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Case Report

Treatment of Periodontal Intrabony Defect Using Autologous Periodontal Ligament Stem Cells: A Case Report of 2 Years Follow-Up and Surgical Re-Entry

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Abstract

Periodontists have been interested in regenerating tooth-supporting tissues destroyed by periodontal diseases. Currently regeneration of periodontal damaged tissue still remains great challenge. Stem cell-based therapy raised novel therapeutic strategies for periodontal regeneration. To date, substantial advances have been made in stem cell-based periodontal regeneration with autologous periodontal ligament stem cell niche. Currently there is dearth of evidence regarding the success of this therapy, especially evidence for the effectiveness of autologous periodontal ligament stem cells. We present a case report of a 38-year-old male patient having periodontal osseous defect w.r.t 36 was treated with autologous periodontal ligament stem cell niche harvested from third molar. Surgical re-entry at 2 years revealed bone formation w.r.t 36. At one year, 75% radiographic bone gain was accomplished. The improvement in the clinical and radiographic parameters reinforced by the re-entry surgery findings strongly suggest that A-PDLSCs Niche may be a cost-effective substitute to implants and tooth supported prosthesis in situations where conventional periodontal therapy would yield compromised outcomes.

Keywords: *Intrabony Defect; Autologous; Periodontal Ligament Stem Cells; Surgical Re-Entry; Regeneration*

Introduction

Periodontitis is an inflammatory disease and is the most common cause of tooth loss in adults. World Health Organization (WHO) has reported that 10 - 15% of the world populations suffer from severe periodontitis [1]. Moreover 50% of Indian population suffers from periodontitis [2]. Following disease control, the ultimate goal of periodontal therapy is regeneration and its aims at re-formation of all components of the periodontium: gingival connective tissue, periodontal ligament, cementum and alveolar bone.

The current regenerative techniques have limited success rates especially in advanced periodontal defects. The human clinical trial on stem cells based using *ex vivo* stem cell culture for periodontal regeneration is promising [3]. However Vandana., *et al*. 2015 proposed direct application of autologous periodontal ligament stem cells (PDLSCs) overcoming the limitations and concerns of *ex-vivo* stem cell culture methods like high cost, technique sensitivity, loss of stemness during cell passage, genetic manipulation and tumorigenic potential [4]. The presence of PDLSCs in soft-tissue scrapings of roots of extracted molar has been reported [5]. Based on this report, stem cell as-

sistance in periodontal regeneration technique (SAI-PRT), the PDL tissue adherent to tooth root and alveolar socket comprised of PDLSCs along with its niche (PDL tissue niche) components were gently removed using sterile curette and mixed with gelatin sponge (Abgel®©™) to form a transferable mass which was placed in the periodontal defect. The clinical studies on SAIPRT [6-9] included both clinical and radiographic evaluation parameters to demonstrate evidence of periodontal regeneration without the direct evaluation of regenerated tissues such as bone. The true methods of evaluation are re-entry and histologic methods. Re-entry procedures typically involve reflapping a site at some time after surgical therapy in order to directly compare new bone levels to initial bone levels. Although this method can measure the gross behavior of bone, bone measurements do not reflect connective tissue attachment levels and cannot distinguish bone that is attached to the root surface via a periodontal ligament and are, therefore, inappropriate for evaluation of periodontal regenerative therapy. The re-entry is possible with patients consent to visualize and evaluate regenerated bone macroscopically which otherwise is interpreted as bone fill radiographically. The re-entry method doesn't allow those microscopic changes such as periodontal ligament (PDL) and cementum regeneration. The surest method to overcome shortcoming of re-entry are histologic methods, which can be attempted for an experimental hopeless tooth that has undergone regenerative methods. However, the re-entry method can be still be attempted for those teeth that has undergone regenerative methods without any extraction This Stem cell Assistance In Periodontal Regeneration Therapy (SAIPRT) was tried in the treatment of intrabony defect and followed up for 2 years radiographically and a surgical re-entry was done to assess periodontal regeneration.

Case Report

An apparently healthy 38 year old male patient reported to the Department of Periodontics, College of Dental Sciences, Karnataka with the chief complaint of bleeding gums since 1month. Based on this history, clinical findings and radiographic evaluation diagnosis of localized periodontitis (periodontal pocket) was reached upon.

The study protocol was approved by Institutional review board of College of Dental sciences ((Ref.No.CODS/977/2015=2016) and was in compliance with the Rajiv Gandhi University of Health Sciences, India.

