Treatment of a Large Cystlike Inflammatory Periapical Lesion Associated with Mature Necrotic Teeth Using Regenerative Endodontic Therapy

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Abstract

Introduction: Regenerative endodontic therapy is currently used to treat immature permanent teeth with necrotic pulp and/or apical periodontitis. However, mature teeth with necrotic pulp and apical periodontitis have also been treated using regenerative endodontic therapy. The treatment resulted in resolution of apical periodontitis, regression of clinical signs and symptoms but no apparent thickening of the canal walls, and/or continued root development. A recent study in an animal model showed that the tissues formed in the canals of mature teeth with apical periodontitis after regenerative endodontic therapy were cementumlike, bonelike, and periodontal ligament–like tissue with numerous blood vessels. These tissues are similar to the tissues observed in immature permanent teeth with apical periodontitis after regenerative endodontic canal therapy. Methods: A 23-year-old woman had a history of traumatic injury to her upper anterior teeth when she was 8 years old. Subsequently, #8 developed pulp necrosis and an acute apical abscess and #7 symptomatic apical periodontitis. The apex of #8 was slightly open, and the apex of #7 was completely formed. Instead of nonsurgical root canal therapy, regenerative endodontic therapy was attempted, including complete chemomechanical debridement on #8 and #7. This was based on the premise that filling of disinfected root canals with the host’s biological vital tissue might be better than filling with foreign materials. Results: After regenerative endodontic therapy of #8 and #7, there was radiographic evidence of periapical osseous healing and regression of clinical signs and symptoms. The pulp cavity of #8 decreased in size, and the apex closed. The pulp cavity of #7 appeared to be obliterated by mineralized tissue. These indicated ingrowth of new vital tissue into the chemomechanically debrided canals. Conclusions: Regenerative endodontic therapy of mature teeth with apical periodontitis and apical abscess can result in the regression of clinical signs and symptoms and healing of apical periodontitis but no apparent thickening of the canal walls or continued root development. Filling of the disinfected canals with the host’s vital tissue may be better than with foreign materials because vital tissue has innate and adaptive immune defense mechanisms. (J Endod 2014;40:2081–2086)

Key Words

Apical periodontitis, mature teeth, necrotic pulp, regenerative endodontic therapy, root canal therapy, vital tissue

Regenerative endodontic therapy has been suggested as treatment of immature permanent teeth with necrotic pulp and/or apical periodontitis. It has the potential to restore tooth vitality, increase thickening of the canal walls, and/or encourage continued root development (1). Regenerative endodontic therapy has been performed on mature permanent posterior teeth and anterior teeth with necrotic pulp and/or apical periodontitis in humans (2, 3) and animals (4). The treatment resulted in the resolution of apical periodontitis and regression of clinical signs and symptoms but no apparent thickening of the canal walls or continued root development. An outcome can be considered success of endodontic therapy, i.e., resolution of periapical lesion and regression of clinical signs and/or symptoms.

The purpose of this case report was to describe treatment using regenerative endodontic procedures of a large cystlike inflammatory periapical lesion associated with 2 traumatized maxillary permanent anterior teeth with infected necrotic pulps and apical periodontitis in an adult patient. The rationale of performing regenerative endodontic therapy was based on the premise that filling of the disinfected root canals with the host’s vital tissue might be as good as or better than that with foreign material such as gutta-percha because vital tissue has innate and adaptive immune defense mechanisms. In addition, most vital tissues are capable of perceiving external stimuli because of sensory innervation.

Case Report

A 23-year-old woman presented to the faculty practice clinic at Faculty of Dentistry, University of Benghazi with the chief complaint of pain and swelling in the maxillary right anterior region. The patient gave a history of trauma to her maxillary anterior teeth when she was 8 years old. She did not seek dental treatment at the time of trauma. During the past 15 years, she had several episodes of pain and...
swelling; however, she did not go for any dental treatments. The patient did not have any significant medical history contradictory to nonsurgical root canal therapy.

**Clinical Examination**

**Extraoral Examination.** Neither facial discoloration nor extraoral swelling or sinus tract was noted. There were no palpable lymph nodes in the head and neck.

