and lamellar bone. Moreover, ongoing remodeling and transition from woven, primary bone to lamellar, secondary bone could be observed.

However, there were significant differences regarding the stage of remodeling process, as well as the type of bone tissue, depending on the zone. Thus, two distinct zones were distinguished: the coronal zone corresponding to the cortical bone of the alveolar crest, representing about 1/3 of the alveolar process height, and the apical zone, the rest of 2/3, extending towards the maxillary sinus (Figure 6).

In both coronal and apical zone, there was an association of woven (primary, immature) bone and lamellar (secondary, mature) bone. The two types of bone could be differentiated based on particular features: the characteristic appearance of the bone matrix, the arrangement of the collagen fibers and the morphology of the osteocytes. The woven bone consisted of intertwined collagen fibers with a random orientation, large amounts of interfibrillar proteoglycans and acidic proteins, but lower mineral density in the matrix, and numerous isodiametric osteocytes. Lamellar bone exhibited orderly arrangement of the collagen fibers, higher mineral density in the matrix and flattened osteocytes with their short axis parallel to the thickness of the lamellae (Figures 7C and 8C).

By the amounts of woven and lamellar bone tissue, the intensity of the remodeling process could be assessed. Therefore, in the coronal zone, where the ratio woven bone/lamellar bone was approximately 1:1, the remodeling seemed to be more advanced (Figure 7C); in the apical zone, the ratio was approximately 2:1, suggesting that remodeling was less pronounced (Figure 8C).

Discussions

Various studies confirm that sinus lift can be performed without introducing any graft material [10–12, 15–17]. When the Schneiderian membrane is lifted, a blood clot forms between the sinus membrane and floor. This blood clot appears to be of crucial importance in bone formation and also maintaining the space between the sinus membrane and floor [15–17]. The exact mechanism of bone formation is not entirely understood. The osteoprogenitor potential of the Schneiderian membrane (cells in its structure, which determine bone formation) seems to have a key role [18, 19]. On the other hand, other researchers believe that the osteogenic potential is a characteristic of the maxillary sinus floor, particularly of the maxillary tuberosity and also the maxillary and mandibular periosteum. Their conclusion is based on the capacity of the maxillary and mandibular periosteum to form osseous structures after ectopic transplantation, on account of the cells that expressed osteogenic markers [11, 20].
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Figure 4 – Dental implants failure and xenograft material infection: (A) Bone resorption around the implant in position 2.5; (B) Wound aspect after total removal of implants in relation to teeth 2.5, 2.6 and infected grafting material; (C) Filling the entire bone defect with PRGF (fractions 1 & 2); (D and E) Panoramic X-ray and CBCT images at eight months after implants removal from positions 2.5, 2.6 and xenograft removal from sinus. PRGF: Plasma rich in growth factors; CBCT: Cone-beam computed tomography.

Figure 5 – Implants insertion in 2.5 and 2.6 positions at eight months after filling bone defect with PRGF: (A) Bone healing at eight months; (B) Implant bed preparation with a trephine bar and concomitant bone harvesting for histological assessment; (C) Harvesting second bone from the place of the third removed implant for histological assessment; (D) Second and third implant inserted at the same place of the implants were removed; (E) Covering the entire wound with fibrin membrane; (F and G) Panoramic X-ray and CBCT images taken after four months of implants placement in the same place of initial implants; (H) Intraoperative image of implants osseointegration after four months. PRGF: Plasma rich in growth factors; CBCT: Cone-beam computed tomography.
Figure 6 – (A–C) The new bone formed in the intervention area: (A) The coronal zone contained dense bone tissue consisting of bone lamellae oriented in concentric layers; (B) The apical zone contained trabecular bone – anastomosing network of bone trabeculae delimiting areoles (Goldner’s trichrome staining).

Figure 7 – High density bone in the coronal zone: (A and B) Bone lamellae showing tendency to organize into concentric layers to form osteons in the periosteal surface of the alveolar crest and in the deeper area (arrows); (C) Proportion between woven bone (thin arrows) and lamellar bone (thick arrows) (Goldner’s trichrome staining).

Figure 8 – Trabecular bone in the apical zone: (A) Short anastomosing trabeculae delimiting large areoles; (B) Bone lamellae organized in parallel bundles at the surface of the areoles; (C) Proportion between woven bone (thin arrows) and lamellar bone (thick arrows) (Goldner’s trichrome staining).
What happened, in fact, in this particular case? Because of the infection, a vigorous curettage of the osseous sinus walls and floor was necessary, with a consecutive bleeding, for stimulating its osteogenic capacity. The autologous osseointegrated bone preserved the sinus membrane in an elevated position after removal of the infected osseous graft material. In this context, the clot (formed out of fraction 2 – PRGF and fraction 1 – fibrin), which was introduced in the sinus through a small access window, was maintained inside the sinus cavity. Moreover, the blood clot alone has osteoconductive properties [11]. It is worth pointing out that one study obtained good results with blood harvested from a peripheral vein, which led to bone formation when introduced into the sinus after sinus membrane elevation [21]. Platelets and later neutrophils and macrophages, which accumulate in the blood clot, are a source of growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), as well as a large spectrum of other bioactive molecules. PDGF has a mitogenic and chemoattractant potential for osteogenic cells and can temporarily suppress their differentiation. PDGF induces blood vessel formation and acts synergistically with VEGF and bFGF in this process [4]. A simple rationale would be that, if such promising results were obtained after employing blood clot only, using PRGF should lead to much better results given the fact that growth factor concentration is two to three times higher than the peripheral blood. Furthermore, PRGF is free from leukocytes, which, in an inflammatory environment, are able to secrete pro-inflammatory cytokines, enzymes and reactive oxygen species; these molecules have harmful effects on tissues and increase the inflammatory response [14].

