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Case Report

Root development of immature necrotic permanent teeth following regenerative endodontic process: Case series

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ABSTRACT

Regenerative endodontics is an expedient therapeutic strategy for necrotic teeth with open apex. The promising result of clinical research in the regenerative endodontic treatment field is published. The main goal of this case series is to present the radiographic and clinical findings of the regenerative endodontic procedure.

Key Words: Apexification, apexogenesis, regenerative endodontics

INTRODUCTION

Root canal treatment of premature permanent teeth has a long history of challenges. Although the success rate of apical barrier formation with calcium hydroxide is considerable, it is essential to conduct long-term follow-ups on these teeth. Issues such as inability to manage infection, reoccurrence of infection, and cervical root fractures may arise.[1,2]

Regenerative endodontics is a biological field that attempts to substitute necrotic pulp and reconstruct the new pulp tissue. Continuation of root formation and mitigating the traditional root canal treatment are the most important advantages of the regeneration approach.[3,4]

Cell-based transplantation therapy and cell homing are two approaches that can be used for the reconstruction of the pulp-dentin complex.[5,6] In cell-based transplantation therapy, transfer of autogenous or allogeneic stem/progenitor cells via intravenous can be administered. Even so, economic and ethical concerns are the limitations of this technique.[7,8] In the cell-homing approach, activated signaling pathways can absorb endogenous stem cells into the injured tissue.[6]

In the field of pulp regeneration, this approach might be easy and cost-effective and also can be administered easily by a less-trained clinician.[9] Stimulation of the

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periapical area via over-instrumentation can result in the organization of blood clots as a scaffold and chemotaxis of blood platelet-derived growth factors and mesenchymal stem cells into the canal space. Dental papilla is the source of stem cells delivered to the root canals.[9]

Studies showed that a blood clot can act like a perfect scaffold in most (regenerative endodontic treatment) RET and promising results have been published.[10,11] In addition to blood clots, several biological scaffolds such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) are introduced and can improve healing results because they contain platelets, growth factors, and cytokines.[12]

MATERIALS AND METHODS

The present study was confirmed by the faculties of dentistry, health, and advanced technologies in medicine, Isfahan University of Medical Sciences (IR.MUI.DHMT.REC.1403.153).

CASE REPORTS

Case 1

A 10-year-old female was referred to the Endodontic Department of Isfahan University of Medical Sciences with a chief complaint of pain in her mandibular left second premolar. The pain was lingering, vigorous, localized, and sharp. Her medical and dental history was not considered contributing. In the intraoral soft tissue evaluation, there was no swelling or sinus tract. Clinical examination revealed deep caries on the distal surface of the second premolar. The tooth was sensitive to palpation and percussion tests. The tooth mobility and periodontal probing were WNL. Sensitivity tests revealed no response

Figure 1: Preoperative.

Figure 2: Preoperative.

Figure 3: Postoperative.

Figure 4: Postoperative.

Figure 5: 3-months follow-up.

Figure 7: 12-months follow up.

Figure 6: 6-months follow up.

Figure 8: 18-months follow up.

to cold spray (Luber, Iran) and electric pulp test (EPT) evaluations. In the radiographic examination as shown in Figure 1, deficient root formation, expanded periodontal ligament space, and periapical radiolucency were detected in the mandibular left second premolar. A diagnosis of necrotic pulp with an open apex and symptomatic apical periodontitis was made.

Case 2

A 29-year-old female with the chief complaint of tooth discoloration in upper incisors was referred to the Endodontic Department of Isfahan University of Medical Sciences. The history of trauma many years ago was mentioned. The medical and dental history was noncontributory. Sensitivity tests showed no response to cold and EPT tests. Pulp and periapical diagnosis for the right maxillary central incisor was necrosis and chronic apical abscess, and for the left maxillary central incisor was necrosis and symptomatic apical periodontitis. Radiographic evaluation as shown in Figure 2 revealed that the central incisors had immature root formation. Considering the incomplete root formation, a regenerative endodontic procedure was scheduled.