**Intraoral Examination.** The patient’s oral hygiene was acceptable. The crowns of all maxillary anterior teeth were intact. Well-circumscribed swelling measuring approximately 2 × 2 cm in diameter was located on the palatal surface involving the periapical areas of teeth #8 and #7 (Fig. 1). The swelling was tender to palpation and slightly fluctuant. No sinus tract was observed. Tooth #8 was discolored and displaced labially (Fig. 1). It was tender to percussion and periapical palpation on the labial surface. The tooth did not respond to either thermal or electric pulp tests (EPTs). Tooth #7 was slightly tender to percussion and palpation but not discolored. It responded erratically and inconclusively to thermal and EPT. Periodontal probing of #8 and #7 was within normal limits (3–4 mm in pocket depth).

**Radiographic Findings**

A periapical radiograph showed a well-circumscribed osteolytic lesion measuring approximately 15 × 17 mm in diameter involving the entire apical root of #7 and the mesial aspect of the root of #6 and extending upward to the floor of the nasal cavity (Fig. 2A). In addition, a separate small ill-defined osteolytic lesion was associated with the root apex of #8 (Fig. 2A). The 2 osteolytic lesions appeared to merge. The root apex of #8 was slightly open, and the pulp cavity was completely formed root, and the apex curved distally (Fig. 2A). The pulp cavity was narrow but could be seen extending to the apex on radiographs.

Cone-beam computed tomographic imaging in a coronal view indicated that a large osteolytic lesion involved the entire root of #7 and the mesial root surface of #6 and extended upward to the floor of the nasal cavity (Fig. 3A). In a sagittal view, the osteolytic lesion had perforated a large portion of the palatal cortical bone plate and a small portion of the buccal cortical bone plate (Fig. 3B).

**Diagnosis and Treatment Plan**

Although the large periapical osteolytic lesion seemed to primarily involve #7, it responded inconsistently to pulp tests. Tooth #8 had a small periapical osteolytic lesion and did not respond to repeated pulp tests. The clinical diagnosis of #8 was an acute apical abscess because of apical swelling and pain, no response to pulp tests, labial displacement, discoloration of crown, and sensitivity to percussion. The treatment plan for #8 was to perform regenerative endodontic therapy. It was decided to continue to observe #7 because of an inconclusive diagnosis of the pulp-periapical tissue complex. The treatment plan for #8 was explained to the patient, and consent was obtained. The patient was scheduled for regenerative endodontic treatment.

**Treatment Procedures**

**First Treatment Visit.** Local anesthesia was not administered. Tooth #8 was isolated with a rubber dam. The crown of the involved tooth and the surrounding rubber dam were disinfected by swabbing the area with 30% hydrogen peroxide followed by Betadine (Tizaro Suppl Limited, London, UK). The canal was accessed through the lingual surface. A straw-colored fluid drained through the access cavity. The access cavity and canal were gently irrigated with 2.5% sodium hypochlorite (Clorox; Nobelwax Factories for Chemicals, Kaliobeya, Egypt). A #50 hand K-file was used to estimate the working length (WL) (1 mm short of the radiographic apex) radiographically. More exudate drained through the access cavity when the palatal swelling was pressed. The canal was sequentially instrumented to a #80 hand K-file to the WL and irrigated with copious amounts of sodium hypochlorite followed by sterile saline solution. The canal was dried with sterile paper points. Triple antibiotic paste consisting of metronidazole 500 mg (Flagaz, Amriya Pharm Ind, Alexandria, Egypt), ciprofloxacin 200 mg (Ciproflozazine, European Egyptian Pharm Ind), and minocycline100 mg (Minocin; Wyeth, Guangzhou, China) mixed with sterile saline solution to a creamy consistence was delivered into the canal using a Lentulo spiral into the apical portion of the canal. A sterile cotton pellet was placed into the canal below the cementoenamel junction (CEJ), and the access cavity was sealed with intermediate restorative material (IRM; Dentsply DeTrey, Konstanz, Germany).

**Second Treatment Visit.** One week after the first treatment visit, the tooth was asymptomatic, and the palatal swelling subsided. The IRM together with the cotton pellet was removed from the access cavity. Triple antibiotic paste was removed from the canal by irrigation with copious amounts of sodium hypochlorite. Some yellow straw-colored fluid continued to seep out of the access cavity. The canal was sequentially reinstrumented to a #100 hand K-file to the WL and irrigated with copious amounts of 2.5% sodium hypochlorite. The canal was dried and dressed with triple antibiotic paste again. The access cavity was closed with a cotton pellet and IRM.

