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Research Article

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Treatment of Medication-Related Osteonecrosis at Dental Implants Utilizing CO_2 (9.3 µm) Laser and Sticky Bone: A Case Series

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ABSTRACT

Introduction: Medication-related osteonecrosis of the jaw (MRONJ) is a significant challenge for clinicians with limited treatment options. In this case series, a CO2 laser (9.3µm) was utilized in conjunction with platelet-rich fibrin (PRF) mixed with allograft to create sticky Bone.

Materials & Methods: Four consecutive patients with MRONJ at implant sites were treated at a private practice setting. The necrotic bone was removed, and the sites were irradiated with a CO2 laser and ethelylenediaminetetraacetate (EDTA). Platelet-rich fibrin (PRF) mixed with BioOss Collagen particulate to create sticky bone to graft in the defect sites and secured with a solid-PRF membrane. Herbal-based mouthrinses in place of chlorehexidine was utilized as a post-surgical rinse. Follow-up time for the cases ranged from 6 months to 7 years.

Results: All patients healed uneventfully without any post-operative complications. In one case, a new implant was placed without any post-operative complications with a 2-year follow-up.

Conclusion: This case series demonstrates successful outcomes of treating MRONJ at implant sites utilizing CO2 laser to decontaminate the implant surface and sticky bone for regenerative therapy. Additional controlled clinical studies are necessary to validate this technique.

Keywords: Medication-Related Osteonecrosis of the Jaw, MRONJ, Platelet-Rich Fibrin

Introduction

Medication-related osteonecrosis of the jaw (MRONJ) remains a significant challenge for clinicians due to its complex etiology and limited treatment options, as well as an expanding list of contributing medications.1 Originally termed bisphosphonate-related osteonecrosis of the jaw (BRONJ) by Marx in 2003 for its primary association with bisphosphonates in cancer and osteoporotic patients, the name change to MRONJ reflects the inclusion of other medications, such as angiogenesis inhibitors, anti-rheumatics, and RANKL medications [1-3]. Concerningly, the introduction of new medications associated with MRONJ directly reflects a rapid increase in the prevalence of the disease [3].

Bisphosphonates possess anti-osteoclastic properties to prevent bone loss, and, similar to the other medications associated with MRONJ, also function as strong angiogenesis inhibitors, dramatically lowering tissue oxygenation [3-5]. While the intention in cancer patients is to reduce the amount of blood flow to the tumor, the decrease in oxygenation can promote the invasion of oral anaerobic bacteria, leading to infection

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of the exposed necrotic bone characteristic of the disease [6]. Additionally, anti-resorptives and immune modulators interfere with immune-cell activation and cytokine signaling that are normally involved in inflammation resolution [7]. The American Association of Oral and Maxillofacial Surgeons (AAOMS) released a series of position papers starting in 2007 in response to the increasing caseload experienced in private practice [1,8-10]. Recent literature has suggested an association between MRONJ and dental implants, with reports of both MRONJ lesions triggered by implant surgery, and also dental implant presence alone triggering necrosis [11]. MRONJ lesions have even been reported to occur at dental implants that were placed prior to the patient beginning anti-resorptive medication [12]. A recent systematic review by Nisi et al [13]. included 24 articles reporting on peri-implantitis-induced MRONJ (Pi-MRONJ) and 111 total patients with MRONJ occurrence, highlighting the potential for dental implant and peri-implantitis to trigger MRONJ lesions in susceptible patients.

Currently, treatment options for MRONJ are frequently conservative and include bone sequestrum excision, local debridement, and a combination of systemic antibiotic therapy and/or administration of anti-microbial rinses, with chlorhexidine being the most recommended by the AAOMS [1,8]. However, platelet-rich fibrin (PRF) is a 100% autologous second-generation platelet concentrate that has emerged as a valuable adjunct in various oral surgery procedures due to its angiogenic potential, wound-healing support, and analgesic properties [14,15]. It is well documented that PRF can aid in both the treatment and prevention of MRONJ lesions owing to its regenerative capabilities [16,17].

