

# Regeneration of Pulp and Radicular Tissues in a Nonvital Avulsed Tooth with Open Apex: A Case Report

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## ABSTRACT

**Aim and background:** The management of avulsed immature teeth poses a significant challenge to clinicians, as prolonged dry time before reimplantation may lead to replacement resorption or ankylosis.

**Case description:** Recent studies have shown promising results with the use of an intracanal proprietary pharmaceutical preparation, followed by sealing of the orifice with mineral trioxide aggregate (MTA). Angiography suggested the presence of vascularized tissue after 1 year, indicating successful regeneration of pulpal tissue in the radicular area.

**Conclusion:** Despite an unfavorable crown-root fracture leading to tooth extraction after 9 months, histological examination revealed regular root dentin formation, indicating a favorable outcome.

**Clinical significance:** These findings offer hope for the management of avulsed immature teeth and underscore the importance of early intervention and appropriate treatment selection.

**Keywords:** Avulsed tooth, Case report, Endodontics, Mineral trioxide aggregate, Open apex, Radiculogenesis.

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## INTRODUCTION

Oral injuries are frequent, particularly in school-aged children, and are mainly caused by dental trauma to the front teeth. The leading causes are falls (20%), sports injuries (10%), violence (9%), and road traffic accidents (6%). Contributing factors to oral injuries include inadequate lip closure and protruded anterior teeth.<sup>1</sup>

Losing a permanent tooth during the developmental years may result in significant atrophy of the alveolar bone.<sup>2</sup> The maxillary anterior teeth are most commonly affected by avulsion, particularly before root development is complete and between the ages of 7 and 10 years.<sup>3</sup> Reimplantation of these immature teeth results in the formation of the apex, but their thin dentinal walls and wider pulp chambers make them more susceptible to subsequent fractures.<sup>4</sup> According to research, the apex forms in nearly all environments where the apex stays open.<sup>5</sup> The success rate of an avulsed tooth is also affected by extraoral time and transport media.<sup>6,7</sup>

Pulp revascularization is a technique that has been shown to promote the development of roots. This technique results in an increase in the length of the root, the closure of the apex, and the formation of root dentin in necrotic immature teeth. As a result, it is considered a preferred technique over apexification.<sup>8</sup> The standard treatment protocol for root canal therapy involves a passive decontamination process using an irrigant, followed by the application of an antibiotic paste as an intracanal dressing, inducing bleeding and ultimately sealing the cavity. However, this technique can be challenging and uses a triple antibiotic paste that may cause tooth discoloration. The procedure aims to stimulate the formation of pulp and dentin-like tissue to promote root end closure. A new sol-gel preparation called Rationale use of Antibiotics for Disinfection and Regeneration (RADAR) has been developed for root canal therapy.<sup>9</sup> This sol-gel pharmaceutical preparation consists of selected antimicrobials and antiviral drugs, including moxifloxacin, doxycycline, and nystatin, in a chitosan base. The concentration of these drugs is adjusted based on the minimum inhibitory

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concentration (MIC) and minimum bactericidal concentration (MBC) values of the pathogens found in the nonvital pulp. RADAR is unique because it releases the antimicrobials in a pH-dependent manner and acts as a scaffold for regeneration. Its rheology and penetration properties are temperature-dependent, allowing it to be tailored to

the specific needs of each case.<sup>10</sup> This case report has been prepared following the PRactical Implementation of Coordinated Efforts (PRICE) guidelines (2020) and outlines the successful management of an avulsed immature maxillary central incisor, including the regeneration of pulp and dental tissues after reimplantation.<sup>11</sup>

