Regenerating a vertical bone defect consequent to peri-implantitis: a GBR case with an equine enzyme-treated bone substitute and a resorbable equine collagen membrane

Rigjenerimi i nje defekti vertikal te kockes konsekuent i peri-implantit: nje rast GBR me nje zevendesues kocke te trajtuar me enzime ekuine dhe nje membrane kolagjeni te riabsorbueshme ekuine (me origjine nga kali)

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Running title: Managing a vertical bone defect consequent to peri-implantitis.

Keywords: peri-implantitis, bone substitutes, collagen membrane, guided bone regeneration

ABSTRACT

Objective. Peri-implantitis leads to gradual peri-implant bone loss. The aim of the present report is to report a case where a vertical bone defect, caused by peri-implantitis, was managed successfully by vertical GBR with an equine bone graft and equine collagen membranes. ***Methods.*** A patient already rehabilitated with an implant/tooth-supported bridge presented with severe bleeding on probing and vertical bone loss. After periodontal/peri-implant probing and intraoral X-ray evaluation, a peri-implantitis was diagnosed. A treatment plan was carried out, calling for the extraction of an adjacent lost element, soft tissue healing, fixture decontamination and vertical GBR. Controls followed at 1, 8 and 12 months after regenerative surgery. At 8 months a second implant was placed and the patient definitively rehabilitated. ***Results.*** Radiographic exams at 8 and 12 months showed radio-opacity at the grafted sites to gradually increase over time and bone levels preservation. The regenerated bone allowed for the successful insertion and osseointegration of the second implant. ***Conclusions.*** When vertical GBR is performed according to a strict, detailed protocol it can be successfully applied to manage also bone loss due to peri-implantitis. Using an equine enzyme-deantigenic bone graft may be helpful in achieving the formation of proper newly-formed bone that could allow fixture osseointegration. Its association with resorbable collagen membranes spares the patient a second surgery. Further studies should be performed to investigate the association of these two biomaterials in the management of vertical bone loss due to peri-implantitis according to GBR principles.

INTRODUCTION

Peri-implantitis is a biological complication of implant therapy, involving inflammation of soft tissue around the implant and the gradual loss of marginal bone around the fixture[1,2]. Etiology of peri-implantitis is related to bacterial plaque accumulation, beginning already at implant uncovering, and the consequent development of inflammation[3]. This reversible condition, if left untreated, may lead to the progressive destruction of the tissues supporting the implant and ultimately to its failure[4]. When bone resorption reaches the implant apical end the endosseous stability, and therefore the fixture, are lost[5].
Bleeding on probing is usually the first detectable sign of peri-implantitis[4,6]. Additional symptoms are much less frequent and comprise suppuration, mucosal recession and swelling of the peri-implant mucosa. Diagnosis is confirmed when, in addition to bleeding, peri-implant probing depth is ≥5 mm and peri-implant bone resorption is ≥2 mm[7].

Fjale kyce: peri-implantit, zevendesues kocke, membrane kolagjeni, rigjenerimi i guiduar i kockes

ABSTRAKTI

Objektivi. Peri-implantiti çon në humbje peri - implantare graduale te kockave. Qëllimi i këtij raporti është te raportoje një rast ku defekti vertikal i kockës , i shkaktuar nga peri - implantiti , u menaxhua me sukses nga GBR-ja vertikale me një graft kockor ekuin (me origjine kali) dhe membrana kolagjeni ekuine. ***Metoda.*** Pacienti i rehabilituar me një ure te mbeshtetur mbi implant paraqet gjakderdhje të rënda ne sondim dhe humbje vertikale te kockes. Pas sondimit periodontal / peri – implantar dhe pas vlerësimit me rreze X intraoral, eshte diagnostikuar nje peri-implantit. Nje plan trajtimi eshte hartuar, qe parashikon ekstraksionin e një elementi fqinje te humbur, shërimin e indeve të buta, dekontaminimin e fixture dhe GbR-ja vertikale. Kontrollet ndiqen në 1 , 8 dhe 12 muaj pas kirurgjise rigjeneruese. Per 8 muaj nje implant i dyte eshte vendosur dhe pacienti eshte rehabilituar perfundimisht. ***Rezultatet.*** Testet radiografike ne 8 dhe 12 muaj shfaqen radioopacitet ne zonat e grafteve qe gradualisht rritej me kalimin e kohes dhe nivele kockore te ruajtura. Kocka e rigjeneruar lejonte inserimin e suksesshem dhe osteointegrimin e implantit te dyte. ***Konkluzione.*** Kur kryhet GBR-ja vertikale sipas nje protokolli strikt dhe te detajuar, mund te aplikohet me sukses per te menaxhuar humbjen e kockes nga peri-implantiti. Te perdoresh nje graft kockor ekuin te trajtuar me enzima mund te jete i dobishem ne marrjen e nje formacioni kocke te re per te qene, qe mund te lejoje osteointegrimin e fixture. Shoqerimi i tij me nje membrane kolagjeni te riabsorbueshme i kursen pacientit nje kirurgji te dyte. Studime te metejshme duhet te kryhen per te hetuar lidhjen e ketyre dy biomaterialeve ne menaxhimin e humbjes vertikale te kockes nga peri-implantiti sipas parimeve te GBR-se.

HYRJE

Peri-implantiti eshte nje komplikim biologjik i terapise implantare, qe perfshin inflamacionin e indit te bute perreth implantit dhe humbjen graduale te kockes marginale perreth fixture. Etiologjia e peri-implantitit eshte e lidhur me akumulimin e pllakes bakteriale, qe fillon ne pjesen e zbuluar te implantit dhe si rrjedhoje zhvillimin e inflamacionit. Kjo gjendje e kthyeshme, nese lihet patrajtuar, mund te coje ne shkaterrimin progresiv te indeve qe mbeshtesin implantin dhe si perfundim ne deshtim te implantit. Kur rezorbimi i kockes arrin fundin apikal te implantit stabiliteti endooseal dhe si rrjedhoje fixture humbasin.
Gjakderdhja gjate sondimit eshte ndoshta shenja e pare e dallueshme e peri-implantitit. Simptoma shoqeruese jane shume me te rralla, dhe perfshijne supuracion, recesion dhe enjtje te mukozes peri-implantare. Diagnoza eshte konfirmuar kur pervec gjakderdhjes, thellesia e sondimit te peri-implantitit eshte ≥5 mm dhe rezorbimi i kockes peri-implantare eshte ≥2 mm[7].
Debati per trajtimin me efektiv te peri-implantitit eshte akoma i

