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CASE REPORT

Management of endo-perio lesion with autologous stem cell therapy

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Abstract

The objective of periodontal therapy is the regeneration of tooth-supporting tissues. Various treatment modalities, such as the use of bone grafting materials, guided tissue regeneration, and delivery of enamel matrix derivatives or growth factors, are applied with large variability in regenerative outcomes. However, a case report was done by utilization of autologous dental pulp stem cells and periodontal ligament stem cell niches in the treatment of bone loss associated with endodontically and periodontally involved teeth. An autologous periodontal ligament stem cells niche adherent to the root and dental pulpal stem cells from dental pulp directly into the selected osseous defect following extraction of the impacted tooth in the same patient. The results of this case reported that the dental pulpal stem cells and periodontal ligament stem cells niche with gelatin sponge resulted in a significant amount of bone fill and reduction in probing pocket depth.

Key words: Apicoectomy, gelatin, mesenchymal stem cells, periodontal pocket, stem cell niche

Introduction

The periodontal and pulpal lesions are interrelated, as the inflammatory substances produced by both lesions are detected in variable degrees in the periodontal and pulpal tissues. Hence, it is designated as endo-perio lesions.

The differential diagnosis of endodontic and periodontal will typically be tough; however, it is important to form an accurate diagnosis so that suitable treatment may be provided. When it comes to identifying and predicting the prognosis of the affected teeth, endodontic-periodontal diseases provide complications to the practitioner. The development and evolution of such lesions are significantly influenced by etiologic agents, including bacteria, fungi, and viruses, as well as a number of contributory factors such as trauma, root resorptions, perforations, and dental malformations.

Successful endodontic treatment would typically result in the healing of the endodontic component in the case of a combined endo-perio lesion. As a result, the prognosis would ultimately depend on the efficacy of the periodontal repair or regeneration begun by either of the treatment methods. In such circumstances, surgical apicoectomy has a very good prognosis and may result in saving the patient's natural dentition.[1]

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such as the use of bone grafting materials, guided tissue regeneration, and delivery of enamel matrix derivatives or growth factors, are applied with large variability in regenerative outcomes.[2-4]

Periodontal regeneration additionally needs consideration of many biological features including the appropriate progenitor cells, signaling molecules, and matrix scaffold in an orderly temporal and spatial sequence. In this context, the use of tissue engineering has fueled an increase in interest in exploring cutting-edge regeneration methods using autologous mesenchymal stem cells,[5] particularly dental pulp stem cells (DPSCs) and periodontal ligament stem cells (PDLSCs).

The dental pulp may be a niche housing neural-crest-derived stem cells. This niche is definitely accessible in routine clinical practice, presumably providing a prompt out-there supply of stem cells for clinical periodontal regenerative therapy.[6] Human DPSCs are isolated and characterized as a population of multipotent stem cells capable of differentiating *in vitro* in dental pulp-like structures, osteoblasts, and endotheliocytes.[7,8]

Human studies have incontestable that DPSCs once transplanted with a biocompatible scaffold into periodontal defects, have the properties to regenerate periodontal tissues.

A study by Aimetti M *et al*., in a clinical and radiographic finding and reentry procedure, suggests that the application of autologous DPSCs may be a clinically relevant procedure in treating deep periodontal osseous defects.[9]

Periodontal ligament stem cells (PDLSCs) can serve as a cell source, simply accessible from soft tissue adherent to an extracted tooth, and provide excellent therapeutic effects in promoting periodontal regeneration. *Ex-vivo* cultivated PDLSCs isolated from soft-tissue adherent to extracted teeth have incontestable the power to regenerate periodontal tissues (cementum, periodontal ligament, and alveolar bone) in experimental animal models[10] and human studies.[11]

Based on growing analysis of the biological importance of niche/microenvironment on residing stem cells in physiologic and post-injury status is the inspiration for this study. Periodontal regeneration in humans utilizing *ex-vivo* cultivated PDLSCs and bone graft materials has only been documented in a few investigations.[11,12] According to Vandana KL *et al*., the autologous stem cell assistance in periodontal regeneration technique, which adheres to the tissue engineering concept and makes use of PDLSCs (cells), niche (growth factors), and gelatin sponge (scaffold), has been successful in treating periodontal osseous defects on both the clinical and radiographic levels.[13-16]

In this case report, an attempt was made to use autologous DPSCs and PDLSCs in the therapy of bone loss related to teeth with endodontic and periodontal problems. These cases are treated by endodontists and periodontists, respectively.