The compulsory inclusion criteria for SAI-PRT is systemically healthy periodontitis patients who had periodontal pocket depth of ≥ 5 to 8 mm following phase I therapy-scaling and root planning (SRP) in vital, asymptomatic tooth with radiographic evidence of angular bone loss and presence of at least one tooth that needs to be extracted due to impaction or non-functional reasons; those who consented the tooth extraction were included in the study. Patient showing unacceptable oral hygiene during pre-surgical period, patients suffering from any known systemic diseases e.g. uncontrolled diabetes, anticoagulant therapy, immunosuppressive therapy etc. mobile teeth and teeth with gingival recession, pregnant or lactating subjects, Smokers and alcoholics were excluded from the study.

Following etiotropic phase, a full-thickness mucoperiosteal flap was raised. Complete debridement of the intrabony defect of 36 was done and followed by extraction of the impacted maxillary left third molar.

The transplant consisted PDL soft tissue adherent to root of an extracted third molar and the extraction socket [5] which harbored the PDLSCniche and mixed with Abgel®©™ transferred to the selected intra-bony defect. The pre-sutured knot was tightened and periodontal dressing was placed. Post -operative instructions were given and suture removal was done after 10 days (Figure 1a to 1e).

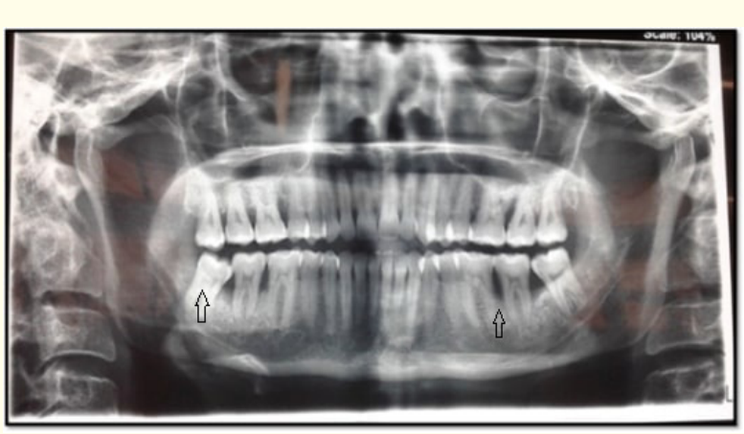

Figure 1a: *OPG showing 36 with osseous defects; 48 indicated for extraction from the same patient.*

Figure 1b: *Intrabony defect after reflection of mucoperiosteal flap w.r.t 36.*

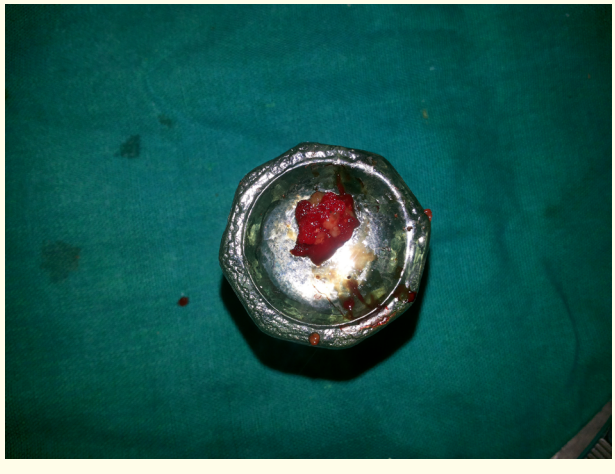

Figure 1c: *Transferable mass consisting of A-PDLSCniche in soft tissue adherent to extracted third molar with Abgel®©™.*