The debate on the most effective treatment of peri-implantitis is still ongoing, as it was underlined in the last Cochrane Group meta-analysis[8] comparing: use of local antibiotics versus ultrasonic debridement, the benefits of adjunctive local antibiotics to debridement; different techniques of sub-gingival debridement; laser versus manual debridement and chlorhexidine irrigation/ gel, systemic antibiotics plus resective surgery plus two different local antibiotics with and without implant surface smoothening and nanocrystalline hydroxyapatite versus deproteinized bovine bone and resorbable barriers. Conclusions of such meta-analysis still leave the main question unanswered, and doubts still remain if a surgical approach should be preferred to non-surgical ones, as no prospective studies are available comparing the two. Concerning the surgical approach involving bone regeneration by grafting bone substitutes, encouraging results were observed. When deproteinized bovine bone was grafted, a significant probing depth reduction was observed ranging from 2.6 mm at 6 months[9] to 5.1/ 5.4 mm after 3-7.5 years[10]. Yet, current clinical literature does not provide indications about the kind of bone graft (i.e. synthetic, heterologous, homologous, autogenous) that should be preferred. Deproteinized bovine bone, for example, has good osteoconductive properties but may also display a low resorption capacity[11] implying a substantially different behaviour than autogenous bone as far as the resorption kinetic is concerned. Alternative xenografts have been devised with the aim of better mimicking the resorption of autogenous bone. Among these, one is an enzyme-treated form of equine bone. The enzymatic process used to clean this material may preserve type I bone collagen component in its native non-denatured state thanks to the selective use of digestive enzymes and a temperature process never high enough to cause substantial changes to some biological and mechanical properties of the origin material. These features should allow an improved bone-regeneration process, given the well-known biological properties of collagen, when preserved,[12-19] and the importance of unaltered apatite crystal features for cell adhesion. Indeed, when human osteoclasts were cultured over a collagen-preserving form of this equine, enzyme-treated bone substitute[20], their adhesion and activity was significantly higher than that the same cells displayed over deproteinized bovine bone[21]. This difference has been cited as one possible reason explaining why grafting sinuses with an enzyme-treated, equine bone graft caused greater new bone formation than grafting deproteinized, heat-treated bovine bone in a recent randomized clinical trial.[22] Given the well-known similarities of mammals as far as the bone apatite physical structure, micro- and macro-morphology, and collagen sequence homology are concerned[23], xenografts presenting one or more of these features preserved, should show a remodelling behaviour similar to that of autogenous bone. Indeed, when sites augmented with equine bone alone were compared to others augmented with the same material added with autogenous bone, immunohistochemical tests showed no differences between the two regarding the expression of some biochemical markers of bone regeneration[24].

Enzyme-deantigenic equine bone has already been used in the clinical practice as a scaffold in bone regeneration of different bone defects[22, 24-29], and has also been applied in orthopaedic regenerative surgery[30,31]. It has also been recently used to treat cases where of implant threads exposure [32], and to manage a severe case of peri-implantitis[33], allowing to save an implant that would have been probably lost otherwise. To our knowledge, the last work cited is the only case of peri-implantitis treatment with such bone substitutes that has been reported thus far. Additionally, in that case, no membrane was placed to cover the graft because of technical particularities of the approach applied. The aim of this study, therefore, is to present how a severe vertical bone defect, consequent to peri-implantitis, was treated by grafting an enzyme-deantigenic, equine bone graft after proper implant surface debridement and decontamination,

hapur, sic eshte theksuar ne meta-analizen e fundit te Cochrane Group duke krahasuar: perdorimin e antibiotikeve lokale kundrejt debridementit ultrasonik (heqja e indit te infektuar, te nekrotizuar), benefitet e antibiotikeve lokale shoqerues ndaj debridementit; teknika te ndryshme te debridementit subgingival; debridementi me lazer kundrejt atij manual dhe irrigimi/xheli me klorheksidine, antiobiotiket sistemike plus kirurgjia rezektive plus dy antibiotike te ndryshem lokale, me ose pa lemimin e siperfaqes se implantit dhe hidroksiapatit nanokristaline kundrejt kockes bovine te deproteinizuar dhe barrierave te rezorbueshme. Konkluzione te te tillave meta-analizave e lene serish pa pergjigje pyetjen kryesore, dhe dyshimet mbesin nese qasja kirurgjikale duhet preferuar ndaj asaj jokirurgjikale, duke qene se nuk ka studime prospektive qe ti krahasoje keto te dyja. Persa i perket qasjes kirurgjikale qe perfshin rigjenerimin e kockes nga graftet kockore zevendesuese, rezultate inkurajuese jane vene re. Kur kocka e bovines e deproteinizuar eshte graftuar, nje reduktim domethenes i thellesise se sondimit eshte vene re nga 2.6 mm ne 6 months[9] deri ne 5.1/ 5.4 mm pas 3-7.5 vitesh. Sidoqofte, literatura klinike aktuale nuk jep indikacione persa i perket tipit te graftit kockor qe duhet preferuar (sintetik, heterolog, homolog, autogen). Kocka e bovines e deproteinizuar, per shembull, ka veti te mira osteoinduktive por mund te shfaqe gjithashtu nje kapacitet te ulet rezorbimi duke implikuar nje sjellje ndryshe nga kocka autogjene persa i perket rezorbimit kinetik. Ksenografte alternative jane shpikur me qellim qe te imitojne me mire rezorbimin e kockes autogjene. Midis tyre, nje eshte forme e trajtuar me enzime e kockes ekuine. Proces enzimatik i perdorur per te pastruar kete material mund te ruaje tipin I te komponentit te kolagjenit kockor ne gjendjen e tij autoktone te padenatyruar fale perdorimit selektiv te enzimave digjestive dhe te nje procesi temperature asnjehere te larte mjaftueshem per te shkaktuar ndryshime te medha te vetive biologjike dhe mekanike te materialit te origjines. Keto veti duhet te lejojne nje proces rigjenerimi te permiresuar, duke marre parasysh vetite biologjike te kolagjenit, kur ruhen, dhe rendesine e vetite apatite te paprekura te kristalit per adezionin e qelizave. Ne fakt, kur osteoklastet njerezore jane mbjellur si kulture mbi nje forme te kesaj ekuine te prezervuar me kolagjen, zevendesuesja e kockes e trajtuar me enzime, adezioni i tyre dhe aktiviteti ka qene ne menyre domethenese me i larte se ai qe te njejtat qeliza shfaqen ndaj kockes bovine te deproteinizuar. Kjo diference eshte cituar si nje arsye e mundshme qe shpjegon pse sinuset e graftuara, me nje graft kocke ekuine te trajtuar me enzime, shkaktojne me teper formim te kockes se re se sa graftet e deproteinizuara, kocke bovine e trajtuar me nxehtesi, ne nje prove klinike te kryer se fundmi.