Case Report

An apparently healthy 28-year-old female patient reported to the department of periodontics, with a complaint of pain in the lower right front tooth region associated with pus discharge for 1 month. On intraoral examination, gingival recession and deep periodontal pocket with grade I mobility were found to be present in relation with 43 [Figure 1a]. A radiovisiography showed extensive periodontal bone loss surrounding the tooth root along with apical radiolucency [Figure 1b]. The nonvitality of 43 was confirmed by electric pulp testing. The treatment plan included root canal treatment for 43 along with open flap debridement of periodontal osseous defects and the use of autologous DPSCs and PDLSCs niche for bone regeneration.

Following the initial phase of scaling and root planning, a full-thickness mucoperiosteal flap was raised, and complete debridement of the intrabony defect of 43 [Figure 1c] followed by root canal therapy and apicoectomy was done [Figure 1d]. For harvesting stem cells, the healthy impacted maxillary right third molar indicated for extraction was removed carefully in the same patient with the patient's consent. The two types of stem cells, DPSCs and PDLSCs were procured from extracted impacted tooth.

The vital pulp from the extracted tooth was extirpated using a barbed broach and mixed with cut pieces (1 mm × 1 mm) of gelatin sponge (Abgel®©™) in a sterile dappen dish [Figure 1e]. The autologous dental pulp tissue containing DPSCs was not adequate to fill the osseous defect surrounding the endo-perio-affected tooth 43, which was overcome by using the PDL tissue (harboring PDLSCs niche) adherent to the extracted tooth root to prepare the transplant. The third molar extraction socket, which included the PDLSCs, was collected by gently scraping the tooth root and removing the socket with a sterile curette [Figure 1f]. The transplant was made up of periodontal ligament soft

