Management of failed regenerative endodontic treatment of a necrotic immature molar: a case report with six-month follow-up

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Abstract

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"Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy"

Abstract

This is a report of the management of failed regenerative endodontic treatment of a necrotic immature molar. Mineral trioxide aggregate (MTA) and bioceramic-based root canal sealers yielded satisfactory outcomes in terms of lesion healing. Little is known about the biological and clinical aspects of regenerative endodontic treatment.

KEYWORDS

Regenerative endodontics, Immature necrotic teeth, Platelet-rich fibrin, Mineral Trioxide Aggregate, Bioceramic-based root canal sealer

Introduction

The management of necrotic immature permanent teeth has always posed a challenge to dental practitioners due to the thin dentin walls, wide open apex, and difficulty cleansing the root canal system of non-vital immature teeth. Furthermore, pulp necrosis can arrest root development and lead to fragile dentin walls which are more prone to fractures[1]. Therefore, every attempt should be made to maintain the pulp vitality of immature teeth.

Traditionally, apexification with calcium hydroxide was an acceptable approach for inducing a calcified apical barrier in non-vital immature teeth. However, this method has several disadvantages, including multiple visits, long-term treatment, and reinfection possibility. This could have led to the use of mineral trioxide aggregate (MTA) as an alternative to calcium hydroxide[2,3], which yielded satisfactory outcomes in terms of dentin bridge formation[3] and resolving periapical lesions[4]. Unfortunately, both procedures are unable to induce maturation and natural development of the root canal system.

Recently, regenerative endodontic procedures (REPs) have been proposed as a conservative alternative to apexification to treat non-vital immature teeth. Regenerative endodontic procedures (REPs) aim to thicken and elongate the root canal walls, induce apical closure, promote the dentin-pulp complex formation, and restore physiologic functions. Namely, regenerative endodontic procedures (REPs) aim to mimic the cellular and molecular mechanisms happening during tooth maturation. This treatment method has been considered a "paradigm shift"[5]. The three key ingredients for regenerative endodontic treatment are stem cells, growth factors, and scaffolds. Firstly, Stem cells are able to proliferate and differentiate to induce hard tissue formation. Secondly, growth factors regulate the stimulation of several cellular activities such as migration, proliferation, differentiation, and apoptosis. Lastly, scaffolds serve as an extracellular matrix to support tissue ingrowth and provide correct localization for cells, scaffolds can be either natural or synthetic[5,6]. Platelet-rich fibrin (PRF) is a synthetic scaffold of autologous fibrin that is loaded with platelet cytokines, leukocyte cytokines, and bioactive molecules[6]. It was first developed in France by Choukroun et al. in 2001[6,7]. However, few failed cases of (REPs) have been presented in the literature with different successful retreatment approaches[8,9,10].

This report presented a case of management of failed regenerative endodontic treatment of a necrotic immature molar using mineral trioxide aggregate (MTA) apical plug and bioceramic-based root canal sealer.

Case report

An eight-year-old boy was presented to the department of pediatric dentistry, Damascus University, in August 2021; he was referred to evaluate the right permanent mandibular first molar after incomplete treatment by a general dentist. The patient's parents reported a previous spontaneous pain lasting for hours and aggravated when the patient lay down for which his dentist performed an emergency treatment. There was no relevant medical history. In clinical assessment, extraoral examination revealed no swelling or facial asymmetry. Intraoral examination showed a temporary filling of zinc-oxide eugenol (ZOE) cement (Zitetemp, Prevest DenPro®, Lewes, DE, USA) in the right permanent mandibular first molar. In the diagnostic test, the tooth was tender to percussion and palpation. However, the tooth was unresponsive to different sensitivity tests. Adjacent gingiva showed a normal probing depth with physiological tooth mobility. Intraoral radiographic examination showed immature roots, wide open apices, periapical radiolucency, and lamina dura widening (Figure1). Regenerative endodontic treatment using platelet-rich fibrin (PRF) was considered an optimal treatment option and written informed consent was provided by the patient's legal guardians.

