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Rescue of "Hopeless" Avulsed Teeth using Autologous Platelet-Rich-Fibrin following Delayed Reimplantation: Two Cases Report

Save the avulsed teeth by autologous PRF

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Abstract

BACKGROUND

Tooth avulsion is one of the most severe types of dental trauma. Most avulsed teeth will undergo ankylosis and replacement resorption after reimplantation in the long term and have the worst prognosis after dental trauma. The aim of this work is to improve the success rate of avulsed teeth after delayed reimplantation by adoption of autologous platelet-rich fibrin (PRF).

CASE SUMMARY

In case 1, a 14-year-old boy fell and knocked out his left upper central incisor for 18 h prior to his arrival to the department. The diagnoses were avulsion of the tooth 21, lateral luxation of the tooth 11 and alveolar fracture of the teeth 11 and 21. In case 2, a 17-year-old boy fell 2 h prior to his presentation to the hospital and had his left upper lateral incisor completely knocked out of the alveolar socket. The diagnoses were avulsion of the tooth 22, complicated crown fracture of the tooth 11, and complicated crown-root fracture of the tooth 21. The avulsed teeth were reimplanted along with autologous PRF granules and splinted using a semiflexible titanium preshaped labial arch. The root canals of the avulsed teeth were filled with calcium hydroxide paste, and root canal filling was performed 4 wk after reimplantation. The reimplanted teeth showed no symptoms of inflammatory root resorption or ankylosis at the 3-, 6-, and 12-month follow-up examinations after reimplantation with autologous PRF. In addition to the avulsed teeth, the other injured teeth were treated using corresponding conventional treatment methods.

CONCLUSION

The presented cases provide examples of PRF successfully reducing pathological root resorption of the avlused teeth, and the application of PRF may provide new healing opportunities for traditionally "hopeless" avulsed teeth.

Key Words: Avulsion; Periodontal healing; Platelet-rich fibrin; Ankylosis; Delayed reimplantation; Case report

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Core Tip: Tooth avulsion is one of the most severe types of dental trauma. Most avulsed teeth will undergo ankylosis and replacement resorption after delayed reimplantation and generally experience the worst prognosis. It was previously proven by us that the autologous PRF could effectively help to control the occurrence and development of initial root resorption. In this report, we present two clinical cases of avulsed teeth by delayed reimplantation with application of autologous PRF. Ideal periodontal healing over 12 mo of follow-up suggests that PRF, as an adjuvant therapy, may provide new insights and perspectives on the management of traditionally hopeless avulsed teeth.

INTRODUCTION

Tooth avulsion is defined as a complete displacement of the tooth from its original alveolar socket and it is one of the most severe types of dental trauma. Permanent tooth avulsion accounts for 0.5-3% of dental trauma, while some literature points out that its incidence could be as high as 16% [1,2]. A recently presented study in China showed that 8% of all dental injuries were tooth avulsion and were more likely to occur in teenagers 7-20 years old, generally including more boys than girls [3]. The prognosis depends on the measures taken at the site of the accident, such as immediate replantation of avulsion teeth, feasible preservation medium for the avulsed tooth, and the timely and professional dental treatment performed after avulsion [4]. It was pointed out that a delay of more than 5 min could be defined as delayed replantation, affecting tooth survival [5]. Unfortunately, in most cases, an avulsed tooth is kept out of the alveolar

socket for a significantly long time or is stored under improper conditions, which eventually contribute to periodontal ligament cell necrosis and result in ankylosis and replacement resorption of the tooth root after reimplantation [6]. The commercial enamel matrix protein Emdogain has been used clinically. However, its effectiveness in preventing root resorption has not been demonstrated either [12].

Platelet-rich fibrin (PRF) is a second-generation platelet concentrate that is prepared from the patient's own blood without the use of an anticoagulant through a single-step centrifugation process [13,14]. It is classified as L-PRF or PRF based on its leukocyte content, standard PRF or advanced PRF depending on the centrifugation process, and comes in a membrane or injectable form depending on the centrifugation process and consistency of the final product [15]. The main scaffold component of PRF is fibrin, which develops a 3-dimensional mesh crossover structure that is visible under a scanning electron microscope, with a large interfiber space, which contains large numbers of red blood cells, white blood cells, and clusters of platelets [16,17]. The fibrin network of PRF protects platelets from immediate activation but progressively activates them during the process of fibrin degradation, slowly releasing growth factors, eventually prolonging the duration of growth factors in PRF and achieving wound healing promoting effect [18,19]. Thus, PRF has the potential to enhance tissue regeneration, accelerate wound healing, and induce stem cell differentiation through the consistent release of multiple growth factors [20,21]. Our previous study demonstrated that autologous PRF could effectively promote the periodontal healing of avulsed teeth after delayed replantation in dogs and thus control the occurrence and development of initial root resorption[20].