In the first appointment, local anesthesia lidocaine with epinephrine 1:100,000 (Darupakhsh Co., Tehran, Iran) was administered. For isolating the tooth after dental clamp placement, a liquid dam (Cobult Co., Tehran, Iran) was injected at the surface between the clamp and tooth margin, and then access cavity preparation was made. After locating the canal and necrotic tissue extirpation, extensive and irrigation with 20 ml of 1.5% sodium hypochlorite (NaOCl) for 5 min was done and then irrigated with saline

Figure 9: 12-months follow up.

Figure 10: 6-months follow up.

(20 mL/canal, 5 min), with an irrigating needle placed nearly 1 mm from root end, to minimize cytotoxic effects on the stem cells in the apical tissues. Then the canal was dehydrated using paper points.

Then the tooth was sealed with 4 mm glass ionomer cement (Fuji II LC Gold, GC Corp, Tokyo, Japan) as a temporary restorative material in case 1 and zinc polycarboxylate in case 2 after calcium hydroxide (Golchadent, Tehran, Iran) was placed into the canal. Two weeks later, the patient returned for a follow-up appointment.

In the second appointment, in case 2, the sinus tract was not healed, and we decided to try the DAP paste in the root canal for 2 weeks. After 2 weeks, the patient was completely asymptomatic anesthesia with 3% mepivacaine (Darupakhsh Co., Tehran, Iran) without vasoconstrictor was applied. A dental dam and a liquid dam (Cobult Co., Tehran, Iran) were used to isolate the tooth. Paper points were used to dry the canal after copious irrigation with 20 ml of 17% EDTA. To fill the canal with blood to the level of the cementoenamel junction, the canal system was overinstrumented (K file #25), then white Mineral Trioxide Aggregate (MTA) (Tabriz, Iran) in case 1 and RetroMTA in case 2 as capping material was placed. A 4 mm layer of glass ionomer (Fuji II LC Gold, GC Corp, Tokyo, Japan) was applied over the capping substance and light-cured for 40s before restoring the tooth with a composite restorative material [Figures 3 and 4].

The patient was recalled every 6 months for evaluation of clinical signs and symptoms along with radiographic examinations [Figures 5-10]. There was no pain or discomfort or palpation, and no sinus tract was seen. Resolusion of apical radiolucency was detected 3 and 12 months after treatment in cases 1 and 2, respectively. Increased thickness of root walls was seen in 6 months after treatment in both cases. There was no response to the cold or electric pulp tester during pulp sensibility testing.

DISCUSSION

Regenerative endodontics is an expedient therapeutic strategy for necrotic teeth with open apex, with hopeful results of clinical research in the RET field being published.[13] In agreement with AAE clinical considerations for a regenerative procedure, three goals might be achieved: removal of symptoms and bone curing (primary target), root development (secondary goal), and positive feedback to sensibility examination (tertiary goal).[14] The preliminary index of favorable results of RET is healing evidence of apical periodontitis and lack of clinical signs and symptoms.[15] Furthermore, no signs of infection in 96% of REP cases, and complete elimination of apical periodontitis 2.5 years after REP was reported by a systematic review.[16] Another efficient review and meta-analysis showed a healing rate of REP of more than 90%.[17]

The increase in length and wall thickness of root canals has been identified as the supplementary goals of REP.[15] A systematic review reported that the published rate of success of secondary goals is variable and shows a growth in root length and root wall thickness in 62% of cases. Moreover, there was apical closure and complete root development in 45% of cases.[16] Based on a quantitative meta-analysis, REP has shown a 76% increase in root lengthening,

an 80% increase in root thickening, and a 77% reduction in apical narrowing. This indicates a good rate of root development after REP. However, when a 20% radiographic alteration is used as a threshold, the rate of root development decreases, making a clinical assessment of significant root growth after RET unpredictable.[17] Considering the tertiary goal, an incidence of 25% was reported for positive feedback to electric pulp examination in necrotic premature permanent teeth by a meta-analysis of randomized controlled trials.[18]