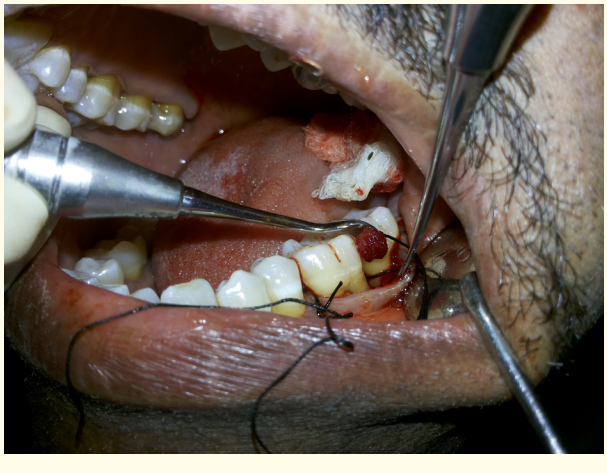

Figure 1d: *Placement of transplant mass w.r.t 36.*

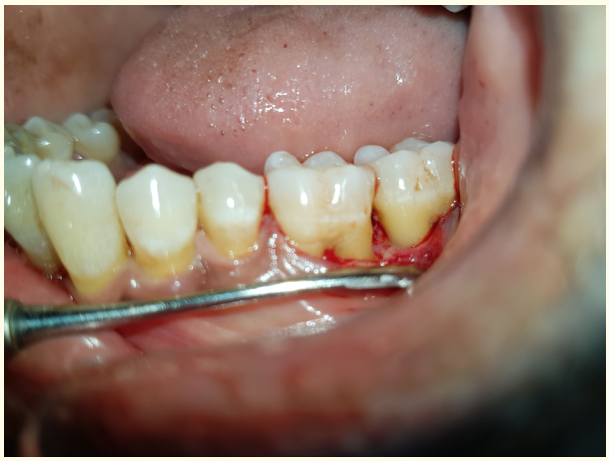

Figure 1e: *Surgical re-entry at 9th post-operative month revealing bone formation.*

Two year follow-up revealed 5mm reduction in periodontal pocket and gain in attachment level of 5mm measured from a fixed reference point (stent) with negligible change in gingival marginal position which did not cause root exposure (gingival recession).

The treated defect area was reentered to appreciate the significant bone fill at 36 after 9 months (Figure 1e). Healing was uneventful and at 24 months of follow-up, there was substantial defect fill in the treated area, representing a significant clinically appreciable bone formation.

Radiographic evaluations were performed at baseline, six months, nine months, twenty four months using IOPA. The percentage of defect fill was 75% with minimal alveolar crestal changes and there was change in radiodensity as calculated by Image J analyser. The mean density changes observed was 64.52 at 6 months to 81.5 and 91.1 at 9 and 24 months respectively in the defect area suggestive of improvement in newly formed bone (Figure 2a to 2g).