In this report, we present two clinical cases of delayed reimplantation of avulsed teeth using autologous PRF granules with a 12-month follow-up. In both cases, the avulsed teeth were separated from the alveolar socket by far more than the optimal reimplantation time of 5 minutes, and the residual periodontal ligament tissue on the root surface was either damaged or seriously polluted, which basically belonged to "hopeless" teeth. By simultaneous reimplantation of avulsed teeth, together

with autologous PRF, the injuried teeth showed no symptoms of inflammatory root resorption or ankylosis in both of two cases, suggesting that the application of PRF may offer new therapeutic opportunities for traditionally "hopeless" avulsed teeth.

CASE PRESENTATION

Chief complaints

Case 1: A 14-year-old boy was referred to the Department of General Dentistry and Emergency of the Fourth Military Medical University with complaint of his left upper central incisor fallen out for 18 h and with pain. **Case 2:** A 17-year-old boy visited the Department of General Dentistry and Emergency of the Fourth Military Medical University with complaint of his left upper lateral incisor being completely fallen out for 2 h.

History of present illness

Case 1: The patient accidentally fell down 18 h prior to presentation and knocked out his left upper central incisor. The patient was conscious, with the vital signs being stable.

Case 2: The patient suffered avulsion of left upper lateral incisor from an accident fall, and came to the hospital 2 h later. The patient was conscious, with the vital signs being stable.

History of past illness

Case 1 and 2: The patients did not have a relevant medical history. They did not report any history of drug allergies or systemic diseases and exhibited no apparent dental treatment contraindications.

Personal and family history

Cases 1 and 2: There were no specific family health histories.

Physical examination

Case 1: After excluding damage to other important organs, an oral examination was performed. There was no obvious contribution of his general medical history to the injury, and an examination revealed no evidence of nerve injury. We performed clinical examinations, and the extraoral findings did not reveal serious wounds. Intraoral examination found that the tooth 21 was missing, and the alveolar nest was empty. Blood clots had formed in the alveolar socket, and there was no obvious lacerated wound in the gums. The crown of the tooth 11 was shifted to the palatal side and had occlusal interference. Tooth H was retained on the lingual side of the tooth 13 and was loose (Figure A-B). The avulsed tooth was wrapped in dirty dry paper sheets (Figure 1C).

Case 2: Intraoral examination found that the tooth 22 was missing and the corresponding alveolar socket was empty, with blood clots filling it. The patient had a complicated crown fracture of the tooth 11 and a complicated crown-root fracture of the tooth 21, with the fracture surfaces being approximately 4 mm below the enamel-dentinal junction (Figure 2A-B). The avulsed tooth was wrapped in dry paper sheets, and there were a large number of pollutants on the periodontal ligament tissues of the root surface (Figure 2C).

Laboratory examinations

Case 1 and 2: These cases did not have any laboratory examinations.

Imaging examinations

Case 1: Digital-X radiograph (FOCUS, Instrumentarium Dental, Finland) revealed that the alveolar socket of tooth 21 was empty and that there were no high-density foreign body images. The periodontal membrane space was widened of tooth 11, without significant root fracture (Fig.3A). By cone-beam computed tomography (CBCT) (Hires3D, Beijing, China), the lip side of the alveolar bone wall of the tooth 21 was fractured (Figure 3B).

Case 2: Periapical radiography found that the alveolar socket of tooth 22 was empty, and there were no high-density foreign body images(Figure 4A). CBCT revealed no alveolar fracture around the empty tooth socket (Figure 4B) and the fracture position of tooth 21 was approximately 3mm above the top of the alveolar crest(Figure 4C).

FINAL DIAGNOSIS

Case 1

Based on the history and findings of the imaging examinations, the diagnoses for this patient were lateral luxation of the tooth 11, avulsion of the tooth 21 and alveolar fracture of the teeth 11 and 21.

Case 2

The diagnoses of this patient were avulsion of the tooth 22, complicated crown fracture of the tooth 11, and complicated crown-root fracture of the tooth 21.

