Maturogenesis and Osseous Healing of a Necrotic Immature Premolar using Revascularization Procedure - A Case Report and Review of Literature

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Abstract
Immature permanent teeth with pulpal necrosis present a clinical challenge to endodontists. Since debridement of pulp canal space is difficult, there is an increased possibility of root perforation and cervical root fracture due to thin root dentine and the presence of an open immature root apex jeopardize the apical seal of a root canal treatment resulting in subsequent failure. Regenerative endodontic Procedures provide an unconventional approach which relies on the principle of tissue engineering. The treatment outcomes of revascularization of necrotic immature permanent teeth have been shown to promote tooth maturogenesis and bone healing. This report presents a case of revascularization of a necrotic left mandibular premolar with apical periodontitis and interseptal bone defects using minimal canal instrumentation and calcium hydroxide paste as a root canal disinfectant. At a following visit, blood clot was evoked in the canal by irritating periapical tissues and the canal properly sealed with mineral trioxide aggregate, glass ionomer cement and composite resin. The case was followed for thirty-eight-month and deemed to be clinically normal with a positive response to cold test (Endo-frost, Roeko, UK). Radiographic evaluation showed root maturogenesis and complete osseous healing which was evident in the apical and interseptal bones.

Keywords: Apexification; Immature permanent tooth; Necrosis; Pulp revascularization

Introduction
Immature permanent teeth with pulpal necrosis present a clinical challenge to endodontists, with the facts that debridement of pulp canal space is not guaranteed, there is an increased possibility of root perforation and cervical root fracture due to thin root dentine and the presence of an open immature root apex jeopardize the apical seal of a root canal treatment resulting in subsequent failure. Regenerative endodontic Procedures provide an unconventional approach which relies on the principle of tissue engineering.\textsuperscript{[1-3]}

Conventionally, necrotic immature permanent teeth were treated with traditional calcium hydroxide apexification techniques or more recently MTA was used to treat immature teeth with pulp necrosis in a single visit setting.\textsuperscript{[4]}

However, apexification with calcium hydroxide has several drawbacks, including unpredictability of treatment time, several recall visits are needed to place and replace calcium hydroxide to avoid possible weakening of the root structure and subsequent root fracture, also root dentin does not increase in thickness and remain stunted.\textsuperscript{[3,5-7]}

A new treatment modality of revascularization of immature necrotic permanent teeth was introduced in the past several years. The concept of revascularization was first established by Ostby \textsuperscript{[8]} in 1961, and in 1966, Rule and Winter \textsuperscript{[9]} reported

root development and apical barrier formation in cases of pulpal necrosis in children.

Successful Revascularization of an immature permanent tooth with increased root length and root dentin width have been reported after appropriate canal disinfection and the presence of a scaffold (blood clot) in the canal space for both human and in animals.\textsuperscript{[10]}

Revascularization procedures in general require the use of an intracanal disinfectant which is regarded as a major prerequisite for success.\textsuperscript{[2,3,5,11,12]}

The triple antibiotic paste (TAP) consisted primarily of a mixture of ciprofloxacin, metronidazole and minocycline which has been reported to be effective in bacterial elimination and canal disinfection.\textsuperscript{[13]}

Calcium hydroxide has been extensively used as an intracanal medicament in mature and immature permanent teeth owing...
to its known antibacterial effects. Its increased PH impedes bacterial proliferation and it has also been reported to decrease the likelihood of discoloration following revascularization procedures. On the other hand, high PH of Calcium hydroxide can prevent vital tissue growth in the root canal space and the difficulty of its complete washout might lead to diminished space required for tissue regeneration. Moreover, Calcium hydroxide can induce a hard tissue response instead of pulp-like structures. [14,15]

The treatment outcomes of revascularization have been shown to result in increased thickening of the canal walls by deposition of hard tissue and/or encourage continued root development in immature permanent teeth with necrotic pulp tissue and/or apical periodontitis/abscess. [6]

This case report presents a thirty-eight-month follow-up of a necrotic immature mandibular premolar with apical periodontitis treated with revascularization procedures using calcium hydroxide with iodoform paste (Mitapex) as a root canal disinfection dressing material. The tooth showed continued root development, apical closure and osseous healing.