Duke marre parasysh ngjashmerite e njohura te mamaleve persa i perket struktures fizike apatite te kockes, mikro dhe makro morfologjise, dhe homologjise se sekuences se kolagjen, ksenograftet qe shfaqin nje ose me shume te ketyre vetive te ruajtura, duhet te tregojne nje sjellje rimodelimi te ngjashme me ate te kockes autogjene.

Në të vërtetë, kur vendet e augmentuara me vetëm kocke ekuine janë krahasuar me të tjerët te augmentuara me të njëjtin material te shtuar me kocke autogene, testet immunohistokimike nuk treguan dallimet në mes të dyve në lidhje me shprehjen e disa shënuesve biokimike të rigjenerimit kockor.

Kocka ekuine e trajtuar me enzima-deantigjenike tashmë është përdorur në praktikën klinike si një tribunë në rigjenerimin e difekteve te ndryshme kockave, dhe gjithashtu është zbatuar në kirurgjine ortopedike rigjeneruese. Ajo ka qenë gjithashtu e përdorur ne kohët e fundit për të trajtuar rastet kur kemi raste te ekspozimit te implantit, dhe per te menaxhuar një rast të rëndë të peri-implantitit, duke lejuar të ruhet një implant që do të kishte qenë ndoshta i humbur. Ne njohurine tone, puna e fundit e cituar është e vetmi rast i trajtimi te peri-implantitit me zëvendësues të tilla kockave që ka qenë i raportuar deri tani. Përveç kësaj, në këtë rast, nuk ka membrane te vendosur për të mbuluar graftin për shkak të veçantive teknike të qasjes

applying concomitantly resorbable equine collagen membranes as a protection.

MATERIALS AND METHODS

A 55 female year-old patient with no past medical history, rehabilitated with a fixed bridge from teeth 1.1 to 1.3, supported by an implant at 1.2, presented for periodical controls showing – at periodontal/peri-implant probing and intraoral X-ray examination – with an appearance consistent with severe perimplantitis around the implant at 1.2 (Figure 1). Peri-implant probing depths were measured at six points around the implant (three on the buccal side/three on the palatal side) and averaged. Average probing depth was 5.3 mm. (min. 4.0 mm./max. 6.0 mm.). Tooth 1.1 was deemed lost and was extracted. After soft tissue healing, still profuse class 3 bleeding on probing[4] around the implant at 1.2 and vertical volumetric loss were observed (Figure 2).

Therefore, a procedure calling for implant debridement and bone regeneration of the bone defect, followed – after bone healing – by the placement of a second fixture, was proposed. The patient gave her informed consent.

Antibiotic prophylaxis (Amoxicillin/Clavulanic acid, Augmentin, Glaxo-SmithKline, Verona, Italy), 2 g, 1 hour before surgery and then 1 g every 12 hours for 6 days, was initiated and the patient was subjected to a mouth rinse with Chlorhexidine 0.2% (Corsodyl, Glaxo-SmithKline, Verona, Italy) for one minute, and instructed to perform mouth rinses with Chlorhexidine 0.2% (Corsodyl, Glaxo-SmithKline, Verona, Italy) once every 8 hours on the following 14 days. Pain management (Sodium naproxen, Synflex, Recordati, Milano, Italy), 550 mg, 1 hour before surgery and then every 12 hours for three days was also initiated. Local anaesthetic was administered by means of an infiltration with 1% Articaine with Adrenaline 1:100000. The tooth was extracted atraumatically (not shown) and complete soft tissue healing waited for. After performing antibiotic prophylaxis, pain management therapy and local anaesthesia as before, a full-thickness mucoperiosteal flap was detached to expose the underlying bone tissue, observing a vertical bone defect (Figure 3). The granulation tissue was debrided with hand curettes (Mini-Five Gracey, Hu-friedy, Chicago, Illinois, USA) and ultrasonic scaling tips. Surfaces were then decontaminated with a 83 mg/ml Tetracycline Chlorhydrate solution (Ambramicina, Scharper, Milano, Italy), for 10 minutes and a 3% Hydrogen Peroxide solution (Hydrogen Peroxide 3%, Pharma Trade Company, Brugherio, Monza Brianza, Italy). Receiving bone was further prepared by drilling it with a tungsten carbide round bur to favor bleeding and osteoprogenitor cells arrival. Collagen membranes (Biocollagen BCG-01, Bioteck, Arcugnano, Vicenza, Italy) were placed, still dry, on the palatal side of the defect to help granules containment (Figure 4a). The membranes stuck in the position they were placed thanks to the blood-collagen adhesive/hemostatic interaction, and no further fixation was needed. The defect was then grafted with a 1:1 cancellous-cortical mixture of enzyme-deantigenic equine granules (Bio-Gen Mix, BGM-05, Bioteck, Vicenza, Italy), after hydrating them for some minutes in sterile saline (Figure 4b). The membranes previously placed were then adapted to cover the defect, and an additional one was added to create a double protective layer. (Figure 4c).

Horizontal mattress suture, to create a first closure line, and single stitches to create a second one followed (Cytoplast PTFE Suture 4-0, Osteogenics Biomedical, Lubbock, USA) (Figure 5). The patient was recalled after eight days for suture removal, and controls followed at 1 and 8 months after surgery. Eight months after surgery, after patient preparation as previously described, a second implant was placed in position 1.1. A further follow up control followed at 12 months after the regenerative surgery, and the patient was finally rehabilitated.

së aplikuar. Qëllimi i këtij studimi, pra, është të paraqesë se si një defekt i rëndë vertikal i kockave, konsekuent i implantitit, u trajtua me nje kocke ekuine te trajtuar me enzime deantigjenike, pas debridementimit dhe dekontaminimit te siperfaqes se implantit, duke aplikuar njëkohësisht membrana te rezorbueshme te kolagjenit si një mbrojtje.