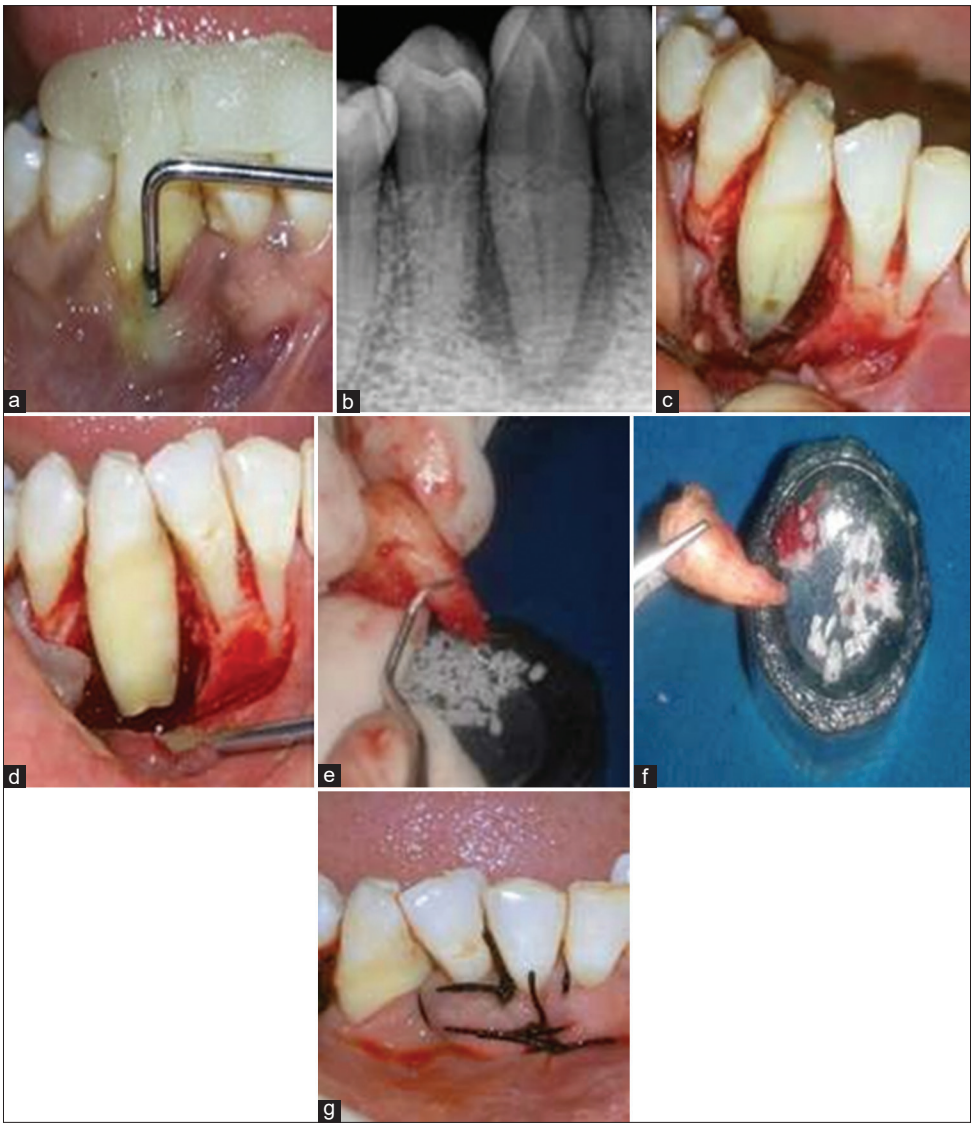

Figure 1: Clinical procedure: (a) Baseline probing pocket depth with respect to 43, (b) Baseline radiovisiography, (c) Intrabony defect in 43 region, (d) Apicoectomy with respect to 43, (e) Soft-tissue adherent to the root of an extracted third molar, and the extraction socket harboring the periodontal ligament stem cells and Abgel®©™ (1 mm × 1 mm), (f) Transferable mass consisting of soft-tissue adherent to extracted third molar, cementum scraping, and scraping from alveolar socket mixed with Abgel®©™, (g) Autologous stem cell niche transplant placement and closure

tissue that was adhering to the root of the withdrawn third molar. Dental pulp containing DPSCs was extirpated with broaches. Both the harvested tissues were mixed with cut gelatin sponge pieces (Abgel®©™) separately in the sterile dappen dishes. Transferable mass containing PDLSCs niche was transplanted into defect lateral to the tooth and DPSCs transplant was placed in the apical portion of the tooth root. The presutured knot was secured [Figure 1g] and a periodontal dressing was placed. Postoperative instructions were given and suture removal was done after 10 days.

Clinical parameters were assessed using a standardized periodontal probe (UNC 15, Hu-Friedy, USA). Radiographic measurements were analyzed using Image analyzer software at baseline [Figure 2a], 1 month [Figure 2b], 3 months [Figure 2c], 9 months [Figure 2d], and 12 months [Figure 2e].

A one-year follow-up revealed that the initial probing depth of 21 mm reduced to 16 mm; the initial clinical attachment level (CAL) of 24 mm was improved to 17 mm as a result of stem cell therapy, from a fixed reference point (stent). The percentage of defect fill was 80% with minimal alveolar crestal changes and there was a change in radiodensity from a mean baseline value of 59.97 was improved to 66.15 at 9 months (as calculated by histogram) using the ImageJ analyzer observed in the defect area suggestive improvement in newly formed bone.