Case Report

A 10-year-old Saudi female presented to King Khalid University, College of Dentistry, outpatient clinics, for evaluation of her mandibular left first premolar. The medical history was of no relevance. There was history of pain on biting, whilst her mother was anxious about some swelling of the gingiva adjacent to the offended tooth. Intraoral examination revealed deep occlusal caries with heavy plaque accumulation on the lower left quadrant indicating it as a non-chewing side [Figure 1]. Sensibility testing of the mandibular left first premolar was not responsive to both cold and electric pulp sensibility testing as compared to the remaining teeth in the lower left arch which showed a positive response. Periodontal examination revealed normal periodontal health around the offended tooth with no probing depths greater than 3 mm. The tooth revealed grade I mobility and the crown showed a deep carious lesion.

Radiographically, the mandibular left first premolar had; radiolucency involving enamel, dentin and exposing the dental pulp, an increased periodontal ligament space and apparent peri-apical radiolucency. The apex was Blunderbuss and dentinal wall were thin at the apical third of the root. Bone rarefaction was obvious at the interseptal bone both mesial and distal sides of the offended tooth. Agensis of the left second mandibular premolar was also evident [Figure 2].

On the basis of the clinical and radiographic examination, the tooth was diagnosed as being necrotic with acute apical periodontitis which was a result of untreated dental caries and consequent pulpal involvement. Regenerative endodontic procedure was planned considering the age of the child, immaturity of the root apex, the thin root dentin, apical radiolucency and the rarefied interseptal bone. The primary goal was to promote maturogenesis of the root and healing of the periradicular and interseptal lesion.

Detailed information regarding the benefits, hazards, possible side effects and other possible treatment alternatives were offered for the child’s legal guardian and a written informed consent was obtained.

Local anaesthesia using 2% lidocaine with vasoconstrictor was administered and rubber dam isolation achieved.

Access cavity was prepared; a wide single canal was detected. Working length was estimated with a periapical radiograph taken with a size 15 K-file (Sybron Endo, Orange, CA, USA) inserted inside the canal.

The canal was minimally instrumented and copiously irrigated with 20ml of 1.5% sodium hypochlorite followed by 17% EDTA. This was followed by dryness of the canal using paper points then calcium hydroxide with iodoform paste (Metapex) was used as dressing and tooth temporary restored with Glass Ionomer Cement Fuji IX (GC, IL, USA). Next recall visit was scheduled three weeks from the first appointment. However, patient failed to attend her appointment and came after 3 months instead. Patient reported no symptoms following the first appointment and pain disappeared completely. Therefore,
the second visit was initiated; a periapical radiograph was taken and showed Metapex was in place with good apical and coronal adaptation [Figure 3].

Figure 3: Periapical radiograph taken 3month following the first visit showing Metapex inside the root canal, reduced periradicular radiolucency and increased interseptal bone trabeculation.

A 3% mepivacaine without a vasoconstrictor was used in order to facilitate intracanal bleeding. Under rubber dam isolation, bleeding was evoked by over-instrumenting the canals beyond the apical foramen to allow the influx of blood containing mesenchymal stem cells from periapical tissues to the root canal space using a NiTi H-file (Dentsply Tulsa Dental, TN, USA). Then blood clot formation was initiated by applying a damped cotton pellet to canal orifice for 15 minutes to produce a natural scaffold for the regenerative procedure [Figures 4A and 4B].

Figure 4: Clinical picture of the tooth (A) bleeding has been evoked by over-instrumenting the periapical tissues with a NiTi H-file. (B) Clot formation below the cement-enamel junction.

Access cavity was then sealed with an inner layer of 2 mm of ProRoot white MTA (Dentsply Tulsa Dental, TN, USA) using an amalgam carrier (CF-II® Hu-Friedy, USA) and a Buchanan Plugger (Sybron Endo, Orange, CA, USA) and an outer layer composed of GIC Fuji IX and an acid etched composite resin restoration [Figures 5A and 5B].