## CASE DESCRIPTION

An 8-year-old female patient presented to the Department of Pediatric and Preventive Dentistry with a complaint of tooth loss in the upper front tooth region due to a fall from a tree while playing. The patient arrived with the teeth wrapped in a dry handkerchief after 2 hours of the incident. Clinical examination revealed Ellis class V trauma with tooth 11, class IX trauma with tooth 52, and Ellis class I fractures with teeth 32 and 42.<sup>12</sup> Radiographic examination showed complete loss of 11 and revealed no alveolar bone fracture. On the patient's insistence and after obtaining their informed consent, reimplantation of 11 was done following the Dental Trauma Guidelines given by the International Association on Dental Traumatology (IADT) wherein it states that in order to retain the height, breadth, and shape of the alveolar bone while temporarily restoring function and esthetics, replantation is used. Future treatment choices and the ability to be removed are also made possible through replantation. Depending on the patient's development and the risk of tooth loss, patients should be informed about the possibilities of decoronation or autotransplantation if the tooth becomes ankylosed and infrapositioned. Ankylosis and resorption progress at varying and unexpected rates due to above mentioned causes.<sup>1</sup> The state of the periodontal ligament (PDL) cells and the root maturity affect the course of treatment for PDL cell avulsion. The length of time spent outside of the mouth and the kind of storage media employed both affect PDL cell survival. Dry time is critical for PDL cell survival since most cells die after 30 minutes of extra-alveolar dry time. A complete history must thus include information regarding the tooth's dry period prior to replantation or storage.<sup>13</sup> In this case, the tissue of the PDL was scraped, followed by extraoral access opening, pulp extirpation and the tooth was repositioned in the socket. Radiographic confirmation was done followed by flexible splinting for 14 days (Figs 1 to 3). A pharmaceutical preparation—RADAR—was placed for disinfection and sealed with mineral trioxide aggregate (MTA). On the next appointment, after 24 hours, the moist cotton pellet was removed and the orifice was sealed with composite. Administration of tetanus toxoid vaccination was done intramuscularly.

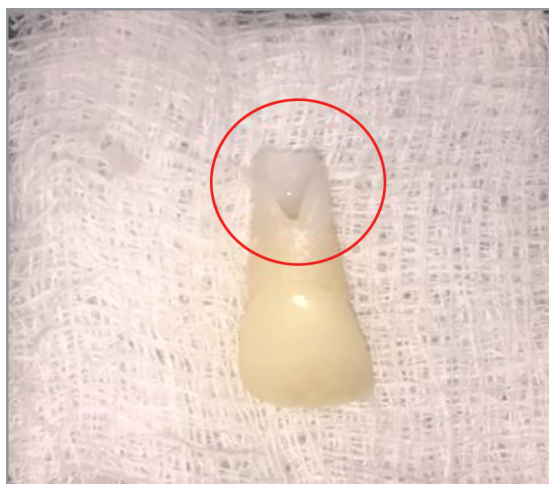


Fig. 1: Avulsed tooth

After 1 year, 6.1 mm increase in the length of the anatomically formed root, along with apical closure was evident radiographically (Fig. 4). On deep vein thrombosis (DVT) examination, the regular dentin deposition and formation of the regular root morphology was seen in continuation with the replanted root segment, suggesting



Fig. 2: Showing Ellis class V trauma with 11, class IX trauma with 52, and class I fracture with 32 and 42 on clinical examination



Fig. 3: Radiograph on 14-day follow-up



Fig. 4: Radiograph on 1-year follow-up



complete maturation of the tooth. Angiography was performed by injecting radiopaque contrast dye at the level of external carotid artery. The lateral view revealed the blood vessel entering the pulp space through the apex of the tooth, suggesting the presence of vascularized tissue in both existing and newly formed root segments (Fig. 5). After 9 months, the patient reported with an unfavorable crown-root fracture of the same tooth. As the prognosis of the tooth was poor, extraction was planned (Fig. 6). Following extraction, the histology of the apical third of the root was studied. Histological examination suggested formation of dentinal tubules under 40x magnification (Fig. 7). There was evidence of palisading arrangement of cells with nuclei, suggestive of odontoblasts. The connective tissue architecture consisted of fibroblasts with small vacuolar spaces of varying sizes in the matrix, resembling the pulpal tissue (Fig. 8).

## DISCUSSION

Despite the extraoral dry time of 2 hours which exceeded the recommended 60-minute timeline, the patient and her family insisted on reimplantation of the tooth to prevent the loss of space, maintain the alveolar ridge and restore esthetics. To prevent ankylosis, a nonrigid splint with a wire diameter of <0.4 mm was utilized.<sup>1,14</sup>