MATERIALE DHE METODA

Nje femer 55 vjece pa histori te shkuar mjekesore,rehabilitoi me nje ure fikse nga 1.1 te 1.3, mbeshtetur nga nje implant te 1.2, e shfaqur per kontrolle periodike- gjate sondimit periodontal-peri implantar dhe ekzaminimit me rreze X- me nje pamje konsistente dhe peri implantite te renda perreth implantit 1.2 (fig 1). Thellesia e sondimit te peri-implantitit eshte matur ne gjashte pika perreth implantit (tre ne anen bukale, tre ne anen palatinale) dhe eshte mesatarizuar. Thellesia mesatare e sondimit ishte 5.3 mm (min. 4.0 mm./max. 6.0 mm.). dhembi 1.1 eshte konsideruar i humbur dhe eshte ekstraktuar. Pas sherimit te indeve te buta, serish eshte vene re gjakderdhje ne klasen trete gjate sondimit rreth impantit te 1.2 dhe humbje vertikale volumetrike jane vene re. (figura2). Keshtu qe eshte propozuar nje procedure qe kerkon debridementin e implantit dhe rigjenerimin e kockes te defektit kockor, e ndjekur- pas sherimit te kockes- nga vendosja e nje fixture te dyte. Pacientja dhe konsentin e saj te informuar. Antibiotiku prophylaxis (Amoxicillin/Clavulanic acid, Augmentin, Glaxo-SmithKline, Verona, Italy), 2 g, eshte dhene nje ore para kirurgjise dhe me pas 1 g cdo 12 ore per 6 ditet e ardhshme, dhe pacienti perdori dhe shpelares goje Chlorhexidine 0.2% (Corsodyl, Glaxo-SmithKline, Verona, Italy) per 1 minute, dhe u udhezua ta perdorte shpelaresin cdo 8 ore ne 14 ditet e ardhshm. Menaxhimi i dhimbjes (Sodium naproxen, Synflex, Recordati, Milano, Italy), 550 mg, 1 ore para kirurgjise dhe me pas cdo 12 ore per 3 ditet ne vazhdim. Jane administruar anestetike lokale me infiltracion1% Articaine me Adrenaline 1:100000. Dhembi eshte ekstraktuar pa trauma dhe indet e buta u sheruan plotesisht. Pas perdorimit te antiobiotiko profilaksise, terapise se menaxhimit te dhimbjes dhe anestezise lokale, nje flap mukoperiostal i plote eshte shkeputur per te ekspozuar indin kockor nen te, duke vene re nje defekt vertikal te kockes. (figura 3). Indi I granulacionit eshte debriduar me kyreta (Mini-Five Gracey, Hu-friedy, Chicago, Illinois, USA) dhe maja ultrasonike. Siperfaqet me pas jane dekontaminuar me 83 mg/ml Tetracycline Chlorhydrate solucion (Ambramicina, Scharper, Milano, Italy), per 10 minuta dhe 3% solucion Hydrogen Peroxide (Hydrogen Peroxide 3%, Pharma Trade Company, Brugherio, Monza Brianza, Italy). Kocka me pas eshte preparuar duke e frezuar me nje freze karbidi tungsten te rrumbullaket per te favorizuar gjakderdhjen dhe ardhjen e qelizave osteoprogenitore. Membranat e kolagjenit (Biocollagen BCG-01, Bioteck, Arcugnano, Vicenza, Italy) jane vendosur, akoma te thata, ne pjesen palatinale te defektit per te ndihmuar kontrollin e granulave(Figure 4a). membranat qendrojne ne pozicionin qe jane vendosur ne saje te interaksionit gjak-kolagjen adeziv/ hemostatic, dhe nuk eshte I nevojshem nje fiksim I metejshem. Defekti me pas eshte graftuar me nje miksture kortikale-kanceloze 1:1 te granulave me enzime deantigjenike ekuine (Bio-Gen Mix, BGM-05, Bioteck, Vicenza, Italy), pasi jane hidratuar per disa minuta ne saline sterile(Figure 4b). membranat e vendosura me pare jane adaptuar per te mbuluar defektin, dhe nje membrane me teper eshte shtuar per te krijuar nje shtrese mbrojtese te dyfishte. (Figure 4c). Sutura horizontale dyshek, per te krijuar nje linje te pare te mbylljes, dhe qepje teke per te krijuar nje te dyte(Cytoplast PTFE Suture 4-0, Osteogenics Biomedical, Lubbock, USA) (Figure 5). Pacienti eshte thirrur pas 8 ditesh per heqjen e suturave, dhe kontrrollet jane kryer per 1 muaj dhe 8 muaj pas kirurgjise. 8 muaj pas kirurgjise, pas preparimit te pacientit sic eshte shpjeguar me siper, nje implant I dyte eshte vendosur ne pozicionin 1.1. Nje kontrroll I metejshem I kryer pas 12 muajshpas kirurgjise rigjeneruese, dhe pacienti eshte rehabilituar perfundimisht.

RESULTS

Healing after the regenerative surgery was uneventful. After eight months, intraoral X-ray showed the graft was integrated with the surrounding vital bone tissue (Figure 6) and bone levels recovered up to the implant neck. Additionally, radio-opacity – similar to that of the surrounding bone – suggested proper graft remodeling. No bleeding at probing around the implant was observed. Average peri-implant probing depth was 3.0 mm (min 3.0 / max. 3.0 mm). Bone healing was deemed sufficient to place an implant at position 1.1. Intraoral X-ray at 12 months from the regenerative surgery showed radio-opacity to increase at the grafted site (Figure 7) and proper osseointegration of the implant at position 1.1. Probing depths were unchanged. Bleeding was absent at both locations. Both implants were surrounded by bone tissue, reaching the first thread for the implant at 1.1 and being slightly more apical for the one at 1.2. Final rehabilitation followed.

DISCUSSION

The possibility of treating patients showing peri-implantitis and peri-implantitis-caused bone loss with a combination of implant surface detoxification and a vertical ridge augmentation procedure according to the principles of Guided Bone Regeneration (GBR) in association with titanium-reinforced e-PTFE membranes was proposed, since 1992, by different authors[34-36]. The present case was performed according to the technique presented by Tinti and Benfenati in 2001[36], using a resorbable collagen membrane instead of a non-resorbable one. A resorbable membrane does not call for removal, thus sparing an additional surgery to the patients. Results of the present case may be regarded as highly satisfactory. The peri-implantitis treatment and the concomitant bone grafting managed to stop bone resorption around the implant. Additionally, the grafted areas showed a gradual radio-opacity increase that was consistent with complete or nearly complete bone graft remodeling, and new bone formation. Accordingly, it could be observed that the resorbable membrane worked properly and allowed effective protection of the graft and exclusion of the soft tissues. It should be observed that the membrane was positioned in a double layer: this might have contributed to the result observed, having possibly increased the covering total resorption time. Such hypothesis should be tested in further cases, according to proper research protocols.