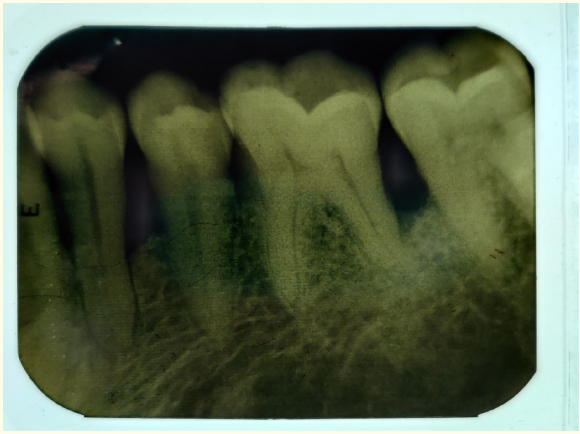

Figure 2a: *Baseline IOPA at 36.*

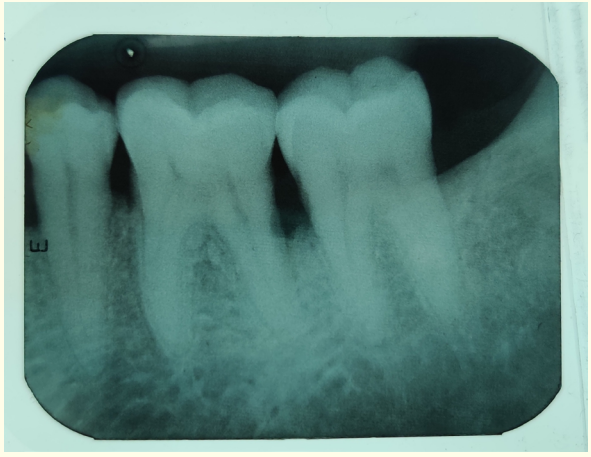

Figure 2b: *6months IOPA, osseous defect in 36 (Intrabony).*

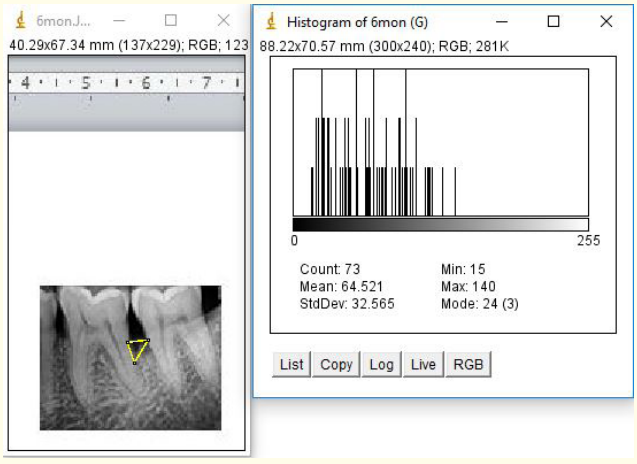

Figure 2c: *Radiographic bone density at 6 months.*

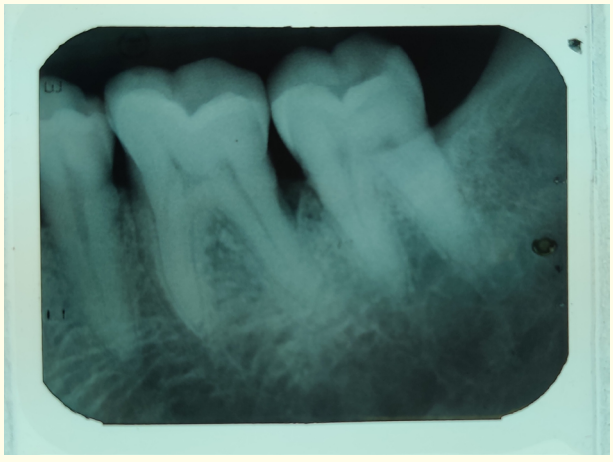

Figure 2d: *9 months IOPA changes in the bone fill at 36.*

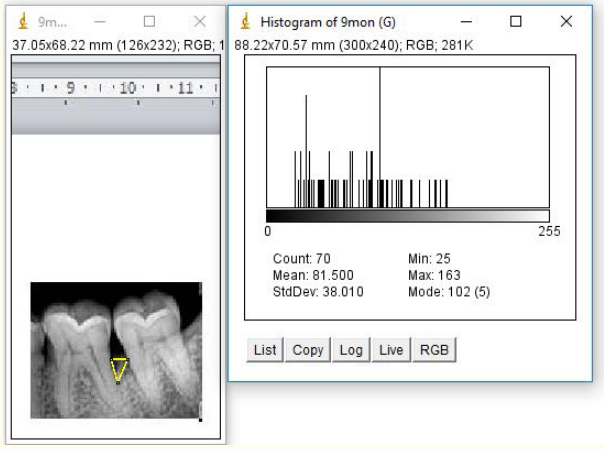

Figure 2e: *Radiographic bone density at 9 months.*

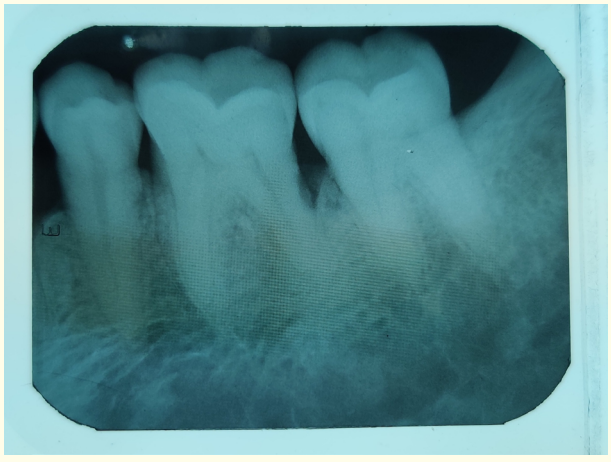

Figure 2f: *24 months IOPA changes in bone fill at 36.*

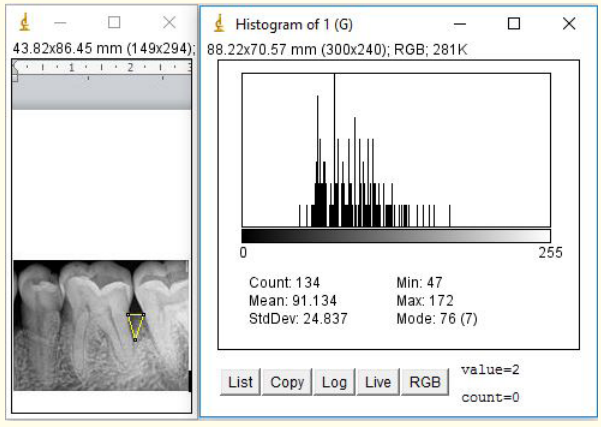

Figure 2g: *Radiographic bone density at 24 months.*

Discussion

Stem cells are responsible for the growth, homeostasis and repair of many tissues. The maintenance and survival of stem cells is regulated by inputs from their local microenvironment, often referred to as the 'stem cell niche'. The stem cell niche hypothesis was developed in 1978 by Schofield, who proposed that stem cells reside within fixed compartments, or niches, which are conducive to the maintenance of definitive stem cell properties [10].