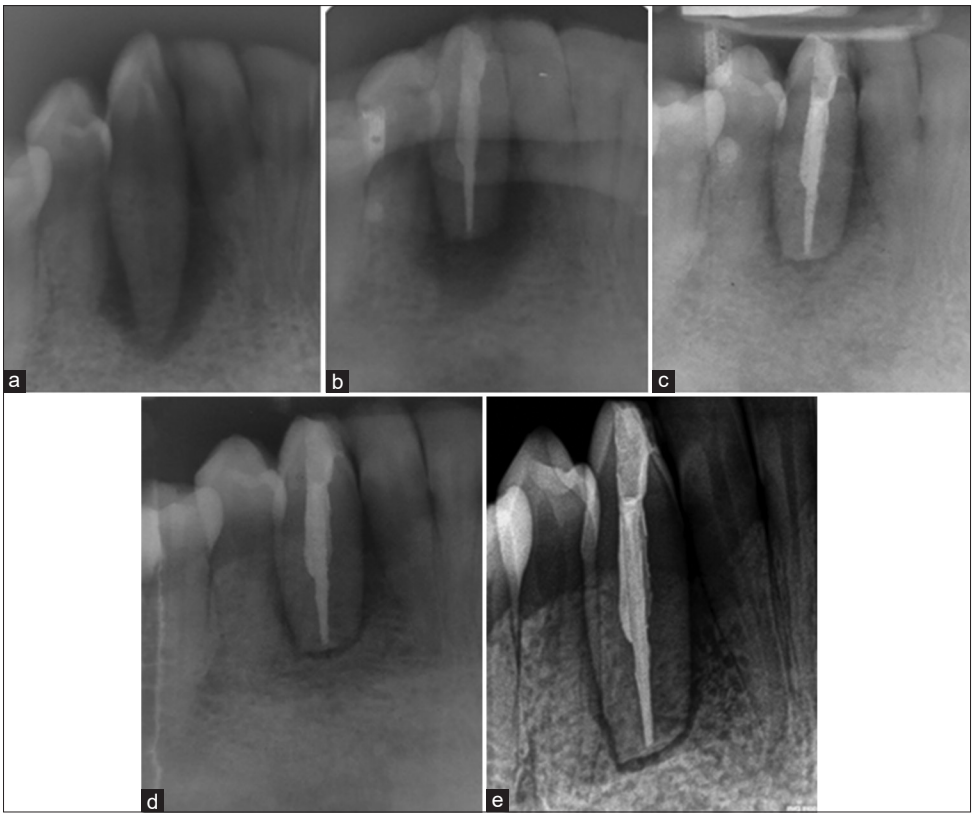

Figure 2: Radiographic evaluation: (a) Radiovisiography 43 region– baseline, (b) Radiovisiography 43 region– 1 month, (c) Radiovisiography 43 region– 3 months, (d) Radiovisiography 43 region-9 months, (e) Radiovisiography 43 region– 12 months

Discussion

Although the repair or regeneration of periodontal tissues is debatable if connected to an endodontic lesion, the healing of one is very predictable. In the case of a primary endodontic and secondary periodontal involvement, endodontic therapy should typically come before periodontal pocket elimination procedures. However, endodontic therapy would primarily resolve the endodontic component of involvement and have little impact on the periodontal lesion. Therefore, a thorough diagnostic examination usually will indicate the primary etiology and, thereby, direct the proper course of the treatment plan as presented in this case.

In this case, both endodontic and periodontal regenerative treatments are done simultaneously in a single appointment. Periodontal regeneration has been tried with a variety of grafting materials. The latest is the use of stem cells in periodontal regeneration.

Stem cells are in charge of the growth, homeostasis, and repair of many tissues. The conservation and survival of stem cells are regulated by inputs from their native microenvironment, often known as the "stem cell niche." The stem cell niche postulation proposed that stem cells reside within fixed compartments, or niches, that are conducive to the maintenance of definitive stem cell properties.

PDLSCs appear to play a crucial part in the regeneration of periodontal tissues as progenitor cells that coordinate the process. They can differentiate into osteoblasts, cementoblasts, chondrocytes, and adipocytes since they are heterogeneous, clonogenic, extremely proliferative, and multipotent cells. It should come as no surprise that they encourage the neoformation of periodontal tissues, such as bone, cementum, and sharpey-like periodontal ligament fibers. The primary cell types in charge of maintaining tissue homeostasis in the alveolar bone, cementum, and periodontal ligament, respectively, are osteoblasts, cementoblasts, and fibroblasts. As a result, it is critical to consider how PDLSCs function as a source of differentiation for these cells.[17] By expressing a number of neural growth and differentiation factors, PDLSCs have demonstrated significant neurotrophic benefits in peripheral nerve damage. Schwann cell (SC) transplantation is a potential method for repairing peripheral nerves. One cell source that can develop into SC-like cells is PDLSCs.[18]

In this case, we utilized transplantation of autologous DPSCs and PDLSCs niche in the treated periodontal intrabony defect of an endodontically affected tooth that contributed to periodontal bone regeneration. The existence of a healthy impacted tooth that needs to be extracted is the basic need of this procedure to procure DPSCs and PDLSCs.