Significantly, new bone-implant contact was observed around both implants, suggesting the possibility of a new osseointegration process to have occurred. This is consistent with current knowledge about the remodeling properties of the bone graft being used, which is known to generate a significant amount of newly-formed bone[22] that, being vital, has theoretically the capability of osseointegrating again with implants already present. If *de novo* osseointegration really occurred around the two implants that could have happened because of the peculiar features of the bone substitute being grafted. Bone regeneration, in fact, could have possibly been facilitated by the use of a xenogeneic bone tissue not undergoing substantial modifications because of the mild treatment applied to make it biocompatible, confirming what was already observed in previous *in vitro*[20] and clinical studies where histological and histomorphometric analyses were performed[22,24,25,27].
Finally it should be observed that, even if the success of the present case might have been facilitated by the use of a physiologic remodeling graft, and the patient was spared additional surgery as a resorbable membrane was used, proper attention was paid – and should ever be paid – to following a strict surgical protocol as the predictability of a vertical GBR procedure is highly technique-sensitive[37]. Constant care, in fact, should be taken in avoiding membrane exposure, by managing flaps properly to achieve a tension-free suture.

REZULTATI

Sherimi pas kirurgjise rigjenerative ishte I qete. Pas 8 muajsh grafia me rreze x intraorale tregon qe grafti eshte integruar me indin kockor vital perreth (Figure 6) dhe nivelet e kockes u ngriten deri ne qafen e implantit. Per me teper radio-opaciteti – i ngjashem me ate te kockes perreth, tregonte rimodelim te mire te graftit. Nuk eshte vene re gjakderdhje perreth implantit gjate sondimit. Thellesia mesatare e sondimit rreth implantit eshte 3.0 mm (min 3.0 / max. 3.0 mm). Sherimi I kockes eshte vleresuar I mjaftueshem per te vendosur nje implant ne pozicionin 1.1. grafia intraorale x ne 12 muaj nga kirurgjia rigjenerative tregon radio-opacitet te rritur ne anen e graftuar. (fig 7) dhe osteointegrim te mire te implantit ne pozicionin 1.1. thellesite e sondimit mbeten te pandryshuara. Gjakderdhja mungonte ne te dyja vendndodhjet. Te dy implantet jane te rrethuara nga ind kockor, duke arritur fijen e pare per implantin 1.1 dhe duke qene lehtesisht me apikal per implantin 1.2. Rehabilitimi final ka pasuar.

DISKUTIM

Mundesia e trajtimit te pacienteve qe kane peri-implantit dhe peri-implantit qe shkakton humbje te kockes, me nje kombinim te detoksifikimit te siperfaqes se implantit dhe nje procedure augmentimi vertikale me kurriz sipas parimeve te Guided Bone Regeneration (GBR) ne asocijim me membranat titanium-reinforced e-PTFE, eshte propozuar qe ne 1992, nga autore te ndryshem. Rasti i tanishem eshte kryer sipas teknikes se paraqitur nga Tinti dhe Benfenati ne 2001, duke perdorur nje membrane te rezorbueshme kolagjeni ne vend te nje te parezorbueshme. Nje membrane e rezorbueshme nuk ka nevoje per tu hequr, duke i kursyer keshtu pacientit nje kirurgji shtese. Rezultatet e rastit prezent mund te vleresohen si shume te kenaqshme. Trajtimi i peri-implantitit dhe grafti kockor concomicant arriten te ndalojne rezorbimin e kockes perreth implantit. Per me teper, zona e graftuar tregon nje rritje graduale te radioopacitetit qe eshte e perbere totalisht ose pothuajse totalisht nga rimodelimi me graft i kockes, dhe formimi i ri i kockes. Sipas kesaj, mund te thuhet se membrana e rezorbueshme funksionoi sic duhet dhe lejoi mbrojtje efikase te graftit dhe ekskluzim te indeve te buta. Duhet vene re qe mebrana eshte vendosur ne shtrese te dyfishte, kjo mund te kete kontribuarne rezultatet e observuara, duke rritur ndoshta kohen totale te rezorbimit. Hipoteza te tilla duhen testuar ne raste te metejshme, sipas protokolleve te duhura kerkimore. Ne menyre domethenese, kontakti i ri kocke-implant eshte vene re perreth dy implanteve, duke sugjeruar mundesine e ndodhjes se nje procesi te ri osteointegrimi. Kjo eshte ne perputhje me njohurine aktuale persa I perket vetive te rimodelimit te graftit kockor te perdorur, qe eshte i ditur te prodhoje nje sasi domethenese te kockes se re te formuar, qe duke qene vitale, ka teorikisht aftesine e osteointegrimit serish, me implantet tashme prezente. Nese osteointegrimi de novo ndodhi vertet perreth dy implanteve, kjo mund te kete ndodhur per shkak te cilesive te vecanta te kockes zevendesuese qe eshte graftuar. Rigjenerimi i kockes, ne fakt, mund te jete lehtesuar nga perdorimi i kockes i kockes ksenogjenike qe nuk i eshte nenshtruar modifikimeve substanciale per shkak te trajtimit te bute te aplikuar per ta bere biokompatibel, duke konfirmuar cfare ka qene observuar me kohe ne in vitro-t e meparshme dhe studimet klinike ku analiza histologjike dhe histomorfometrike jane kryer.
Si perfundim duhet vene re qe megjithese suksesi i rastit prezent mund te jete lehtesuar nga perdorimi i graftit rimodelues fiziologjik, dhe pacientit i eshte kursyer kirurgji shtese duke qene se nje membrane e rezorbueshme eshte perdorur, nje vemendje e duhur i eshte kushtuar – dhe i duhet kushtuar gjithmone- per te ndjekur nje protokoll kirurgjikal strikt, duke qene se te parashikosh nje procedure vertikale GBR eshte nje teknike shume sensitive. Ne fakt, duhet patur kujdes te vazhdueshem per te shmangur ekspozimin e membranes, duke menaxhuar flapet sic duhet per te arritur nje suture pa tension.

CONCLUSIONS

When a GBR protocol is followed strictly, with proper attention to all procedural details, vertical regeneration may be effective to manage vertical bone loss caused by peri-implantitis. Grafting an enzyme-treated equine bone graft might help achieving proper bone regeneration. The use of a resorbable collagen membrane, applied in a double protective layer, may allow effective protection of the grafting sites and sparing additional surgery to the patient. Further studies should be performed to test the association of these two biomaterials in vertical bone regeneration, according to guided bone regeneration protocols, to restore bone loss caused by peri-implantitis.