**Third Treatment Visit.** Two weeks after the second treatment visit, #8 remained asymptomatic. However, the patient complained of slight pain and tenderness when biting on #7. The tooth did not respond to pulp tests with cold, heat, and EPT at this appointment. The clinical diagnosis of #7 was symptomatic apical periodontitis, and the tooth required treatment.

Local infiltration anesthesia with 3% mepivacaine without vasoconstrictor was administered. The access cavity of #8 was reopened. Triple antibiotic paste was removed from the canal by irrigating with 2.5% sodium hypochlorite solution followed by flushing with saline solution. The canal was dried. A #40 hand K-file was used to penetrate into the periapical tissues and provoke bleeding into the canal up to approximately 3 mm below the CEJ using a surgical microscope. After partial,
coagulation of the blood, a paste of white mineral trioxide aggregate (MTA; Dentsply Tulsa Dental, Tulsa, OK) and sterile saline solution was carefully placed over the blood clot using an amalgam carrier. A moist cotton pellet was placed over MTA, and the access was closed with glass ionomer cement (Fig. 2B).

The canal of #7 was accessed. No vital tissue was noted in the pulp chamber. When a #10 hand K-file was introduced into the canal near the apex, the patient felt pain. Therefore, it was assumed that some vital pulp tissue might have been present in the apical portion of the canal. Another local infiltration of anesthetic containing 3% mepivacaine without vasoconstrictor was administered. The WL (1 mm short of the radiographic apex) was determined radiographically using a #15 hand K-file. The canal was sequentially instrumented to a #35 hand K-file to WL. After instrumentation, triple antibiotic paste was introduced into the canal. The access cavity was closed with a sterile cotton pellet and IRM.

Fourth Treatment Visit. The symptoms associated with #7 subsided 2 weeks after the third treatment visit. At the fourth visit, local infiltration anesthetic with 3% mepivacaine without vasoconstrictor was administered. The tooth was re-entered. The triple antibiotic paste was removed from the canal by irrigating with sodium hypochlorite solution followed by flushing with saline solution. The canal was dried, and a #25 hand K-file was used to penetrate into the periapical tissues and induce bleeding into the canal up to approximately 3 mm beneath the CEJ. MTA paste was placed over the partially coagulated blood clot. A moist cotton pellet was placed over MTA, and the access cavity was closed with glass ionomer cement (Fig. 2B).

Follow-up Examination

At the 6-month follow-up, the soft and hard tissues were within normal limits. There was no swelling or sinus tract. The large cystlike

Figure 2. (A) Preoperative periapical radiograph. A well-circumscribed large periapical osteolytic lesion involving the entire apical root of #7 and the mesial aspect of root of #6 and extending upward to the floor of the nasal cavity. #8 has a small ill-defined periapical osteolytic lesion. (B) Postoperative periapical radiograph. Both #8 and #7 after regenerative endodontic therapy. (C) Six-month follow-up radiograph. The large periapical osteolytic lesion is partially filled with trabecular bone formation, and the density of the lesion increases. (D) One-year follow-up radiograph. The large periapical osteolytic lesion has filled considerably with more trabecular bone formation indicating incomplete healing.
osteolytic lesion had partially filled with trabecular bone formation, and the density of the lesion increased (Fig. 2C). The pulp cavity of #8 had decreased in size and could be seen extending to the apex (Fig. 2C). The pulp cavity of #7 appeared to be obliterated by mineralized tissue, indicating that hard tissue had formed inside the pulp cavity even though the canal was instrumented to a #35 hand k-file. Neither #8 nor #7 responded to pulp tests.

At the 1-year follow-up, the hard and soft tissues were within normal limits. The large cystlike osteolytic lesion had filled considerably with trabecular bone formation, indicating incomplete healing (Fig. 2D). The increase in bone density of the osteolytic lesion was confirmed with the Hounsfield unit. Tooth #8 showed thickening of the canal walls and closure of the apex. The pulp cavity appeared to be obliterated by hard tissue formation in the apical portion (Fig. 2D). The pulp cavity of #7 was similar to the pulp cavity at the 6-month follow-up (Fig. 2D). Neither tooth responded to pulp tests. The patient completely lost contact and could not be located for further follow-up examinations because of unrest in the region.