The primary issue with *ex-vivo* cell culture is the sensitivity of the PDLSCs obtained from the extracted tooth root to continue to live for culture growth. There are several attempts by the researcher to succeed in stem cell survival, as the first step in *ex-vivo* cell culture expansion. Keeping this in mind, the authors of the paper attempted to place the autologous PDLSCs niche (A-PDLSCs Ni) adherent to the root and DPSCs from dental pulp directly into the selected osseous defect following extraction of the impacted tooth in the same patient. In fact, on microscopic examination, this tissue contains all the cells favorable for tissue regeneration.[19] The crucial step of cell survival by direct placement served the best of tissue engineering as chair-side reality instead of arduous laboratory-based sensitive cell culture procedure. They need a protracted life, are safely cryopreserved, and show the ability to interact with biomaterials.[20,21] In addition, they have been used for bone engineering without the need for culture-expanding procedures.[13-16,22,23] Taken together, all of the above-mentioned findings appear to provide the biological rationale for the clinical application of this therapeutic strategy.

In this case study, a gelatin sponge was employed as a scaffold to support osteoblasts and encourage bone regeneration in defective areas because of its flexibility, biocompatibility, and biodegradability.[24]

This technique resulted in successful clinical and radiographic parameters such as clinical attachment gain, decreased probing pocket depth, and satisfactory defect fill of osseous defect over a period of one year. The immediate periodic healing events were uneventful and no adverse reactions were found. Another important feature of direct autologous DPSCs and PDLSCs application in this case report is that the limitations of *ex-vivo* culture, such as high cost, technique sensitivity, loss of stemness during cell passage, genetic manipulation, and tumorigenic potential, were completely avoided.[25]

Based on current literature on the use of *ex-vivo* culture and associated problems, a humble attempt was made to harvest A-PDLSCs niche and DPSCs for direct application using gelatin sponge– scaffold (Abgel®©™**) as a scaffold in the regeneration of intrabony periodontal defect bypassing *ex-vivo* culture was attempted for the first time which satisfied the basic principle of and it abides tissue engineering triad consisting of PDLSCs and DPSCs, tissue niche growth factors as signaling molecules and gelatin sponge– scaffold (Abgel®©™**). Studies done by Vandana KL *et al*. have proved that PDLSCs have shown clinical and radiographical improvements in the treatment of periodontal osseous defects.[13,14,21,23] Based on this, in this case, we attempted to transplant the autologous PDLSCs niche (A-PDLSCs Ni) and extirpated dental pulp with DPSCs directly into the periodontal osseous defects surrounding the endo-perio affected tooth for the first time in literature.

A study by Aimetti M *et al*., in a clinical and radiographic finding and re-entry procedure, suggests that the application of autologous DPSCs may be a clinically relevant procedure in treating deep periodontal osseous defects.[9]

Since there is no bone graft/substitute used in this study it is discernible that the successful clinical and radiographic changes in the treated site are attributable to the DPSCs from dental pulp and PDLSCs present in the transplanted autologous periodontal tissue. This case report is based on the constructive results demonstrated in the published papers, either as case reports or randomized clinical trials by Vandana KL *et al*.[13,16,22] Above mentioned study report is the first of its kind to present chair-side PDLSCs along with niche therapy from the best of tooth waste without *ex-vivo* culture.

Conclusion

The results of this case reported that the DPSCs and PDLSCs niche with gelatin sponge resulted in a significant amount of bone fill and reduction in probing pocket depth.

A simple task of autologous DPSCs and PDLSCs niche procurement and immediate utilization are the major advantages of the current concept, which has emerged as a constructive avenue in the treatment of periodontal osseous defects. The extracted impacted tooth served as the best waste source for DPSCs and PDLSCs without *ex-vivo* culture. Moreover, the clinical feasibility, success, and cost-effectiveness of currently available techniques are encouraging in relatively smaller periodontal osseous defects. However, the clinical utility of this novel idea is suggested. In the field of dentistry, both endodontists and periodontists go hand in hand in treating these types of lesions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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