Laser irradiation has also been proposed as an adjunctive modality in MRONJ treatment due to its ability to remove bone, reduce bacterial burden, and provide biostimulatory effects [18]. Specifically, the CO_2 laser (9.3µm) is particularly useful for both hard and soft tissue removal, given its high affinity for absorption of water and shallow penetration depth [19,20]. Additionally, when treating peri-implantitis, CO_2 lasers (10.6µm) can be utilized without damaging the implant surface when proper parameters are utilized [21,22]. In-vitro, it was demonstrated that irradiation with CO_2 lasers increases the hydrophilicity of titanium surfaces [23]. Additionally, a case series by Romanos and Nentwig demonstrated successful regenerative treatment around 19 implants with peri-implantitis utilizing a CO_2 laser to decontaminate the implant surface [24]. While the majority of the existing literature supports the use of Er: YAG for treating MRONJ, very limited evidence exists documenting the use of CO_2 lasers, with only one case series for a similar indication in treating osteoradionecrosis [25,18,26].

Therefore, the purpose of this case series is to present four cases demonstrating the use of CO_2 laser irradiation combined with a regenerative approach using PRF mixed with xenograft. This case series aims to demonstrate the clinical feasibility of this combined protocol and provide practical insight into managing implant-associated MRONJ lesions.

Methods

Prior to the start of data collection, Institutional Review Board (IRB) Exemption was obtained for the retrospective chart analysis from Sterling IRB (ID: 15998-NEstrin). Four patients with implant-associated MRONJ lesions were treated in a private practice setting by the same clinician (S.F). All four patients underwent surgical regenerative therapy in which a full-thickness flap was reflected after adequate local anesthesia to completely expose the MRONJ lesion. Any loose necrotic bone was removed with rongeurs, and the remaining necrotic bone was removed with a 9.3 µm CO_2 laser (Solea, Convergent Dental, Boston, MA, USA) at 13.9 W. After all necrotic bone was removed, the laser was utilized at 0.4 W for 2 minutes of biostimulation. If attempting to regenerate around the existing implant, 24% ethelylenediaminetetraacetate (EDTA) was placed on the implant surface for 2 minutes, followed by copious irrigation with saline. For PRF preparation, blood was drawn in 10 mL tubes (two blue-top tubes and two red-top tubes) and centrifuged at 700 x g for eight minutes utilizing a horizontal centrifuge (Bio-PRF, Florida, USA). After centrifugation, the red top tubes were flattened for solid-PRF membranes and sticky bone was fabricated by mixing both solid and liquid PRF with 90% anorganic bovine bone/10 % collagen (ABBC; Bio-Oss Collagen®, Geistlich, Wolhusen, Switzerland). The sticky bone complex was then applied over the titanium implant and/or defect and secured with a solid-PRF membrane prior to suturing with 4-0 Vicryl in a single interrupted fashion. Postoperative care included Amoxicillin 500 mg TID for three days, analgesics as required, and a homeopathic oral care recovery kit (StellaLife, StellaLife Inc, IL) for post-operative recovery [27].

Patients were scheduled for follow-up visits at two weeks (for suture removal) and followed during hygiene appointments every 3 months. The four clinical cases are demonstrated in Figures 1-8. This case series has been reported in line with the PROCESS guideline [28].

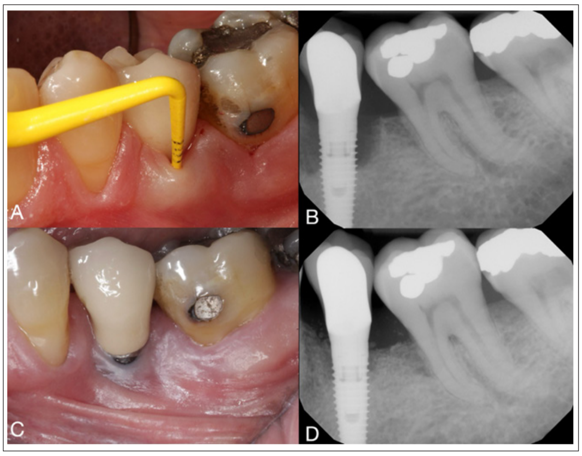

Figure 1: A 71-year-old male on methotrexate for Crohn's disease treatment presented to the clinic with an MRONJ lesion occurring at implant site #20 (placed by a different surgeon). A) Clinical pre-operative photo demonstrating significant probing depth on the buccal aspect. B) Pre-operative radiograph. C) Post-operative clinical photo with lesion resolution. D) 7-year post-operative radiograph