**Discussion**

Shah and Logani (2) and Paryani and Kim (3) reported successful treatment of mature permanent teeth with apical periodontitis using regenerative endodontic therapy. The treatment resulted in resolution of the apical lesion and regression of clinical signs and symptoms. However, no apparent thickening of the canal walls or continued root development was noted.

In present case, we have described the promising treatment of 2 mature teeth with infected necrotic pulps and a large cystlike inflammatory periapical lesion using regenerative endodontic therapy. The large periapical osteolytic lesion has filled considerably with trabecular bone formation, indicating incomplete healing at 1-year follow-up examination. Ideally, a longer period of follow-up examination is required to evaluate the treatment outcome of a large cystlike osteolytic lesion, especially when a new treatment protocol is used. However, the patient completely lost contact and could not be located for further follow-up examinations. Because the periapical osteolytic lesion is a large through-and-through lesion, it might take a longer time to heal or might heal by scar tissue formation (5). Molven et al (6) suggested that cases showing features of incomplete healing (scar tissue) at a 1-year follow-up examination after periapical surgery could be regarded as success. Tooth #8 showed thickening of the canal walls and apical closure. Tooth #7 showed obliteration of the pulp cavity by hard tissue formation. These indicate ingrowth of new vital tissue from the periapical area into the canals after complete chemomechanical debridement of the canals. Both #8 and #7 did not respond to pulp tests, most likely because of an MTA plug extending deep into the coronal portion of the canal.

Nygaard-Ostby (7) and Nygaard-Ostby and Hjordal (8) showed that fibrous connective tissue and cellular cementum from the periapical tissues could grow into the underfilled apical canals of pulpectomized mature teeth after intentional induction of bleeding into the canals. Later, Benatti et al (9) also showed ingrowth of the periodontal ligament, cementum, and bone from the periapical tissues into the underfilled apical canals of pulpectomized mature teeth. In the latter study, intentional bleeding into the canals was not attempted. Recently, in an animal model, the nature of vital tissues formed in the canals of mature teeth with apical periodontitis after regenerative endodontic therapy was described as periodontal ligament, cementum, and bone. Nygaard-Ostby (7) and Nygaard-Ostby and Hjordal (8) showed that fibrous connective tissue and cellular cementum from the periapical area into the canals after complete chemomechanical debridement of the canals. These indicate ingrowth of new vital tissue from the periapical area into the canals after complete chemomechanical debridement of the canals.

Persistence of an intracanal infection is the primary concern in endodontic therapy (16), including nonsurgical root canal therapy, apexification, and regenerative endodontic therapy. In teeth with infected necrotic pulp and apical periodontitis, most anaerobic bacteria colonize in the apical 5 mm of the infected root canals (17), which is difficult to eliminate. Besides copious amounts of antiseptic irrigation and antimicrobial dressing, extensive mechanical debridement of the infected canals to remove biofilm firmly attached to the canal walls and bacterial toxin-contaminated dentin walls is routinely performed in nonsurgical root canal therapy of mature teeth with apical periodontitis. This is not recommended for regenerative endodontic therapy of immature necrotic teeth with thin canal walls. In addition, it is also not recommended to place antiseptic irrigation and antimicrobial intracanal dressing too close to the open apex in order to prevent damage to any remaining pulp tissue or the periapical tissues that could result in the killing of stem cells needed for pulp tissue regeneration. Therefore, root canal disinfection of the immature permanent teeth with apical periodontitis might not be as effective as that of mature teeth with apical periodontitis. Hypothetically, if immature teeth with apical periodontitis could be treated with
regenerative endodontic therapy, it might be possible for mature teeth with similar pathosis to be treated in the same manner.