KONKLUZIONE

Kur nje protokoll GBR-je eshte ndjekur ne menyre strikte, me nje vemendje te duhur ndaj gjithe detajeve proceduriale, rigjenerimi vertikal mund te jete efektiv per te menaxhuar humbjen vertikale te kockes te shkaktuar nga peri-implantiti. Te graftosh nje kocke ekuine te trajtuar me enzime mund te ndihmoje te arrish rigjenerimin e duhur kockor. Perdorimi i nje membrane te rezorbueshme kolagjeni, te aplikuar ne nje shtrese mbrojtese te dyfishte, mund te lejoje nje mbrojtje efektive te vendeve te graftuara dhe te kurseje kirurgji shtese per pacientin. Studime te metejeshme duhen kryer per te testuar asocijimin e ketyre dy biomaterialeve ne rigjenerimin vertikal kockor, sipas protokollit te guiduar te rigjenerimit kockor, per te kthyer humbjen e kockes te shkaktuar nga peri-implantiti.

REFERENCES

1. Algraffee H, Borumandi F, Cascarini L. Peri-implantitis. Br J Oral Maxillofac Surg. 2012 Dec;50(8):689-94
2. [No authors]. Peri-implant mucositis and peri-implantitis: a current understanding of their diagnoses and clinical implications. J Periodontol. 2013 Apr;84(4):436-43.
3. Pontoriero R, Tonelli MP, Carnevale G, Mombelli A, Nyman SR, Lang NP. Experimentally induced peri-implant mucositis. A clinical study in humans. Clin Oral Implants Res. 1994 Dec;5(4):254-9.
4. Mombelli A, Lang NP. The diagnosis and treatment of peri-implantitis. Periodontol 2000. 1998 Jun;17:63-76.
5. Klinge B: Peri-implant tissue destruction. The Third EAO Consensus Conference 2012. Clin Oral Implants Res. 2012 Oct;23 Suppl 6:108-10
6. Klinge B, Hultin M, Berglundh T. Peri-implantitis. Dent Clin North Am 2005;49:661–76.
7. Nguyen-Hieu T, Borghetti A, Aboudharam G. Peri-implantitis: from diagnosis to therapeutics. J Investig Clin Dent. 2012 May;3(2):79-94.
8. Esposito M, Grusovin MG, Worthington HV. Treatment of peri-implantitis: what interventions are effective? A Cochrane systematic review. Eur J Oral Implantol. 2012;5 Suppl:S21-41.
9. Schwarz F, Bieling K, Latz T, Nuesry E, Becker J. Healing of intrabony peri-implantitis defects following application of a nanocrystalline hydroxyapatite (Ostim) or a bovine-derived xenograft (Bio-Oss) in combination with a collagen membrane (Bio-Gide). A case series. J Clin Periodontol. 2006 Jul;33(7):491-9.
10. Froum SJ, Froum SH, Rosen PS. Successful management of peri-implantitis with a regenerative approach: a consecutive series of 51 treated implants with 3- to 7.5-year follow-up. Int J Periodontics Restorative Dent. 2012 Feb;32(1):11-20.
11. Zitzmann NU, Scharer P, Marinello CP, Schupbach P, Berglundh T. Alveolar ridge augmentation with Bio-Oss: a histologic study in humans. Int J Periodontics Restotorative Dent 2001;21:288-295
12. Baslé MF, Lesourd M, Grizon F, Pascaretti C, Chappard D. Type I collagen in xenogenic bone material regulates attachment and spreading of osteoblasts over the beta1 integrin subunit. Orthopade 1998 Feb;27(2):136-142.
13. Green J, Schotland S, Stauber DJ, Kleeman CR, Clemens TL. Cell-matrix interaction in bone: type I collagen modulates signal transduction in osteoblast-like cells. Am J Physiol 1995;268(5 Pt 1):C1090-103.
14. Mizuno M, Fujisawa R, Kuboki Y. Type I collagen-induced osteoblastic differentiation of bone-marrow cells mediated by collagen-alpha2beta1 integrin interaction. J Cell Physiol 2000 Aug;184(2):207-213.
15. Liu G, Hu YY, Zhao JN, Wu SJ, Xiong Z, Lu R. Effect of type I collagen on the adhesion, proliferation, and osteoblastic gene expression of bone marrow-derived mesenchymal stem cells. Chin J Traumatol 2004;7(6):358-362.
16. Gungormus M, Kaya O. Evaluation of the effect of heterologous type I collagen on healing of bone defects. J Oral Maxillofac Surg 2002;60(5):541-545.
17. Gungormus M. The effect on osteogenesis of type I collagen applied to experimental bone defects. Dent Traumatol 2004;20(6):334-337.
18. Regazzoni C, Winterhalter KH, Rohrer L. Type I collagen induces expression of bone morphogenetic protein receptor type II. Biochem Biophys Res Commun 2001;283(2):316-322.
19. Toroian D, Lim JE, Price PA. The size exclusion characteristics of type I collagen: implications for the role of noncollagenous bone constituents in mineralization. J Biol Chem 2007;282(31):22437-22447.
20. Perrotti V, Nicholls B, Piattelli A. Human osteoclast formation and activity on an equine spongy bone substitute. Clin Oral Impl Res 2009;20(1):17-23.
21. Perrotti V, Nicholls BM, Horton MA, Piattelli A. Human osteoclast formation and activity on a xenogenous bone mineral. J Biomed Mater Res A 2009;90(1):238-246.
22. Di Stefano DA, Gastaldi G, Vinci R, Cinci L, Pieri L, Gherlone E. Histomorphometric Comparison of Enzyme-Deantigenic Equine Bone and Anorganic Bovine Bone in Sinus Augmentation: A Randomized Clinical Trial with 3-Year Follow-Up. Int J Oral Maxillofac Implants. 2015 Sep-Oct;30(5):1161-7.
23. Reznikov N, Shahar R, Weiner S. Bone hierarchical structure in three dimensions. Acta Biomater. 2014 Sep;10(9):3815-26.
24. Artese L, Piattelli A, Di Stefano DA, et al. Sinus lift with autologous bone alone or in addition to equine bone: an immunohistochemical study in man. Implant Dent 2011;20(5):383-388.
25. Di Stefano DA, Artese L, Iezzi G, et al. Alveolar ridge regeneration with equine spongy bone: a clinical, histological, and immunohistochemical case series. Clin Implant Dent Relat Res 2009;11(2):90-100
26. Di Stefano DA, Cazzaniga A, Andreasi Bassi M, Ludovichetti M, Ammirabile G, Celletti R. The use of cortical heterologous sheets for sinus lift bone grafting: a modification of tulasne's technique with 7-year follow-up. Int J Immunopathol Pharmacol. 2013 Apr-Jun;26(2):549-56.
27. Pistilli R, Signorini L, Pisacane A, Lizio G, Felice P. Case of severe bone atrophy of the posterior maxilla rehabilitated with blocks of equine origin bone: histological results. Implant Dent. 2013 Feb;22(1):8-15
28. Eser C, Gencel E, Gökdoğan M, Kesiktaş E, Yavuz M. Comparison of autologous and heterologous bone graft stability effects for filling maxillary bone gap after Le Fort I osteotomy. Adv Clin Exp Med. 2015 Mar-Apr;24(2):341-8.
29. Di Stefano DA, Greco GB, Cinci L, Pieri L. Horizontal-guided Bone Regeneration using a Titanium Mesh and an Equine Bone Graft. J Contemp Dent Pract. 2015 Feb 1;16(2):154-62.
30. Santini S, Barbera P, Modena M, Schiavon R, Bonato M. Equine-derived bone substitutes in orthopedics and traumatology: authors' experience. Minerva Chir. 2011 Feb;66(1):63-72.
31. Iorio R, Pagnottelli M, Vadalà A, Giannetti S, Di Sette P, Papandrea P, Conteduca F, Ferretti A. Open-wedge high tibial osteotomy: comparison between manual and computer-assisted techniques. Knee Surg Sports Traumatol Arthrosc. 2013 Jan;21(1):113-9.
32. Di Stefano DA, Andreasi Bassi M, Cinci L, Pieri L, Ammirabile G. Treatment of a bone defect consequent to the removal of a periapical cyst with equine bone and equine membranes: clinical and histological outcome. Minerva Stomatol. 2012 Nov-Dec;61(11-12):477-90.
33. Materni A. Managing an extreme peri-implantitis. Minerva Stomatol. 2013 Sep;62(9):295-305.
34. Jovanovic SA, Spiekermann H, Richter EJ, Koseoglu M.Guided tissue regeneration around titanium dental implants. In: Laney WR, Tolman DE (eds). Tissue Integration in Oral, Orthopedic and Maxillofacial Reconstruction. Chicago: Quintessence, 1992:215.
35. Augthun M, Richter EJ, Hauptmann S, Yilidrim M. Untersuchungen zur Behandlung von tiefen periimplantären Knochentaschen mit ePTFE-Membranen. Z Zahnärztl Implantol 1992;8:246–250.
36. Tinti C, Parma-Benfenati S. Treatment of peri-implant defects with the vertical ridge augmentation procedure: a patient report. Int J Oral Maxillofac Implants. 2001 Jul-Aug;16(4):572-7.
37. Tinti C, Parma-Benfenati S. Vertical ridge augmentation: surgical protocol and retrospective evaluation of 48 consecutively inserted implants. Int J Periodontics Restorative Dent. 1998 Oct;18(5):434-43.