Stem cells, biological scaffolds, and growth factors are the three main elements of tissue engineering that accelerate the regeneration of the dentin-pulp complex.[4,19-22] Among these factors, the effect of scaffolding on the outcomes of REP was widely studied. Based on research, a biological scaffold can ameliorate the reconstruction of the dentin-pulp complex and deposition of mineral content to make resistance of the root canal wall.[20,23,24] In research that evaluates blood clot revascularization, blood PRF, and blood PRP as a scaffold, it was determined that PRF and PRP are more favorable results in apical closure, healing of apical periodontitis, a decrement in the diameter of the root apex and increasing the root length.[25] Prasad *et al*. reported that apical bridge merely forms within permanent incisors that use PRF as a scaffold.[26] However, a systematic review of clinical studies reported that PRF or PRP was not visibly preferable to a blood clot to increase the thickness of the canal walls and continuation of root formation in RET.[27] Furthermore, the mixture of blood clots and platelet-rich fibrin compared to single blood clots did not ameliorate the result of RET.[28] In a network analysis, six scaffolds were evaluated. PRF and PRP exhibited excellent achievement in examining primary and secondary results within 12 months postoperatively, in contrast to the conventional blood clot scaffold protocol. PRP attained the highest success level with statistical significance concerning the increase in root lengthening at 6–12 months.[29]

Disinfection plays a crucial role in regenerative endodontic procedures by influencing the interaction between growth factors, scaffolds, and stem cells, according to a quarter of tissue engineering in endodontics.[30] Various methods have been proposed for disinfecting root canals during revascularization. Usage of triple antibiotic paste (TAP), a composition of metronidazole, ciprofloxacin, and minocycline antibiotics, is recommended by the American Association of Endodontists for this purpose.[14] However, the clinical application of TAP in high concentrations was related to tooth discoloration linked to minocycline-associated.[31] Calcium hydroxide is a strongly suggested intracanal medicament for both multi-visit root canal treatment and RET. The antimicrobial activity of calcium hydroxide is weaker than that of TAP or DAP.[32] Nevertheless, it has been proven to enhance stem cell proliferation[33] and lead to less discoloration.[34]

AAE advocates for the application of bioactive substances like MTA and bioceramic sealers such as Biodentine in regenerative endodontics.[14,35] MTA is favored for its biocompatibility and bioactivity, making it a common choice in these procedures.[36,37] It is available in two forms: white MTA, which is less likely to cause discoloration, and gray MTA.[38,39] Newer materials like Biodentine have been developed to mitigate the discoloration risks associated with MTA.[40,41] Biodentine is a calcium silicate-based material that possesses similar properties to MTA and promotes pulpal healing and mineralization through the release of silicon ions and stimulation of odontoblasts.[42-44]

A comparison was made in controlled clinical research to evaluate the effectiveness of white MTA and Biodentine in REPs. According to the obtained data, no notable distinction was observed between them concerning sinus occurrence, pain, and root length. Nevertheless, Biodentine exhibited a lower incidence of tooth discoloration.[45]

The use of iRoot BP Plus and Bioaggregate in REPs has not been thoroughly researched in clinical settings. Nevertheless, in laboratory studies, Bioaggregate and iRoot BP Plus have been seen to stimulate odontoblastic differentiation and the creation of mineralization nodules.[46,47] Thus, additional research is necessary to explore the capability of iRoot BP Plus and Bioaggregate in REPs, as they might yield encouraging outcomes.

A review by Abdelatif *et al*. evaluated the success rates of pulp regeneration treatments using various bioactive materials in permanent teeth of pediatric patients, following AAE criteria. The findings showed that white MTA was associated with the highest success rates, evidenced by improved periapical healing, promoted root width, and positive responses to vitality tests. The overall success rate of REP indicated in the study is quite promising, with an

impressive 91.20% success. This statistic encompasses both primary and secondary goals of treatment, focusing on periapical healing and the enhancement of root structure through lengthening and thickening. Nonetheless, the data collected indicates a high degree of effectiveness in achieving the desired outcomes within the limits of the study's scope.[48] Thus, various calcium-silicate cements have been used as intracanal coronal barriers, and all of them have shown excellent bioactivity, biocompatibility, and good sealing ability.[40]

CONCLUSION

Regenerative endodontics is an expedient therapeutic strategy for necrotic teeth with an open apex. Our findings indicate a good rate of root development, removing of symptoms and bone curing and positive feedback to sensibility tests after REP.

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Conflicts of interest
The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.

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