TREATMENT

Case 1

We obtained a 10 mL blood sample from the median cubital vein and transferred the blood into a 10 mL glass tube without anticoagulation as soon as possible. The tube was immediately centrifuged at 400 × g for 10 min (TD3, CENCE, China)(Figure 5A). The fibrin clot contains PRF formed in the middle of the tube; thus, the clot was easily separated from the red corpuscles at the bottom (Figure 5B-C). The clot was compressed with sterile dry gauze to remove the fluids trapped in the fibrin matrix. The PRF became a very resistant autologous fibrin membrane, which was then cut into approximately 1 mm^3 granules (Figure 5D). The tooth 21 was reimplanted along with the PRF granules and the tooth 11 received manipulative reduction. Then the teeth were splinted using a preshaped semiflexible titanium labial arch (Titanium Trauma Splint, Zhongbang Titanium Biological Materials Co., Ltd., Xi'an, China) for 4 wk (Figure 6A). The digital-X radiograph immediately after the surgery showed the complete reduction of the tooth 21 and 11 (Figure 7A). According the International Association of

Dental Traumatology guidelines [22], root canal therapy of the avulsed teeth 21 should be started within 7-14 days. As to the teeth 11, it was found negative dental pulp activity, sensitive to percussion, accompanied by small transmission shadow in apical region at return visit after 2 wk. Root canal therapy of the laterally-dislocated tooth 11 and avulsed tooth 21 were performed 2 wk after the first visit, with the calcium hydroxide paste as an intracanal medication sealing for 4 wk. Then, bio-type root canal filling sealer and hot-melt gutta-percha (SuperEndo B&L, Korea) were adopted for root canal filling. After root canal treatment, 11 and 21 teeth were restored with nanoment resin (3M Dental Products, MN, United States). The fixtures were removed 4 wk after the first treatment (Figure 6B and Figure 7B).

Case 2

After obtaining informed consent, blood was collected from the patient, and the PRF was prepared. Then, the tooth 22 was reimplanted with PRF and splinted for 2 wk using a preshaped semiflexible titanium labial arch (Figure 6C). The digital-X radiograph immediately after surgery showed complete reduction of the tooth 22 (Figure 7C). After pulp vitality assessment, the dental pulp of teeth 11, 21 and 22 were removed after 2 wk, with the calcium hydroxide paste as an intracanal medication sealing for 4 wk. Then, bio-type root canal filling sealer and hot-melt gutta-percha (SuperEndo B&L, Korea) were adopted for root canal filling. The fixtures were removed after 2 weeks and the root canal was completed after 6 wk (Figure 6D and Figure 7D). After root canal treatment, 11 and 21 teeth were filled with fiber piles (3M Deutschland GmbH, Germany) and resin (3M Dental Products, MN, United States) and finally repaired with full crown restoration. Teeth 22 was restored with nanoment resin (3M Dental Products, MN, United States).

OUTCOME AND FOLLOW-UP

Case 1

A follow-up examination was performed 3, 6, and 12 mo after the treatment. Clinical examination found that there were no obvious periodontal pocket, tooth discoloration,

or swelling of the gums around the tooth 21 (Figure 8A-B). The radiographic images taken during the follow-up examination showed that the periodontal membrane space was continuous, and no sign of pathological root absorption was observed (Figure 9A-D).

Case 2

A follow-up examination was performed 3, 6, and 12 mo after the treatment. Clinical examination found that there were no obvious periodontal pocket, tooth discoloration, or swelling of the gums around the tooth 22 (Figure 8C-D). The radiographic images taken during the follow-up examination showed that the periodontal membrane space was continuous, and no sign of pathological absorption was observed (Figure 9E-H).

DISCUSSION

Tooth reimplantation is the most important and fundamental treatment for tooth avulsion. The time interval between avulsion and reimplantation was the most important factor for successful reimplantation and is directly related to the number of live periodontal ligament cells on the root surface of the avulsion teeth [16]. If the tooth is not reimplanted as soon as possible, the residual periodontal ligament tissues on the root suface could be damaged or even show necrosis. These conditions can lead to serious pathologic resorption and loss of the reimplanted tooth. Inflammation and replacement root resorption are the most common causes of failure of reimplanatation. The development of the lesion greatly depends on pulp vitality. When the root canal gets infected, microbial toxins can move to the root surface through dentinal tubules, leading to the occurrence of root resorption [6,23]. Inflammatory root absorption on the outer surface can be prevented or controlled by the timely removal of the etiological origin, that is, root canal intervention. The most effective way to prevent the replacement absorption of roots is to immediately replant or put the tooth in an appropriate storage medium [24,25].

It has been reported in the literature that ideal periodontal healing can be achieved when the avulsed tooth is reimplanted within 5 minutes. If reimplantation is delayed

for more than 1 h after avulsion, then complete necrosis of the injured periodontal ligament tissue is expected [22,26]. The storage of the avulsed tooth is also crucial to the periodontal healing process through affecting the viability of the periodontal ligament cells [27]. Unfortunately, due to the lack of common knowledge of early treatment and preservation of the avulsed teeth, few patients save the avulsed teeth in the ideal media in a timely manner. Studies have shown that 28.6% of patients put dislocated teeth in dry tissues for preservation, and only 11% were held in the mouth or placed in milk during the transport to the clinic [28]. In the present cases, the patients washed the avulsed tooth with running water, which removed the periodontal tissues from the root surface. The teeth were then wrapped in paper sheets, and they visited the doctor more than 1 h later, even up to 18 h later. Therefore, the periodontal cells, which are essential for periodontal membrane healing, have been almost destroyed completely.

