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Regenerative endodontic therapy of a non-vital immature permanent tooth with injectable platelet-rich fibrin: An 18-month clinical follow-up case report

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Abstract
Regenerative endodontic procedures (REPs) have emerged as a viable treatment modality for the management of non-vital immature permanent teeth, aiming to promote continued root development and healing. This case report describes an 18-month clinical and radiographic follow-up of a 16-year-old male patient treated with injectable-platelet rich fibrin (i-PRF) in a non-vital immature permanent maxillary central incisor. The protocol followed the most recent American Association of Endodontists (AAE) guidelines. Clinical outcomes demonstrated radiographic signs of continued root development and apical healing, with a shift in the Periapical Index (PAI) score from 4 to 2. The apical response corresponded to Type 3, as per Chen *et al*. classification. The use of i-PRF, owing to its high leukocyte content and regenerative potential, demonstrated encouraging results. The case underscores the biological and clinical benefits of biologically based regenerative techniques.

Keywords: Regenerative endodontics, i-PRF, immature teeth, non-vital permanent tooth, apical response, calcium hydroxide

Introduction
Traumatic dental injuries are highly prevalent, particularly among children and adolescents, accounting for nearly 13% of dental visits in school-aged populations [1]. If improperly managed, they can result in lifelong consequences including tooth loss, esthetic complications and psychological trauma [2]. In recent years, the field of dentistry has shifted towards biomimetic approaches that seek to replicate the original tissue's functional, mechanical, biological, and esthetic properties [3]. The ultimate goal is to maintain long-term vitality and functionality of the tooth by regenerating its natural tissues rather than replacing them.

This regenerative vision was first proposed by Nygård-Østby in the 1960s, who explored the potential for vital tissue regeneration in endodontics [4]. His work laid the foundation for modern regenerative endodontic procedures (REPs), which aim to manage immature non-vital teeth by fostering continued root development, apical closure, and strengthening of the dentinal walls. By preserving the vitality or regenerating functional pulp-like tissue, these procedures offer the potential to retain natural teeth for a lifetime [5].

Traditional apexification techniques using calcium hydroxide or mineral trioxide aggregate (MTA) promote apical closure but fail to stimulate further root development, leaving teeth with thin dentinal walls susceptible to fracture [6,7]. In contrast, REPs have emerged as a superior biological alternative that harnesses the principles of tissue engineering - stem cells, signalling molecules, scaffolds and sterile environment to regenerate pulp-like tissues [8].

Injectable platelet-rich fibrin (i-PRF) has recently gained attention as a biologically active scaffold that enhances healing outcomes in REPs. Derived autologously from the patient's blood, i-PRF is rich in growth factors such as VEGF, PDGF, IGF, and TGF-β1, which are critical for angiogenesis, stem cell recruitment, and tissue regeneration [9-11]. Unlike other platelet concentrates, i-PRF offers a more flexible application due to its injectable nature and sustained release of growth factors over time [12].

Case Report

This case report presents the clinical and radiographic findings of an immature non-vital maxillary central incisor treated with i-PRF in accordance with the latest American Association of Endodontists (AAE) guidelines [13]. Over an 18-month period, the treatment resulted in substantial apical healing, continued root development, and a favorable clinical outcome.

A 16-year-old male presented to the Department of Conservative Dentistry and Endodontics with the chief complaint of discoloration of his upper front tooth. The patient reported no associated pain, swelling, or sensitivity. He had a history of a fall from a bicycle approximately 5 years back about the age of 11 years. The injury resulted in minor bleeding but no fracture or avulsion, and no dental treatment was sought at that time. Since then, the tooth remained asymptomatic until the recent gradual onset of discoloration. The patient denied any history of spontaneous pain, sinus tract, or mobility. Radiographic analysis showed an immature root with a wide-open apex and a periapical radiolucency (Periapical Index Score: 4). A diagnosis of pulp necrosis with chronic apical periodontitis in an immature permanent tooth was established.

The treatment protocol was designed in accordance with the 2021 American Association of Endodontists (AAE) guidelines on REPs [13].