Rational use of Antibiotics for Disinfection and Regeneration, a medicament known for its regenerative properties, was utilized in this case to promote the growth of a new root and the formation of vascularized connective tissue in both the reimplanted and newly formed root segments. The medication was effective in restoring the original morphology of the tooth and there were no clinical symptoms or radiographic evidence of complications or discoloration observed.<sup>15</sup> Upon extraction of the tooth, histological examination revealed the presence of pulpal tissue with peripheral cells resembling odontoblasts and dentinal tubules, 1 year and 9 months post-reimplantation. This could be attributed to the surviving stem cells from apical papilla (SCAP) and dental pulp stem cells (DPSC) under the influence of Hertwig's Epithelial Root Sheath (HERS), which led to the formation of primary odontoblasts and complete root formation and regeneration of the pulp.<sup>9</sup> The regenerated pulp tissue had ingressed into the canal space of the original tooth fragment and regenerated root segment, without inducing bleeding, fulfilling the secondary goals of the regenerative procedure as outlined by the American Association of Endodontists (AAE).<sup>16</sup>

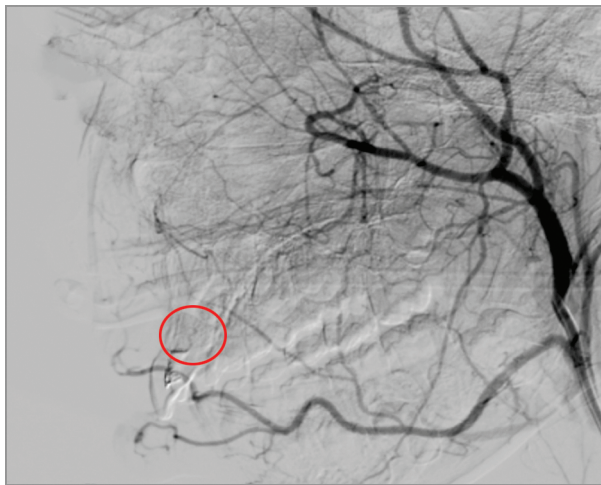


Fig. 5: Angiograph image



Fig. 6: Extracted tooth after 2 years

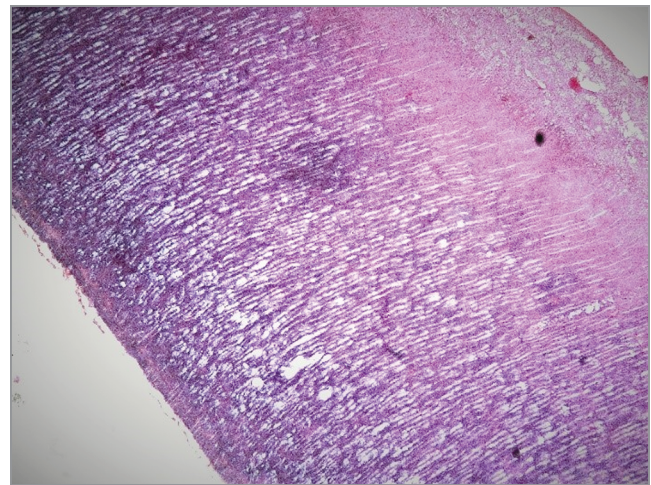


Fig. 7: Presence of physiologic dentinal tubules in apical third of root under 10x magnification

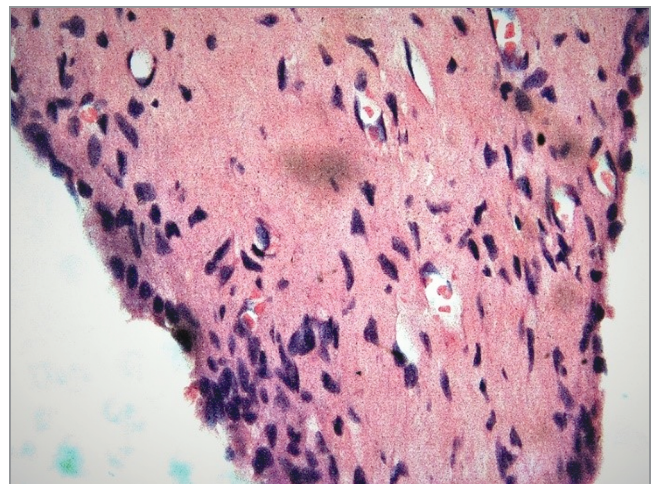


Fig. 8: Histologic section showing cells with palisading nuclei adjacent to the dentinal tubules under 40x magnification suggestive of odontoblasts. Connective tissue shows tissue architecture similar to pulp, with cells resembling fibroblasts in the matrix

Luan et al. have suggested that during the regeneration process, fenestration of HERS may occur, which can lead to the invagination of periodontal tissue at the junction of regenerated and broken fragments.<sup>17</sup> This can increase the likelihood of fractures and weaken the tooth. However, in this case, there was continuous tissue formation, as demonstrated by the fact that the subsequent fracture occurred at a different site from the primary fracture after 1 year and 9 months. Moreover, a partial intracanal calcific barrier was formed at the junction of the existing and newly formed tooth fragments.