In our previous study, we demonstrated that autologous PRF effectively promotes the periodontal healing of avulsed teeth during delayed tooth reimplantation [20]. Similarly, Hiremath *et al* demonstrated that PRF increased the cellular activity of the periodontal ligament cells *in vitro* [29,30]. A previous study reported that when a PRF membrane was used to wrap the root surface and condensed into the canal, it seemed to promote the pulp and periodontal healing of the avulsed teeth, whereas a thick radiolucent area surrounding the root was always obvious even after 24 months of follow-up [31]. Here, PRF granules instead of PRF membrane were adopted; thus, the problem that the PRF graft might prevent the root from fitting into the alveolar bone was avoided. In case 1, the avulsed tooth was reimplanted after 18 h, when its periodontal membrane was necrotic, and the probability of root absorption was greatly increased. Therefore, we used PRF together with tooth replantation to reduce the probability of root resorption. These results were also in line with our expectations, with no signs of root resorption during the 3-, 6-, and 12-month postoperative follow-up. To our knowledge, this is the longest successful delayed replantation of an avulsed tooth reported in the literature thus far. These

results suggest that PRF may provide a new opportunity for traditionally hopeless avulsed teeth.

We assume that PRF promotes the healing of avulsed teeth in two aspects based our previous *in vitro* and *in vivo* studies. Firstly, the periodontal ligament tissues remaining within the original alveolar socket contains periodontal ligament cells and stem cells. During the tissue repair process, multiple growth factors are released by the PRF. Additionally, cell homing will occur, and host stem cells from the circulation will be recruited to the injury region by factors released by the PRF to promote their proliferation and induce their differentiation toward the periodontal membrane, facilitating the formation of periodontal membrane-like structures [20,32]. Secondly, we have shown that PRF consists of concentrated blood platelets, and the α-granules could be activated and degranulated. Thus, many growth factors such as platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), insulin-like growth factor (IGF), epidermal growth factor (EGF), and vascular endothelial growth factor (VEGF) could be released at least a week and up to 4 wk, which means that the PRF supports the regenerative and remodeling environment for a certain period [11,20,31,33-35]. These growth factors increase the mitotic activity of periodontal fibroblasts by 20% – 37% [36], thereby improving the proliferation and periodontal differentiation of target cells and further promote periodontal healing of avulsed teeth [20]. We'd also like to point out that when a variety of growth factors act together, synergistic or even antagonistic effects among them cannot be ruled out. Therefore, the natural proportion of various growth factors is particularly important, which is just one of the important reasons why we choose PRF, which contains a large number of active growth factors. The growth factors in PRF are not only rich in content and variety, but also kept natural proportion under normal physiological conditions. Only by synergic effects of them, can they jointly maintain the balance of tissue environment, and plays an important role in regulating wound healing and tissue regeneration.

Although we did not observe obvious ankylosis in these cases, it is a common finding in patients with avulsed teeth [6,20,37,38]. Previous studies have shown that PRF

can inhibit the osteogenic differentiation of periodontal ligament stem cells *in vitro*, which might contribute to reducing the possibility of ankylosis. There may be three reasons. Firstly, PRF can promote cell proliferation toward fibroblasts and make the tissue repair with more seed cells instead of mobilizing bone stromal cells and bone-derived cells. Secondly, the main component of PRF is the collagen fiber, which could act as a physical barrieris when it was placed in the periodontal space. It can avoid the direct contact between the tooth root and the inner wall of the alveolar socket, thus reducing the bone repair between them [20]. Thirdly, PRF can inhibit the generation of osteoclasts by promoting osteoprotectin secretion. With the inhibition of osteoclasts activity, the opportunity for external resorption can be suppressed to some extent [31]. Of course, the present study also has some limitations, such as a short follow-up time and a small sample size, which makes the long-term effect of PRF in promoting the periodontal healing of avulsion teeth unclear. The observation of the effect of even long-term follow-up with a large sample size is the direction of our future studies.

CONCLUSION

Enriched with growth factors and leukocytes, PRF could help to reduce pathological resorption and promote periodontal wound healing and periodontal ligament regeneration following delayed reimplantation of avulsed teeth. Although the availability of PRF must be demonstrated in more cases, the application of PRF may offer new therapeutic opportunities for traditionally hopeless avulsed teeth.

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