FIGURES

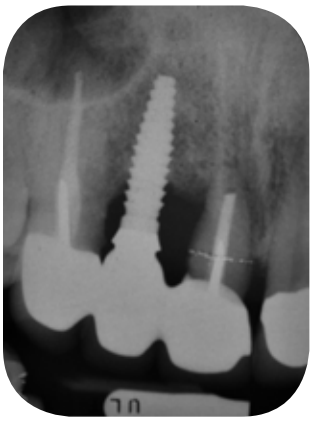

Fig. 1. Intraoral X-ray. The implant in position 1.2 shows a severe peri-implantitis, with appreciable bone loss. Teeth 1.1 is lost. / *Radiografia intraorale. Implanti ne pozicionin 1.2 tregon peri-implantit te rende me humbje te konsiderueshme te kockes. Dhembi 1.1 eshte i humbur.*

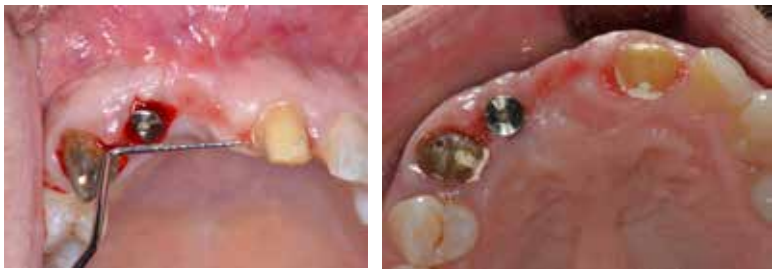

Fig. 2. After 1.1 is extracted and soft tissue healing has occurred, a quite large vertical bone defect can be observed. Profuse bleeding is observed on probing the implant at 1.2.
Pasi 1.1 eshte ekstraktuar dhe ka ndodhur sherimi I indeve te buta nje defekt I madh kockor vertikal eshte vene re. Gjakderdhje e bollshme eshte vene re gjate sondimit te implantit 1.2

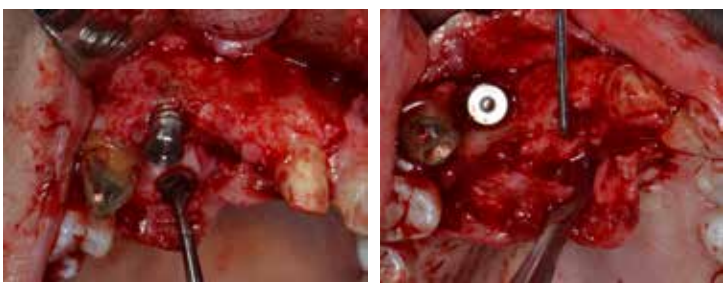

Fig. 3. Upon surgery, the vertical bone defect, causing also some implant threads exposure, may be observed direclty.
Pas kirurgjise, mund te vezhgohet direkt defekti kockor vertikal, qe shkakton gjithashtu mundesi te ekspozimit te implantit.