First Visit

- Access cavity was prepared under rubber dam isolation
- Treatment was done under a dental operating microscope (Labomed Magna, Labomed Inc., USA).
- Canal was gently irrigated with 20 mL of 1.5% sodium hypochlorite (Vishal Dentocare, India) using side-vented irrigation needle for 5 min, positioned about 1 mm from root end, to minimize cytotoxicity to stem cells in the apical tissues.
- Final rinse with 20 mL of normal saline for 5 min
- Canals were dried with paper points
- Intracanal medicament of calcium hydroxide paste (Ultracal XS, Ultradent, USA) was placed.
- Access cavity was temporized with intermediate restorative material (IRM, Dentsply Sirona, York, PA, USA).

Second Visit (After 3 Weeks)

a. Patient was asymptomatic, calcium hydroxide was removed using irrigation and ultrasonic activation (Endo 3 Ultrasonic Endo Activator, Guilin Woodpecker Medical Instrument Co., China).
b. Copious, gentle irrigation with 20ml of 17% EDTA, with passive ultrasonic activation (Endo 3 Ultrasonic Endo Activator, Guilin Woodpecker Medical Instrument Co., China).
c. Canals dried with paper points.
d. i-PRF preparation was done according to Choukroun's low-speed centrifugation concept (LSCC):

- 10 mL of intravenous blood was collected from the median cubital vein into sterile plastic tubes (BioPro i-PRF vaccum testube).
- Centrifugation was done using Duo Quattro Centrifuge (DLAB Scientific Co., Ltd., Beijing, China) at 700 rpm for 3 minutes.
- The upper yellow layer of i-PRF was aspirated near the buffy coat and injected into the canal up to 3 mm below the cementoenamel junction.

e. Collagen matrix (CollaPlug sterile collagen sponge) placed above the i-PRF scaffold
f. A 2-3 mm coronal plug of Biodentine (Septodont, France) was placed.
g. RMGIC was placed above the biodentine layer.
h. Access cavity was restored with resin composite (Te-Econom Plus, Ivoclar Vivadent, Schaan, Liechtenstein).

Fig 1: (a) Duo Quattro Centrifuge (DLAB Scientific Co., Ltd., Beijing, China) set at 700 rpm for 3 minutes; (b) i-PRF aspirated; (c) i-PRF being injected into the canal; (d) i-PRF placed upto 3 mm below the CEJ; (e) Collagen matrix (CollaPlug collagen sponge) placed; (f) About 2 mm of Biodentine placed; (g) RMGIC placed; (h) Composite restoration done.

Results

Radiographic evaluation at 3, 6, 12 and 18 months revealed progressive periapical healing and thickening of the root canal walls observed. At 18 months, PAI score according to Ørstavik *et al.* [14] reduced from 4 to 2. Radiographic evaluation suggested a type 3 apical response according to Chen et. al classification for apical response, indicating continued root development with an open apex [15]. Pulp sensibility tests remained negative at all follow-ups, likely due to limited innervation during the early regeneration phase given the short follow-up duration of only 18 months.

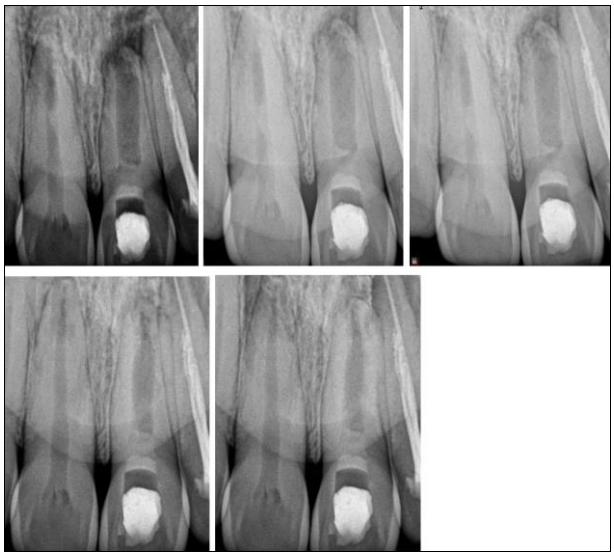

Fig 2: (a) Immediate postoperative radiograph; (b), (c), (d) 3-month, 6-month, 12-month, and 18-month follow-up radiographs.

Discussion

The primary goal of regenerative endodontics is to eliminate symptoms and resolve apical periodontitis while promoting

continued development of the root and surrounding tissues. Unlike apexification with calcium hydroxide or mineral trioxide aggregate (MTA) which do not lead to further root development, REPs enable the formation of root structures resembling natural tissue [13,16].