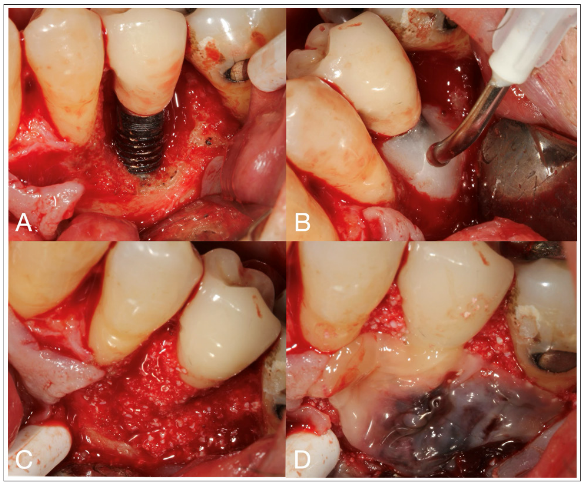

Figure 2: Surgical photos of the same patient. A) Defect after removing the necrotic bone with a CO2 laser (Solea, Convergent Dental, Boston, MA, USA) at 13.9W and 0.4W for 2 minutes of biostimulation. B) EDTA was applied to the implant surface for 2 minutes. C) Sticky bone utilizing PRF with 90% anorganic bovine bone/10% collagen (ABBC; Bio-Oss®, Geistlich, Switzerland) was applied to the defect and secured with D) Solid-PRF membrane before closure

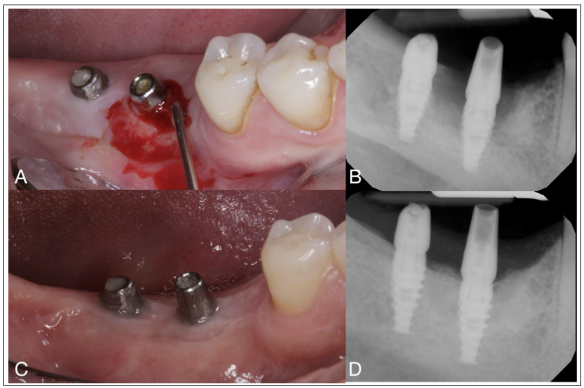

Figure 3: A 45-year-old male on Denosumab for prostate cancer presented with an MRONJ lesion around implant #30 (placed by another surgeon). A) Clinical pre-operative photo demonstrating significant probing depth at implant site #30. B) Pre-operative radiograph. C) Post-operative clinical photograph with lesion resolution. D) 6-month post-operative radiograph

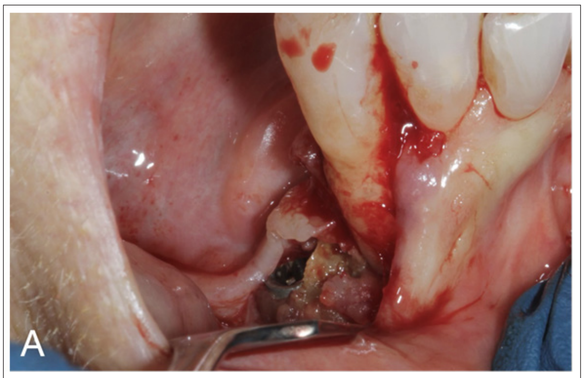

Figure 4: A 62-year-old female on ibandronate sodium for post-menopausal osteoporosis presented with an MRONJ lesion affecting implants #28 and #30, as well as dentition #26-#27. Both #26 and #27 were root canal-treated before surgery by a local endodontist (Dr. Joseph Dibernardo). A) Full-thickness flap reflection revealing necrotic bone, which was sent for biopsy. B) Clinical representation 3-months post-surgery during which both implants were removed, and defects were grafted according to the protocol above. C) 3-year follow-up clinical photograph after ridge augmentation and new implant at site #28

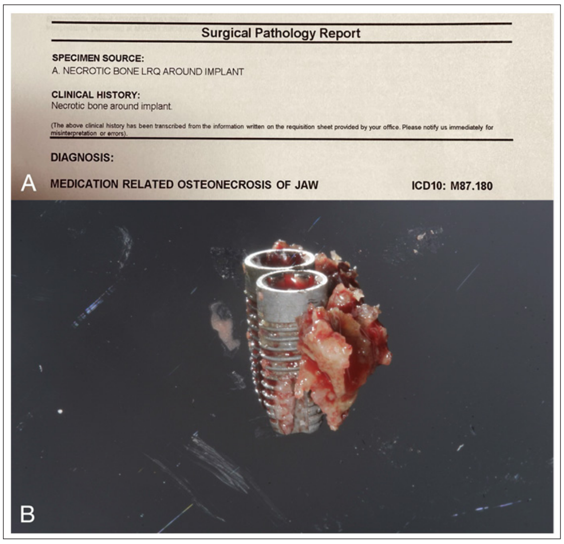

Figure 5: A) Pathology report diagnosing necrotic bone at implant site #28. B) Clinical photograph of removed implant #28 with necrotic bone