Ethical approval was obtained from the institutional review board of Damascus University (N 374/2021), and it was conducted in full accordance with the Declaration of Helsinki. On the first appointment, an inferior alveolar never block (IANB) was administered using Lidocaine HCL 2% with Epinephrine 1:80,000 (2% Lidocaine HCL Injection, Huons Co., Ltd, Seongnam, Korea) followed by rubber dam isolation (Sanctuary®, Perak, Malaysia). The temporary filling was removed using a 2 mm round bur (Dentsply, Maillefer, Ballaigues, Switzerland) in a high-speed handpiece (NSK PANA AIR, Nakanishi Inc., Tochigi-ken, Japan) with copious irrigation. Three canals were detected (mesiobuccal, mesiolingual, and distal). Working length was determined using Root ZX electronic apex locator (J. Morita MFG, Kyoto, Japan) and was confirmed with radiography. Without mechanical instrumentation, the canals were gently irrigated using 20 mL of 1.5% sodium hypochlorite solution (Carmel®; Akka Brothers Co. Carmel Detergent, Damascus, Syria) and then 20 mL of sterile saline solution (SODIUM CHLORIDE 0.9% MIAMED, Miamed Pharmaceutical Industry, Damascus, Syria), during irrigation the side-vented needle was inserted 1 mm short of the WL. Sterile absorbent paper points (Dentsply, Maillefer, Ballaigues, Switzerland) were used to dry the canals. The canals were filled with triple antibiotic paste (TAP) consisting of an equal proportion of ciprofloxacin (Ceproz, ELSaad Pharmaceuticals, Aleppo, Syria), metronidazole (Statizol, ELSaad Pharmaceuticals, Aleppo, Syria), and minocycline (Quatrocin, ALFARES Pharmaceuticals Co., Damascus, Syria) in a concentration of 1mg/mL, mixed with propylene glycol into a creamy paste using lentulo spiral (Dentsply, Maillefer, Ballaigues, Switzerland). The access cavity was sealed with temporary restoration (Cavit, 3M ESPE, St. Paul, MN, USA).

The next treatment session was appointed to be 3 weeks later. An inferior alveolar nerve block (IANB) was administered followed by rubber dam isolation. The access cavity was reopened, the intracanal dressing was flushed out of the canals by sterile saline solution irrigation, then the canals were irrigated with 20 mL of 17% EDTA (EDTA Solution, Prevest DenPro®, Lewes, DE, USA), then finally they were rinsed with sterile saline solution. The canals were dried with sterile absorbent paper points. In the meantime, platelet-rich fibrin (PRF) was prepared by drawing a 5 mL sample of whole venous blood from the patient's right foramen (right median cubital vein). The collected venous blood sample was transferred into a vacutainer tube (Vacuum Blood Collection Red Top Plain Tube, Jiangsu Nuohong Medical Technology Co., Ltd., Anhui, China) without anticoagulant and centrifugated (REMI Laboratories, Mumbai, Maharashtra, India) at 3000 revolutions per minute (rpm) for 10 minutes. Three layers were obtained: an acellular plasma layer (PPP) at the top, a platelet-rich fibrin layer (PRF) in the middle, and a red blood cells layer (RBCs) at the bottom (Figure 2). A sterile tweezer was used to remove the jelly PRF from the vacutainer tube, then it was placed on a sterile dry gauge to squeeze out the fluid present in the fibrin matrix. The freshly prepared PRF was fragmented into small increments which were inserted apically in the root canal up to the middle third and condensed using an endodontic plugger (Elite Dental Products, Daive, Florida, USA). A 2 mm thick layer of white MTA (ProRoot; Dentsply Tulsa Dental Specialty, Tulsa, OK, USA) was placed on the top of the floor of the pulp chamber and then sealed with a wet cotton pellet and temporary filling (Cavit, 3M ESPE, St. Paul, MN, USA) (Figure 3). On the next day, the temporary restoration and the wet cotton pellet were removed and a stainless steel crown (3M ESPE, St. Paul, MN, USA) was adjusted and cemented with luting glass ionomer cement (GC Fuji I, Leuven, Belgium). At 3- and 6-month follow-ups, the tooth was asymptomatic, with no sensitivity to palpation or sensitivity tests. At 9 months follow-up, there was a periapical radiolucency around the distal root, with tenderness to palpation and percussion, and with a negative response to different vitality tests. However, the periapical lesions around the mesial roots were resolved (Figure 4). Therefore, apexification with MTA was considered an optimal retreatment option for the distal root.