Figure 5: clinical picture of the lower left first premolar. (A) ProRoot MTA placed over the induced blood clot as an inner sealing material. (B) Gic Fuji IX and acid etched composite resin restoration used as outer sealing materials.

Patient was recalled six months later and reported no clinical symptoms, the tooth was functioning efficiently and periapical radiograph showed increased root dentin thickness particularly in the apical half of the root, root apex almost closed and marked increase in interseptal bone thickness and trabeculation in both mesial and distal sides [Figure 6].

Figure 6: Periapical radiograph taken 6 months later, showing increased root dentin thickness particularly in the apical half of the root, root apex almost closed and marked increase in interseptal bone thickness and trabeculation in both mesial and distal sides of the tooth.

The tooth was clinically and radiographically followed up for thirty-eight-month. Patient was recalled at year two and three for clinical and radiographic evaluation. The tooth was clinically normal and a positive response was found when cold test was used (Endo-frost, Roeko, UK). Radiographic evaluation showed root maturogenesis and osseous healing; increased width of root dentine which was particularly evident at the apical half, slight lengthening of the root, apex was completely closed and radiopaque tissues were noticeable in the root canal space. Complete osseous healing was evident in the apical and interseptal bones [Figures 7A and 7B].

Figure 7: Periapical radiograph of the lower left premolar taken at follow up appointments. (A) At two-year follow-up, showing complete root maturogenesis and osseous healing. (B) At thirty eight-month follow-up showing hard tissue formation and canal obliteration in apical half of the root.

Discussion

The concept of Regenerative endodontic treatment is not a new topic. Nygaard-Ostby in 1961 investigated the role of blood clot from the apical tissues in healing of infected pulpal and periradicular tissues. [8] Pulp revascularization procedures to be successful requires the existence of a triad consisting of a source of mesenchyme stem cells, growth factors/ signaling molecules and scaffolds so as to provide structural and biological supports for cellular activities. [16]
It is suggested that mechanical cleaning as much as the use of intracanal irrigants and dressing is the most efficacious way to disinfect root canal space of an infected pulp. Nevertheless, in an immature permanent tooth, vigorous intracanal instrumentation and dressing using high concentration of antiseptics may result in damage and cytotoxicity of viable pulpal cells that might be present in the apical area.\[15,17\]

The use of triple antibiotic mixture of ciprofloxacin, metronidazole and minocycline in pulp revascularization procedures as canal disinfectants has been reported in many case reports and case series studies.\[3,5,11,18,19\] On the other hand, Calcium hydroxide has similarly been used meritoriously as an intracanal disinfectant of immature permanent teeth with necrotic pulp.\[20,21\]

Lovelace in 2011 suggested that evoked-bleeding step in regenerative endodontic procedures generates an abundant number of undifferentiated mesenchymal cells into the pulp space, these progenitor cells might play an essential role in regeneration of pulpal tissues.\[22\] Directly over the induced blood clot MTA was applied and compressed to attain an optimal coronal seal.

Mineral Trioxide Aggregate (MTA) was first introduced in the 1990’s and was used as an apical barrier.\[23\] The choice of MTA as an inner sealing material was based on its hydrophilic property that requires moisture to set and the fact that MTA by itself delivers signaling molecules required for stem cells growth and differentiation.\[24\] Although, different terminologies have been used in this context such as pulp revascularization, regenerative endodontics, pulp revitalization and/or pulp repopulation, it is still not well recognized what kind of tissue has actually been renewed.\[3\]

However, in histological studies of animal teeth treated with revascularization procedures, the hard tissues formed in pulp canal spaces were defined to be bone-like or cementum-like tissues and persistent root development was recognized to be due to apical cementum deposition following revascularization procedures.\[2,6,25,26\] Some authors postulated that there may possible be residual vital pulpal tissue in necrotic teeth that induce the regenerative process.\[3,27\]