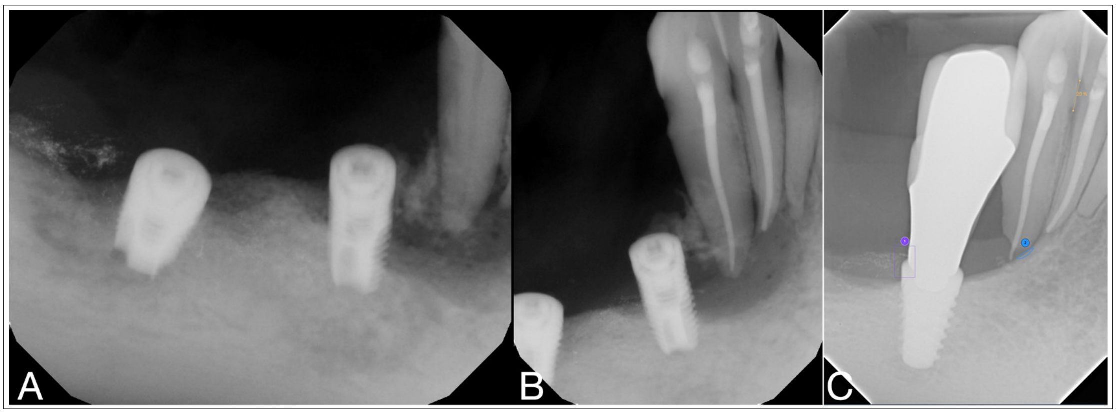

Figure 6: A) and B) represent pre-operative radiographs of MRONJ lesions affecting teeth #26, #27 and Implants #28 and #30. C) 3-year post-operative radiograph after a new implant at #28 was placed