In contemporary nonsurgical root canal therapy, disinfected canals are filled with foreign materials, such as gutta-percha and sealer or cement. They are supposed to act as a physical barrier to entomb the bacteria in the dentinal tubules and to seal the canal from communicating with the periapical tissues. However, the effectiveness of root fillings in entombing the bacteria in the dentinal tubules and in sealing off the complex root canal system has been questioned (18), especially when the intracanal bacterial load was not eliminated by chemomechanical debridement to a level that could be tolerated by the periapical tissues (19). In many cases, the apical 3–4 mm of the canal after chemomechanical debridement is only filled with a single-cone gutta-percha point in nonsurgical root canal therapy; therefore, the bacteria-tight seal of the canal system is questionable (18). If the intracanal bacterial load is effectively reduced, the inflammatory periapical lesions may heal even without root canal fillings (20, 21). The root filling materials are nonvital foreign substances and do not have any defense mechanisms to fight against foreign invaders, such as bacteria. They act as foreign bodies favorable for biofilm formation and can significantly lower the infectious dose of bacteria to produce infection (22).

Although regenerative endodontic therapy of the mature tooth with apical periodontitis has not been shown to encourage increased thickening of the canal walls and/or continued root development, vital tissues such as periodontal tissues (cementum, periodontal ligament, and alveolar bone) have been shown to generate inside the canals (4). Most vital tissues are endowed with innate and adaptive immune defense mechanisms and sensory innervation. Physiologically, the nervous system and immune system are closely coordinated and play a pivotal role in tissue survival, defense, and wound healing (23–25). The regenerated vital tissue in the canals of the mature teeth with apical periodontitis after regenerative endodontic therapy is capable of mounting an immunoinflammatory defense mechanism to fight against bacteria if a minute amount of residual bacteria remain in the canal after chemomechanical debridement. Additionally, vital tissue with sensory innervation is capable of perceiving external stimuli and preparing for defense in coordination with innate and adaptive immune mechanisms.

Retreatment of mature necrotic teeth after attempted regenerative endodontic therapy may be a challenge because of the risk of root perforation while removing the MTA plugs. Nevertheless, the same risk may also occur while removing gutta-percha in root-filled teeth. Another issue is the size of the apical foramen in regenerative endodontic therapy. It appears that enlargement of the apical foramen to at least 1 mm in diameter is not necessary for regenerative endodontic therapy (4, 26–28). The size of a no. 25 hand K-file is approximately 0.25 mm in diameter, and the average size of human cells ranges from 10–100 μm. Therefore, there is no reason why blood-borne cells and other cells including mesenchymal stem cells could not migrate into the canal from the periapical area through the apical foramen with a diameter of 0.25 mm in tooth #7 in the present case if there are chemotactic factors inside the canal. Based on the aforementioned rationales, it may be possible to fill disinfected root canals with the host’s biologically vital tissues rather than with foreign materials even though the vital tissue may not be a true pulp tissue.

The control of root canal infection is paramount to root canal therapy and regenerative endodontic therapy. If an effective disinfection protocol of root canal infection can be developed, it may not be necessary to fill the canals with foreign materials but rather with biologically active host’s vital tissues. However, in such cases that a post is required for adequate coronal restoration, nonsurgical root canal therapy can be performed or regenerative endodontic therapy limited to the apical portion of the canal may be performed.

Endodontics is entering an era of tissue regeneration and tissue engineering. Similar to regenerative endodontic therapy of immature permanent necrotic teeth, we may have to consider more biologically to encourage the host’s natural wound healing process to regenerate the vital tissue in the canal, rather than to fill the canal with nonvital foreign materials of mature necrotic teeth. Given the potential of regenerative endodontic therapy to restore sensation and immune function in mature necrotic teeth, this biologically based treatment is worthy of further investigation. Like regenerative endodontic therapy of immature permanent necrotic teeth, more case reports and case series will help formulate the hypothesis to test the predictability of regenerative endodontic therapy of mature necrotic teeth.

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The authors deny any conflicts of interest related to this study.

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ERRATA
The editor wishes to revise the Case Report Cover leader of the October 2014 issue of Journal of Endodontics (40/10) to “Toothache Caused by Trigeminal Neuralgia of Vestibular Schwannoma.” We apologize to the authors for this error.

For this article (Testarelli L, Plotino G, Al-Sudani D, Vincenzi V, Giansiracusa A, Grande NM, Gambarini G. Bending properties of a new nickel-
titanium alloy with a lower percent by weight of nickel. J Endod 2011;37:1293–5), the authors submitted the Dr Al-Sudani’s affiliation incorrectly.

The correct affiliation is as follows: Dina Al-Sudani, DDS, Department of Restorative Dental Sciences, King Saud University, Riyadh, Saudi Arabia.