Apexification is a method of inducing a calcified barrier at the apex of a nonvital tooth with incomplete root formation.<sup>18</sup> This is performed by the placement of intracanal calcium hydroxide-based medicaments for disinfection. However, the resultant hard tissue barrier does not resemble the anatomy of the physiologic root apex.<sup>19</sup> The popular technique for regeneration, on the other hand, is maturogenesis (the physiological growth of the complete root, not just the apical section).<sup>20</sup> It involves the stimulated regeneration of a functional pulpo-dentin complex in nonvital, necrotic immature permanent teeth. It allows the development of the entire root, by thickening dentinal walls and apical closure.<sup>20</sup> The process involves either revascularization or the application of platelet rich fibrin (PRF), platelet rich plasma (PRP), or a combination of these with MTA.

During the process of revascularization, the use of ethylenediaminetetraacetic acid (EDTA) to chelate the native dentin matrix enables the release of essential growth factors such as dentin sialoproteins [bone sialoprotein (BSP)] and osteopontin (OPN).<sup>21</sup> OPN plays a crucial role in preserving the boundaries between the periodontal cementum, PDL, and bone.<sup>22</sup> The process results in the emergence of a novel root structure, distinguished by the accumulation of cementum, bone, dentin, and periodontal connective tissue. Furthermore, fibrous pulp-like tissue is generated and enveloped within a fully matured root, thereby contributing to the overall complexity of the newly formed root.<sup>23–25</sup> The other technique is disinfection followed by stimulation of the remnants of apical papilla from the periapical tissue and placement of PRF, producing a matrix into which the cells could proliferate and release platelet-derived growth factor (PDGF-AB), transforming growth factor  $\beta$  (TGF- $\beta$ ), and insulin-like growth factors which have been evaluated for their ability to guide the stem cells to differentiate into odontoblast-like cells.<sup>25,26</sup> However, the physiologic pulp parenchyma and dentin, containing odontoblasts are not evident.<sup>27,28</sup>

The literature reviews do not support the findings achieved in this particular case, and as a result, the contemporary terminologies are not befitting the results obtained. Since the embryological process of root formation is termed radiculogenesis, this regeneration of dental pulp and hard tissue in an immature nonvital avulsed tooth is proposed to be coined as “neo-radiculogenesis.” It is a process of regeneration of pulpal and circumpulpal tissues of the root resembling anatomical form in an immature nonvital tooth. The process of neo-radiculogenesis resembles the natural downward proliferation of HERS and the subsequent differentiation of the multipotent stem cells present in the dental papilla. This differentiation leads to the formation of the pulp-dentin complex, which ultimately results in the production of both pulp and dentin tissues on the inner surface of the tooth. Meanwhile, cementoblasts differentiate from the dental follicle to produce cementum, which forms the outermost surface of the root.<sup>29</sup>

## CONCLUSION

In conclusion, the proprietary pharmaceutical preparation has the potential to disinfect and facilitate regeneration for the successful

restoration of function and esthetics. However, extensive dental research is required to confirm the efficiency of the pharmaceutical preparation and elucidate the mechanism of dental tissue regeneration in a nonvital immature tooth.

## Clinical Significance

- Avulsion of permanent teeth in children is a common injury and can lead to severe atrophy of the alveolar bone if not treated promptly and properly.
- Revascularization of pulp in immature teeth is a preferred technique for promoting root development, compared to apexification.
- Rationale use of Antibiotics for Disinfection and Regeneration is a sol-gel pharmaceutical preparation that can be used for disinfection and regeneration of nonvital pulp. It contains moxifloxacin, doxycycline, and nystatin in a chitosan base, which is pH-dependent and releases antimicrobials.
- The success rate of reimplanted avulsed teeth depends on the extraoral time and the transport media used.
- Proper dental trauma management guidelines should be followed, such as the dental trauma guidelines by the IADT, to ensure the best possible outcome for the patient.

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