A conventional Inferior alveolar nerve block (IANB) was administered. After the removal of the stainless steel crown, the tooth was isolated with a rubber dam. The 2 mm thick layer of white MTA was removed with CPR ultrasonic tips (Obtura Spartan Endodontics, Algonquin, IL, USA). After working length determination, the distal root was slightly shaped with stainless steel K-file (Dentsply, Maillefer, Ballaigues, Switzerland), and the mesial roots were prepared using crown down technique. The canals were irrigated using 20 mL of 2.5% sodium hypochlorite solution, followed by 20 mL of sterile saline solution rinsing, then the canals were dried with sterile absorbent paper points. Triple antibiotic paste (TAP) was applied, then the tooth was sealed with a temporary restoration, and the next visit was appointed 21 days later.

On the next visit appointment, an inferior alveolar nerve block (IANB) was administered followed by rubber dam isolation. The access cavity was reopened, and the distal root was rinsed with 20 mL of 2.5% sodium hypochlorite solution, followed by 20 mL of sterile saline solution, and then dried with sterile absorbent paper points. Due to the poor visibility and accessibility in the posterior segment, MTA apical plug was applied in very small increments. At first, 30 gutta-percha cones (Dentsply, Maillefer, Ballaigues, Switzerland) were used to transfer the MTA increments into the apical third, then finally were condensed with the aid of an endodontic plugger into a 5 mm apical plug. A moist cotton pellet was placed over the MTA apical plug, then the tooth was sealed with a temporary restoration.

After 48 hours, an inferior alveolar nerve block was administered, the tooth was isolated, and the access cavity was reopened. The canals were rinsed with 20 mL of 2.5% sodium hypochlorite solution, followed by 20 mL of sterile saline solution, and then dried with sterile absorbent paper points. The canals were sealed with a bioceramic-based root canal sealer (CeraSeal, Meta Biomed, Chungcheongbuk-do, Korea), then a stainless steel crown was adjusted and cemented with luting glass ionomer cement (Figure 5). In the three-month follow-up, the tooth was asymptomatic and the periapical lesion began to resolve (Figure 6). In the six-month follow-up the periapical lesion healed (Figure 7).

Discussion

This article presented a case report on failed regenerative endodontic treatment and its clinical management. Although the success of regenerative endodontic procedures (REPs) was highly reported in the literature[11-21], few cases described unfavorable outcomes and their further management[8,9,10]. The success of regenerative endodontic procedures (REPs) is governed by the stage of root maturation[5,22], the size of the apical diameter[5,23,24], the cytotoxicity of the root canal irrigants, the antimicrobial efficacy of the intracanal medicament, and the long-standing nature of the preceding infection[5].

According to cevek et al.[22] classification of the stages of root maturation, regenerative endodontic treatment (RPT) is suitable for stage 1 (wide divergent apical opening with less than 50% of root length), stage 2 (wide divergent apical opening with 50% of root length), and stage 3 (wide divergent apical opening with 66% of root length). However, for stage 4 (wide open apex with nearly completed root formation), as presented in this case, RPT or apexification with MTA apical plug are both suitable treatment options. In addition, Estephan et al.[23] concluded that teeth with a wider diameter ([?]1mm) showed better treatment outcomes because this allows the influx of blood vessels and stem cells. The aforementioned facts could explain the failure of the present regenerative endodontic treatment.

Regarding the afore irrigation protocol, the American Association of Endodontists (AAE) recommends using 1.5% sodium hypochlorite solution followed by 17% EDTA[25]. This recommendation is based on in vitro studies, which found that sodium hypochlorite has a cytotoxic effect on stem cells from the apical papilla (SCAP)[26,27]. However, to date, the antimicrobial efficacy of sodium hypochlorite has mostly been tested in vitro environment[28]. In addition, a reduced concentration of sodium hypochlorite resulted in decreased bactericidal capacity[29]. Therefore, the intracanal antimicrobial capability of 1.5% sodium hypochlorite seems questionable. This could lead to residual bacteria that compromise the level of disinfection, which is a cornerstone for successful regeneration endodontic treatment[5].

In the present case, the presence of preceding infection could have damaged the stem cells and the tissue-forming cells in the periapical area resulting in unpredictable revascularization[30]. In spite of the immune-regulatory and anti-inflammatory properties of mesenchymal stem cells[31,32], and infection leading mesenchymal stem cells into the site of injury by SDF-1 (stromal cell-derived factor)[33,34], pro-inflammatory cytokines (IL-1 α, TNF- α) are able to inhibit stem cells differentiation[35,36,37]. Furthermore, the presence of lipopolysaccharide (LPS) shifted stem cells from apical papilla (SCAP) from odontogenic to osteogenic phenotype[38].