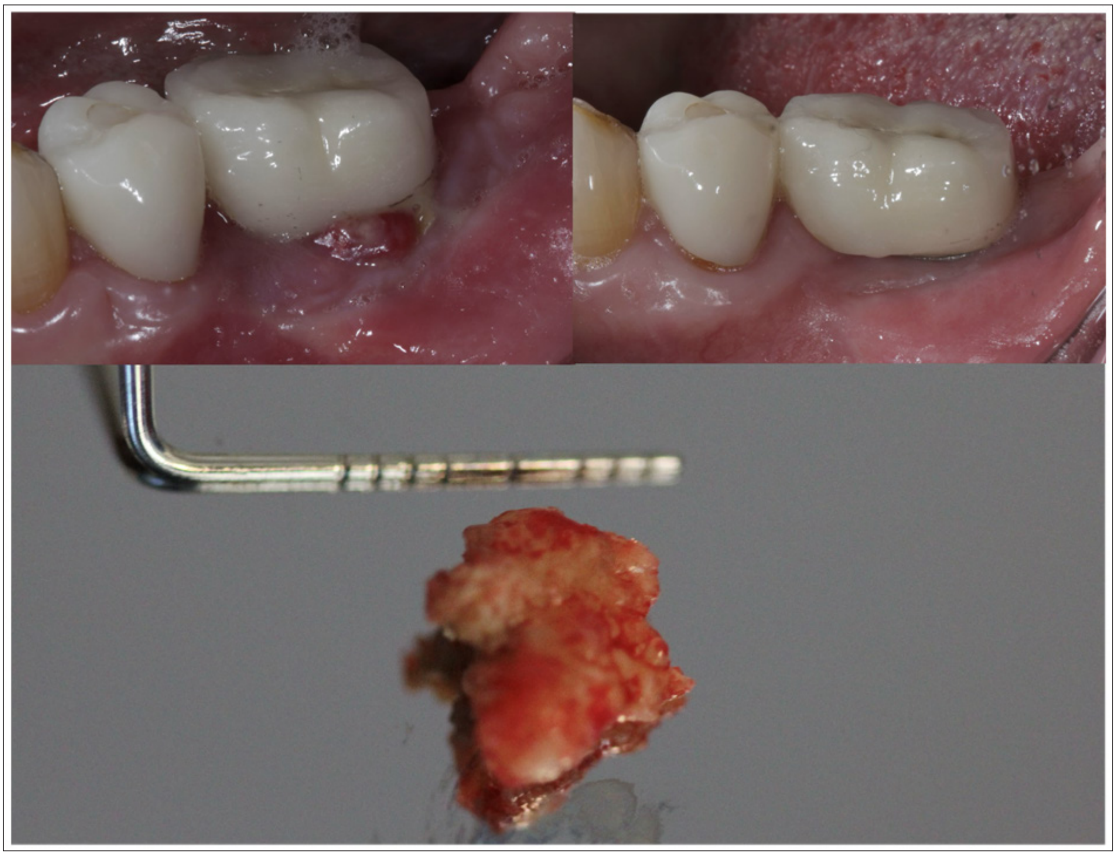

Figure 7: A 65-year-old female on methotrexate for rheumatoid arthritis presented with an MRONJ lesion at implant site #19 (placed 2 years prior). A) Pre-operative clinical photograph. B) 2-year post-operative clinical photograph. C) Necrotic bone removed from the implant site at the time of surgery

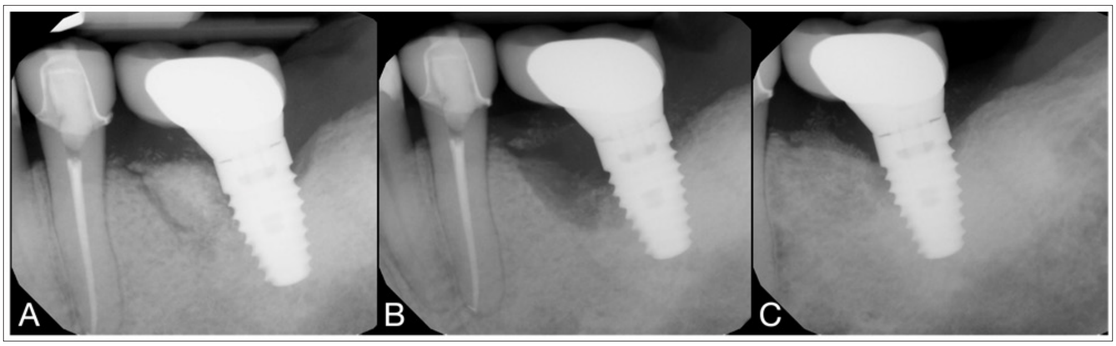

Figure 8: A) Pre-operative radiograph. B) Intra-operative radiograph after removal of necrotic bone. C) 2-year post-operative radiograph

Results

In this case series, four consecutive clinical cases of MRONJ were successfully managed utilizing a combined protocol consisting of surgical debridement with a 9.3 µm-CO2 laser with regenerative therapy utilizing sticky bone via PRF with ABBC. Two female and two male patients were treated with follow-up times ranging from 6 months to 7-years. Two cases included MRONJ lesions due to methotrexate, while the other two cases were associated with ibandronate sodium and denosumab. In three of the cases, successful peri-implant regeneration was completed, while in one severe case, 2 implants were removed before ridge augmentation and new implant placement. All cases demonstrated uneventful post-operative healing with no post-operative infection or recurrent lesions.

Discussion

This case series demonstrated the clinical feasibility of treating implant-associated MRONJ lesions using a combined approach of CO2 laser irradiation in conjunction with ABBC-based sticky bone for a regenerative approach. While previous literature documents occurrences of both implant surgery-triggered MRONJ and implant presence-triggered MRONJ, all four cases included in this case series fell in the latter category, highlighting the plausibility that local inflammation at implant sites may serve as a trigger in susceptible patients [13].

Implant-associated MRONJ is uniquely challenging because these lesions often occur in systemically compromised patients with the usual challenges of treating peri-implantitis, including chronic inflammation and a contaminated implant surface [13]. As is the case with treating peri-implantitis, it is critical to decontaminate the implant surface before attempting regeneration for predictable outcomes [29,30]. While previous evidence exists regarding the use of erbium-doped: yttrium, aluminum, and garnet laser (Er:YAG) for treating MRONJ, the rationale for utilizing the 9.3µm CO2 laser for decontamination is due to its efficiency in both hard and soft tissue management, as well as its safety and shallow penetration depth [25,31]. In peri-implantitis applications, CO2 lasers have been demonstrated to successfully decontaminate the implants without damage/alternating the titanium surface if proper settings are utilized [21,22]. A recent in-vitro study by Romanos et al [23]. demonstrated improved surface wettability/surface energy of rough titanium surfaces with CO2 irradiation, which may support early blood clot stabilization and cellular adhesion conducive to peri-implant regeneration. Additionally, a recent case series including five clinical cases of osteoradionecrosis demonstrated encouraging results utilizing the CO2 laser in sequestrectomy of these lesions, warranting investigation in MRONJ lesions [26].