The use of calcium hydroxide as an intracanal medicament in this case is in line with current literature suggesting it as a more biocompatible alternative to triple antibiotic paste (TAP), which has demonstrated cytotoxicity to apical stem cells. Calcium hydroxide maintains an alkaline pH, which inhibits microbial growth and stimulates hard tissue formation, while not adversely affecting the survival of stem cells of the apical papilla (SCAP) [17].

i-PRF is a second-generation platelet concentrate that is gaining attention for its ease of preparation, autologous nature, and higher concentrations of leukocytes and growth factors compared to traditional PRF and PRP [10,11]. The release of vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGF-β) plays a crucial role in angiogenesis, cellular migration, and proliferation, essential for pulpal regeneration [12].

According to the apical response classification by Chen *et al*., the case in this report exhibited Type 3 response, characterized by continued root development despite the apical foramen remaining open [15]. This finding suggests a successful regenerative process; however, since complete apical closure was not observed, a longer follow-up period would be necessary to evaluate the continued progression of root development.

In the present case, 17% EDTA was activated using passive ultrasonic irrigation (PUI) to promote the release of growth factors and bioactive molecules from dentin, which are crucial for REPs. EDTA is known to demineralize the inorganic portion of dentin, thereby exposing embedded signalling molecules such as transforming growth factor-beta (TGF-β), which play a vital role in the chemotaxis, proliferation, it also facilitates the migration of human dental pulp stem cells (hDPSCs) or stem cells from the apical papilla (SCAP) from dentin during regenerative endodontic procedures [13].

The use of PUI significantly enhances this effect by increasing the contact and penetration of EDTA within the canal system through acoustic microstreaming and cavitation. This has been shown to facilitate a greater release of dentin-derived bioactive factors, which in turn enhances the migration and attachment of SCAP onto dentinal walls, a critical step for successful pulp-dentin regeneration. Thus, the use of EDTA with PUI in this case was aimed not only at conditioning the canal but also at optimizing the biological environment to favour stem cell-mediated tissue regeneration [18,19].

In the present case, a progressive reduction in the periapical index (PAI) score from 4 to 2 over the follow-up period indicated significant periapical healing following the regenerative endodontic protocol. A PAI score of 4 denotes a well-defined radiolucent lesion, while a score of 2 suggests only minor changes in bone structure, reflecting successful resolution of apical periodontitis. This radiographic improvement aligns with the outcomes reported in regenerative endodontic procedures, where resolution of periapical pathology is one of the primary indicators of clinical success. At the 18-month follow-up, a notable increase in root dentinal wall thickness was observed, along with continued root development, which are hallmark features of successful maturogenesis. These findings are consistent with those reported by Banchs and Trope [20], who observed thickening of root canal walls and apical closure following revascularization in immature necrotic teeth. Similarly, Bose *et al* [21] demonstrated statistically significant increases in root length and wall thickness in teeth treated with regenerative techniques compared to traditional apexification. These outcomes are attributed to the recruitment and differentiation of stem cells from the apical papilla (SCAP) in a bioactive environment, which supports the deposition of new hard tissue along the canal walls. Thus, the observed decrease in PAI score and the increase in root dentinal thickness at 18 months in this case support the biological success and regenerative potential of the revascularization approach.

While pulp sensibility testing remained negative during follow-ups, this does not necessarily imply failure of the regenerative process. Studies have shown that reinnervation may take longer than revascularization, and lack of response in the early stages is not uncommon [22,23].

This case also emphasizes the necessity of long-term monitoring in REP cases. Clinical signs, radiographic progression, and potential late pulp responsiveness should all be factored into the long-term prognosis. Future investigations involving histological analysis and stem cell tracking will offer deeper insights into the quality of tissue formed post-regeneration.

Conclusion

Regenerative endodontic treatment using i-PRF in a non-vital immature permanent tooth demonstrated positive radiographic outcomes over an 18-month period, including periapical healing and continued root development. Calcium hydroxide proved to be a suitable intracanal medicament, and the use of i-PRF enhanced healing potential. Continued monitoring is essential to assess long-term success and pulp vitality.

Conflict of Interest

Not available

Financial Support

Not available

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