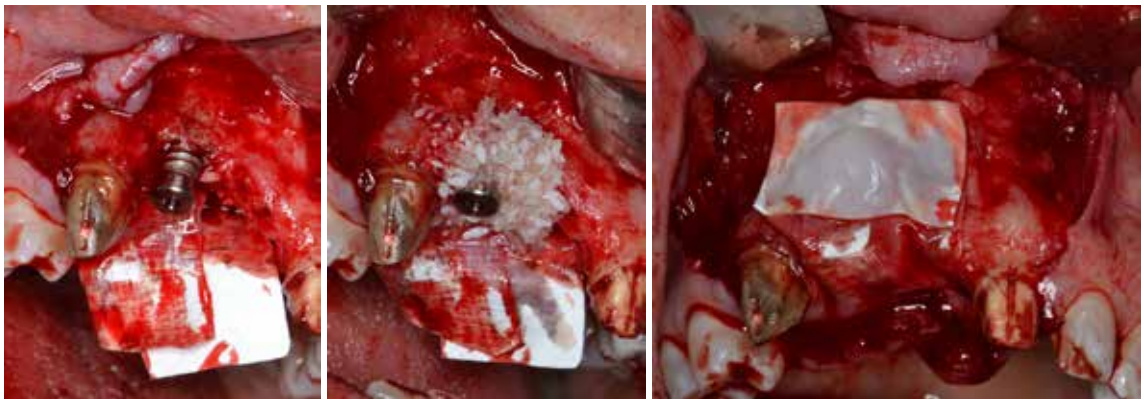

Fig. 4. a) Membranes, still dry, are placed on the palatal side, under the flap. b) The xenogenic granules, after being hydrated, are used to graft the bone defects. c) The defect is covered with the membranes, and an additional one is place for further protection.

Membranat, ende te thata, jane te vendosura ne anen palatinale, nen flap. B) granluat ksenogjenike, pasi jane hidratuar, perdoren per graftin e defektit kockor. C) defekti eshte mbuluar me membrana dhe nje e tille shtese eshte vendosur per mbrojtje te metejshme.

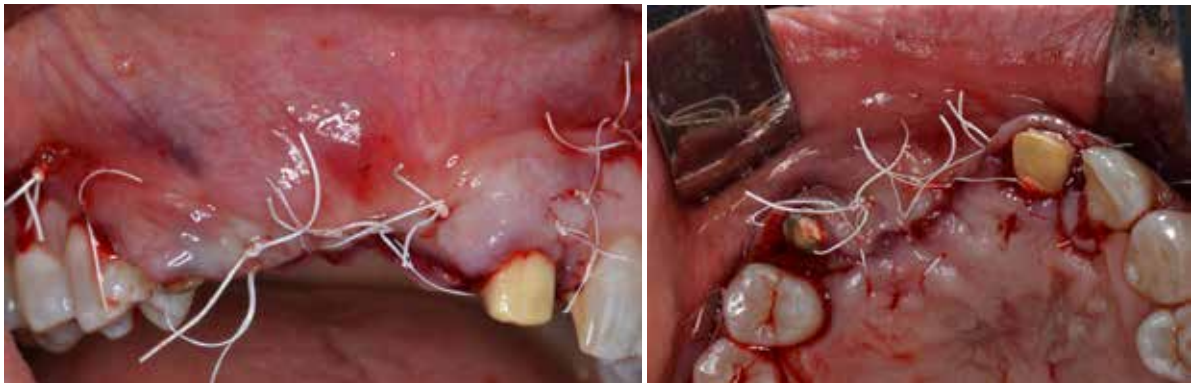

Fig. 5. Suture follows: a first closure line is achieved with horizontal mattress stitches, followed by a second one with single stitches.

Sutura qe ndiqet- nje linje e pare mbylljeje eshte arritur me qepje horizontale dyshek, e ndjekur nga nje linje e dyte me qepje teke.

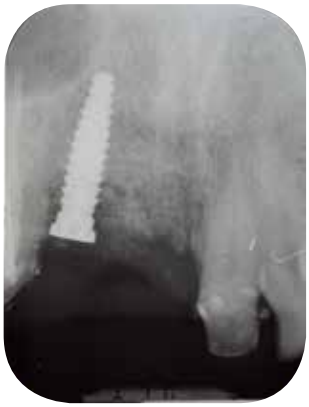

Fig. 6. Intraoral X-ray, 8 months after the regeneration surgery. The grafted zone has a radio-opacity similar to the one of the vital surrounding bone. Peri-implant and ridge bone levels are restored.

Radiografia orale, 8 muaj pas rigjenerimit kirurgjikal. Zona e graftuar ka nje radioopacitet te ngjashme me kocken vitale perreth. Peri-implantiti dhe nivelet kockore jane restauruar.

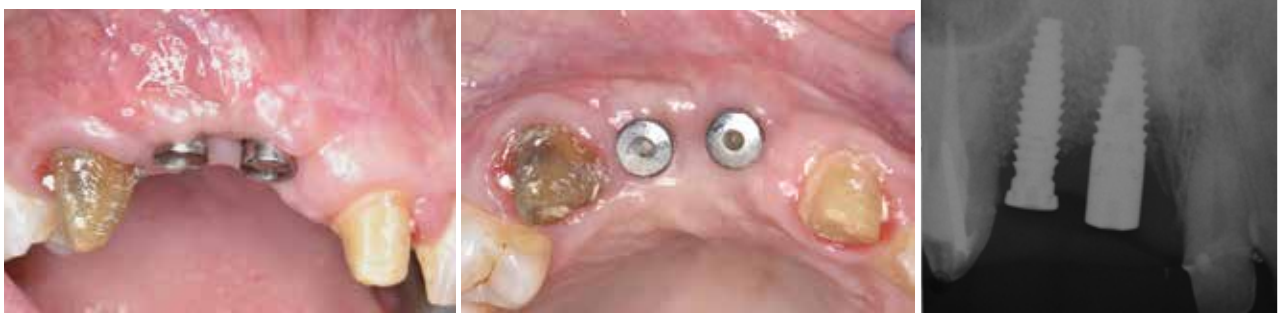

Fig 7. Clinical appearance and intraoral X-ray at 12 months after the regenerative surgery. Soft tissues are healed, and peri-implant bone levels quite well preserved. The implant in position 1.1, placed into regenerated bone, appears surrounded by newly-formed bone.

Pamja klinike dhe radiografia intraorale 12 muaj pas kirugjise rigjenerative. Indet e buta jane sheruar, dhe nivelet kockore te peri-implantitit jane te ruajtura mire. Implanti ne pozicionin 1.1, I vendosur ne kocke te rigjeneruar, shfaqet e rrethuar nga kocke e re e formuar.