Undeniably, the durability of pulpal stem cells and its ability to survive within a necrotic environment has long been documented.\[24,29\] Nevertheless, a recent study on dog teeth has suggested that the newly formed tissue is expected to originate from the periodontal ligament cells comprising cementum, bone, and dentine-like tissues rather than original pulp tissue.\[2,30\] Even with this limited understanding of the regenerative process, many case reports demonstrate evidence of clinical success.\[11,28,31,32\]

The present case report and several previous ones show that revascularization procedure is a possible treatment option which has been termed as a ‘paradigm shift’ that induce root maturogenesis, revitalization and healing of a previously necrotic immature permanent tooth.\[53\] The current case report indicates an effective thirty-eight-month outcome of a revascularization procedure performed in a necrotic immature lower left premolar of a ten-year-old female patient.

The choice of revascularization for this case was based on the fact the tooth was necrotic and immature with an open apex and the surrounding bone was pathologically resorbed. The treatment aimed at inducing maturogenesis of the tooth as long as bony healing. Other options of treatment includes; conventional root canal treatment which would be technically impractical due to the widely open apex and the absence of an apical constriction, apexification with the use of MTA or calcium hydroxide which only guarantee apical closure but not tooth maturation and bone healing. Moreover, the use of Calcium hydroxide dressing for prolonged periods carries the risk of root fracture.\[34\] The American Association of Endodontists considerations for regenerative endodontics indicate that the primary goal of these procedures is the complete absence of symptoms and evidence of osseous healing.\[13\]

In the current case, the patient reported absolutely no symptoms following the disinfection phase (first visit) and throughout the follow-up period. A positive response to Endo-frost spray was evident after 2 years indicating a vital tissue with an organized nerve supply. This finding is not the usual scenario reported in revascularization procedures; in a prospective analytical study of 16 revascularization cases, Kahler et al.\[36\] demonstrated only 5 positive responses to electric pulp tester (EPT) while, other investigators reported negative results for the EPT after regenerative endodontic procedures.\[19,37\] Root maturogenesis is the secondary goal of regenerative endodontic procedure (AAE).

The current case reported an increase in root wall thickness especially in the apical half with calcified tissue evident at the pulp canal space in addition to apical closing and bony healing. However, by comparing the preoperative and postoperative radiographs, it was not possible to confirm that the root length had increased significantly. A retrospective study comparing the effect of different intracanal disinfectants on the outcome of revascularization concluded that Calcium hydroxide when used as a canal disinfectant is efficient in promoting root dentine development when compared to triple antibiotic paste (TAP) and formocresol. However, TAP was superior in inducing root dentin thickness.\[37\]

In the present case report pain was not recounted following the disinfection step of revascularization procedure and the placement of calcium hydroxide paste (Metapex). However, in a study conducted by Ding et al., two patients experienced pain following the application of TAP which necessitated the change of treatment to a traditional apexification procedure instead of revascularization technique.\[18\] The significance of an optimum coronal seal for successful revascularization has been well documented.\[15\] In this case report MTA has been used as an inner layer sealing material whereas GIC Fuji IX and an acid etched composite resin restoration were used as an outer layer sealing materials as recommended by many studies.\[2,3,30\]
The radiographic outcome of this case report was an increase in width of the root dentine which was particularly evident at the apical half of the root, apical closure with resolution of apical periodontitis and a marked healing of bony lesions which was apparent in the interseptal bone mesial and distal to the offended tooth. The presence of a radiopaque material in the pulp canal space was noticeable after two years of the revascularization procedure that subsequently turned into complete canal obliteration in thirty eight-month recall.

**Conclusion**

In conclusion, the authors consider revascularization procedures as an appropriate treatment for necrotic immature permanent teeth with apical periodontitis and/or associated bone defects, which not only result in tooth maturogenesis, but can also promote bony healing. However, case reports on endodontic regeneration have used varying treatment protocols and further clinical trials are required to assess the overall outcomes of the procedures.

**Conflict of Interest**

All authors disclose that there was no conflict of interest.

**References**