A second major component of this protocol was the utilization of sticky bone, utilizing ABBC with PRF. The adjunctive use of PRF in regenerative procedures has been well-documented owing to its 100% autologous platelets aiding in angiogenesis and wound-healing support and has been investigated for both prevention and adjunctive treatment of MRONJ lesions [32]. Additionally, in a recent systematic review by Estrin et al [15]. Including 200 studies in medicine and dentistry, PRF use was consistently associated with significant reductions in pain, one of the major symptoms and characteristics of MRONJ lesions. Clinically, PRF has demonstrated the ability to support predictable soft tissue closure, which is particularly relevant in MRONJ lesions in which achieving a stable, asymptomatic condition with soft tissue coverage is desired as an end-goal [33].

Regarding post-operative protocol, a novel homeopathic, herbal-based recovery kit (StellaLife®) was utilized in place of chlorhexidine (CHX) despite prior guideline-based recommendations by the AAOMS frequently recommending CHX for MRONJ management [1,8]. While CHX possesses powerful antimicrobial properties, its lack of selective cytotoxicity may be a major drawback, as numerous reports have shown its cytotoxicity towards our own cells in the oral cavity and have demonstrated an increased pro-inflammatory response [27,34,35]. In part due to its cytotoxic and pro-inflammatory properties, many countries have entirely banned the use of chlorhexidine as an oral rinse [36]. Due to the above mentioned issues, more natural herbal compounds are increasingly being utilized as potential therapeutic options. Specifically, a novel VEGA Oral Care Recovery Kit (StellaLife®, StellaLife Inc., Aventura, FL, USA) was utilized in this study due to its selective cytotoxicity and ability to decrease bacterial loads while improving wound healing [36-39]. While the use of StellaLife® in the management of MRONJ warrants further investigation, this case series demonstrated the successful utilization of Stellalife® over CHX in the management of MRONJ lesions. Future research with less heterogeneity is necessary, with emphasis on patient-reported outcomes to evaluate their effectiveness in the management of MRONJ lesions of all stages.

Several limitations of this study should be acknowledged. This report represents a small case series without a control group, with many treatment variables. Decontamination protocols included CO2 and EDTA while utilizing PRF and ABBC for regeneration and StellaLife® as a post-surgical antimicrobial rinse. Further studies with larger cohorts and standardized treatment approaches and follow-up protocols are necessary to further evaluate the effects of each treatment approach in managing MRONJ lesions.

Despite the limitations, this case series significantly demonstrates a successful regenerative approach to treating MRONJ lesions, which often clinicians are hesitant to treat, fearing the lesion may not resolve or worsen. This case series successfully incorporated a CO2 laser and PRF laser to regenerate around existing implants and augment the bone in preparation for implant replacement.

Conclusion

Within the limitations of this case series, implant-associated MRONJ lesions were managed successfully using a combined protocol consisting of surgical removal of necrotic bone, CO_2 laser-assisted debridement/decontamination, and regenerative reconstruction using PRF-based sticky bone secured with a solid-PRF membrane. All four cases demonstrated uneventful healing without postoperative infection or recurrent exposed bone during follow-up, ranging from 6 months to 7 years, including one severe case requiring implant removal followed by ridge augmentation and subsequent implant replacement. Although this report cannot isolate the contribution of any single component of therapy, these outcomes support the feasibility of integrating CO_2 laser (9.3µm) decontamination with PRF-based regeneration in complex implant-associated MRONJ defects.

Additionally, StellaLife® was utilized as a postoperative rinse in place of chlorhexidine and was well tolerated by the patients. Further controlled clinical studies are necessary to evaluate this treatment modality in MRONJ management.

Author contributions

Conceptualization, NEE, GER, and NEE.; method¬ology, NEE, SF, and SK; formal analysis, NEE, and SF.; investigation, NEE, and SF.; resources, NEE, SK, and SF; writing—original draft preparation, NEE, PA, and SF.; writing—review and editing, NEE, SK, and PA; supervision, SF, GER; project administration, SF, and GER. All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest

The authors report no conflict of interest.

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