PDLSCs are multipotent and have demonstrated their ability to differentiate into osteoblasts, fibroblasts and tooth cementoblasts and to form cementum- and PDL-like tissues [11].

A gelatin sponge owing to its flexibility, biocompatibility, and biodegradability, and potential to be used as a scaffold to support osteoblasts and to promote bone regeneration in defective areas was considered [12].

The PDLSCs stem cell studies by Feng's (2010) [3] and Chen (2016) [11] have demonstrated the use of *ex-vivo* cultured PDL stem cells along with bone grafts in periodontitis treatment successfully, the periodontal regeneration reported in their studies is due to *ex-vivo* cultured stem cell or due to bone grafts or both is not possible to differentiate. However, the autologous PDLSCs niche application in SAIPRT is devoid of graft usage. Hence periodontal regeneration assessed by clinical, radiographic parameters and re-entry are due to regenerative potential of PDLSCs niche.

Histological evaluation is the only reliable method of determining the efficacy of regenerative periodontal therapies aimed at the creation of a new attachment apparatus consisting of new bone, cementum and Periodontal ligament. Due to ethical considerations, need for controls and limitation of variation, animal models have been created to evaluate periodontal therapy. A model in a nonhuman primate has contralateral defects with the same amount of bone and periodontal ligament loss [13,14]. Periodontal treatment is done on one side and compared histologically to the contralateral side to determine the effect of the treatment on bone and periodontal ligament levels. In this way, it can be accurately determined whether the therapy resulted in repair or regeneration. Thus, histological evaluation can determine the efficacy and safety of periodontal therapies and is especially important when new drugs or devices are being developed and evaluated [15].

The basic problem faced in *ex-vivo* cell culture is that the sensitive nature of the procured PDLSCs from the extracted tooth root to survive for culture expansion. There are several attempts by the researcher to succeed in the stem cell survival, as the first step in *ex-vivo* cell culture expansion. Keeping this in mind, the authors of the paper attempted randomized control trial [16] to place the autologous PDLSCniche [A- PDLSCniche] adherent to the root directly into the selected osseous defect following extraction of impacted tooth in the same patient. In fact on microscopic examination this tissue contains all the cells favourable for tissue regeneration [5]. The crucial step of cell survival by direct placement fulfilled the best of tissue engineering principle as chair side reality instead of arduous laboratory sensitive cell culture procedure.

Based on current literature on use of *ex vivo* culture and associated problems, a humble attempt was made to harvest A-PDLSCniche for direct application using (gelatine sponge) (Abgel®©™**) as scaffold in regeneration of intrabony periodontal defect bypassing *ex vivo* culture was attempted for the first time which satisfies the and it abides tissue engineering triad consisting of PDLSCs (cells), gelatin sponge - scaffold (Abgel®©™**) and growth factors present in the niche. This technique resulted in successful clinical and radiographic parameters such as clinical attachment gain, decreased probing pocket depth and satisfactory defect fill of intrabony defect when evaluated for a period two year. The immediate periodic healing events were uneventful.

As an evidence based approach initiated in 2015, out of 14cases, the first case report of 24 months evaluation is presented in this case report with surgical re-entry. The clinical and radiographic outcome measures are highly successful. changes in bone height, density and volume can be estimated by pre- and posttreatment radiographs but cannot distinguish whether the bone is connected to the tooth by

new periodontal ligament and cementum (true regeneration) Since there are no bone graft/substitute used in this study as used in Feng and Chen study, it is discernable that the successful clinical and radiographic changes in the treated site is attributable to the PDLSCs present in the transplanted autologous PDL tissue the re-entry procedure confirmed the bone regeneration which was otherwise radiographically measured.

To the best of our knowledge, no study was found to use direct autologous PDLSC niche in the treatment of periodontal intrabony defect. The postoperative bone fill was examined through surgical re-entry in this case report, to confirm the defect fill after 24 months, and obvious bone formation was noticed. The SAI-PRT technique is safe as autologous cells are utilized without any adverse affects.

Conclusion

A simple task of autologous PDLSCniche procurement and immediate placement are the major advantages of the current concept, the autologous Stem cell Assistance In Periodontal Regeneration -Technique (SAI-PRT) has emerged as a constructive avenue in treatment of periodontal osseous defects. Moreover, the clinical feasibility, success and cost effectiveness over currently available techniques are encouraging in small periodontal osseous defects. As the periodontal bone formed in the osseous defects as observed in the reentry is strong enough to recommend this novel idea clinically.

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