The repairing process at the site of drilling for implant insertion is similar to the healing of extraction wounds: firstly, an immature, woven bone is formed, which is later replaced by mature, lamellar bone [22–25].

During the formation of woven bone, the mesenchymal cells located in the medullary spaces differentiate into osteogenic cells that line the bone trabeculae. In richly vascular areas, the osteogenic cells give rise to osteoblasts, which form bone matrix and promote the growth of bone trabeculae. In areas with poor capillary blood supply, they form chondroblasts which lay down cartilage [26, 27]. In the present case, the numerous blood vessels that were identified in the areoles sustained the differentiation of the mesenchymal cells into bone forming cells and thus promoted the bone tissue development, without cartilage formation.

In our study protocol, PRGF was selected among the PRP preparations for application in combination with autologous bone in the sinus lift for implant surgery, taking into consideration that the growth factors contained in PRGF stimulate the osteogenic potential of cells at the receiving site [28–30].

PRGF technology enables the effective use of therapeutic potential of platelets and endogenous fibrin and contains growth factors that initiate local regeneration and increase tissue vascularization [29–32].

The areoles in the apical zone contained no significant inflammatory infiltrate, suggesting that the bone formation occurred physiologically, without any inflammatory complications. Since both PRGF and bone were autologous products, the immune reactions were circumvented; moreover, the absence of leukocytes minimized the local concentration of leukocyte-derived pro-inflammatory factors and prevented significant inflammatory reaction at the intervention site.

Another important observation was that in only eight months, the entire intervention area was occupied by bone tissue, suggesting that the repairing processes progressed adequately, with direct formation of bone tissue. An explanation may be that PRGF contains VEGF, a factor that enables the proliferation of endothelial cells and promotes neo-vascularization [29, 33]. Moreover, the formation of the new bone occurred physiologically, with the predominance of lamellar bone and well organized trabeculae; moreover, the regenerated bone had the typical topographical morphology, namely a dense bone tissue on the periosteal surface of the alveolar crest and polymorphic trabeculae in the profound zone.

From structural point of view, the immature woven bone was undergoing remodeling towards mature lamellar bone, both in the superficial zone, where there was a definite tendency to organize into concentric arrays characteristic of compact bone (the osteon formation) and in the profound zone, where bone organized to form trabeculae delimiting the areoles with bone marrow. More advanced remodeling in the cortical bone and the superficial part of the alveolar crest is an advantage because this zone is crucial for implant insertion.

Regarding the quality and quantity of bone tissue at the intervention site, our results are consistent with the preliminary results reported by other clinical and experimental studies. Anitua indicating that PRGF induced the formation of increased amount of mineralized cancellous bone at 10–16 weeks after tooth extraction in humans [28]. An experimental study on rabbits conducted by Molina-Milano et al. reported a higher regeneration in bone defects filled with a combination of autologous bone and PRGF after one and two months, but without significant differences compared with the control [33]. Moreover, PRGF has proven its usefulness in patients with poor bone quality such as smokers who underwent immediate implant placement after extraction. The implants stability improved and the postoperative pain and swelling was reduced [34].

The results of our study are supported by the findings reported by Pal et al. in a study on 100 patients. The dental implants were immediately inserted into infected sockets; the application of the two-time use of PRGF method was superior to the one-time use of PRGF for the stability of dental implants [35]. The novelty of our case resides in the use of PRGF and fibrin clot in the treatment of infectious complications that may occur along implant treatment. Various researchers reported the antimicrobial properties of both platelets and different preparations from PRP [36]. This property is ensured by the release agents, among which we mention: thrombocidins, platelet...
microbicidal proteins (PMPs), platelet factor-4 (PF-4), regulated on activation, normal T-cell expressed and secreted (RANTES), connective tissue activating peptide 3 (immunomodulatory agents with antimicrobial activity) [36]. PRGF possesses an antimicrobial action on four Staphylococcus strains, reaching its maximum effect in the first hours after application [36]. Other studies also confirm that activated platelets, dynamically participate in antimicrobial defense [37–39].

The particular features of the therapeutic method applied in this case were the bone regeneration in the post-explanted and infected sites and the association with the maxillary sinus augmentation procedure complicated with vestibular abscess. The use of PRGF and fibrin clot allowed the re-insertion of dental implants into the same sites and positions, thereby achieving the primary stability of dental implants.

Conclusions

Sinus membrane elevation grafting with only PRGF and fibrin membrane had significant advantages inducing the bone formation within eight months, while sinus membrane tenting was maintained. Histological examination revealed well-consolidated bone trabeculae that enabled the insertion of implants. However, additional long-term clinical data regarding implants inserted at the same time as sinus elevation and PRGF use as a grafting material are needed to draw a more definitive conclusion.

Conflict of interests

The authors declare that they have no conflict of interests.

References


[34] Gangwar S, Pal US, Singh S, Singh RK, Singh V, Kumar L. Immediately placed dental implants in smokers with plasma rich in growth factor versus without plasma rich in growth
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