Mechanical instrumentation was minimal because it could lead to the weakening of the fragile and thin root canal walls[25]. However, the effectiveness of mechanical debridement protocol in regenerative endodontic procedures (REPs) is suspected[5,39]. In the present case report, platelet-rich fibrin (PRF) was used as a scaffold because it is rich in growth factors compared with the blood clot scaffold which could result in favorable treatment outcomes[6].

The American Association of Endodontists (AAE) defines the success of regenerative endodontic treatment by three measures. The primary measure is symptoms resolving and bony healing[25] which is generally achievable[40,41,42] with high probability (91-94%)[41,42]. The secondary measure is root canal lengthening and/or root canal thickening[25] but these outcomes are not always predictable[42,43,44,45]. The tertiary goal is a positive response to pulp vitality tests[25], but it does not indicate pulp tissue regeneration[46]. In the present case report, the mesial roots achieved the primary healing measure. This could be explained by the fact that the size of the preoperative periapical lesion around the mesial roots is smaller than the one around the distal root[5].

As aforementioned, the main reason for failed regenerative endodontic cases is inadequate disinfection, inadequate biofilm removal, and the presence of preceding infection which all lead to root canal reinfection[5].

Mineral trioxide aggregate (MTA) is highly biocompatible[47,48], has good sealing properties, and has a great marginal adaptation[47,49]. In addition, MTA stimulates the formation of dentin bridges[49] and limits bacterial infection when using it as an apical plug[50]. Furthermore, MTA induces bone deposition[49,51] by stimulating growth factors such as bone morphogenetic protein-2 (BMP-2) and transforming growth factor beta-1 (TGF-β1) to achieve osseous healing[52,53,54]. Moreover, MTA has yielded satisfactory outcomes in terms of healing large periapical lesions after six years of follow-up[4]. However, in the present case report, the periapical lesion around the distal root healed only after six months. This could be explained by the well-known fact that regeneration and healing are faster in younger individuals than in older age groups[55,56]. Bioceramic-based root canal sealer was used due to its high biocompatibility[57,58], bioactivity[58], and low cytotoxicity[57,58]. bioceramic sealers are believed to have superior properties compared with other sealers in terms of bone deposition and osteogenic potential[59,60]. Moreover, bioceramic sealers stimulate osteogenic differentiation by inhibiting the expression of inflammatory mediators prompted by lipopolysaccharides (LPS), suggesting that these sealers demonstrate anti-inflammatory properties[60].

The results of the present case report suggest that little is known about the biological and clinical aspects of regenerative endodontic treatment (RPT) and there are many unanswered questions. Moreover, there are still unknown factors that govern the success of RPT. Taking these points into consideration, further studies should be conducted with a large sample size to decipher this medical mystery.

Conflict of interest

The authors declare that there are no conflicts of interest.

Authors' contributions

MK: research concept and design, collection and/or assembly of data, data analysis and interpretation, writing the article. IA: collection and/or assembly of data, critical revision of the article. ML: critical revision of the article. NB: critical revision of the article, final approval of the article.

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Ethical approval

Ethical approval was obtained from the institutional review board of Damascus University (N 374/2021).

Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Consent statement

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy

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Figure legendsFigure 1. Diagnostic radiograph of the right permanent mandibular first molar showed the presence of periapical radiolucency with lamina dura widening.**Figure 2.** Three layers were obtained after centrifugation: an acellular plasma layer (PPP) at the top, a platelet-rich fibrin layer (PRF) in the middle, and a red blood cells layer (RBCs) at the bottom.**Figure 3.** Postoperative radiograph after regenerative treatment and MTA placement.**Figure 4.** Follow-up radiograph after 9 months, a periapical lesion was detected around the distal root and there was bony healing around the mesial roots.**Figure 5.** Postoperative radiograph after MTA apical plug placement and sealing with bioceramic-based root canal sealer.**Figure 6.** Follow-up radiograph after 3 months, the periapical lesion around the distal root began to resolve.**Figure 7.** Follow-up radiograph after 6 months, the periapical lesion healed.

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