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CASE REPORT

Segmental root development of immature necrotic permanent teeth following regenerative endodontic procedures: a case series

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Abstract

Regenerative endodontic procedures (REPs) are frequently utilized to treat immature permanent teeth with necrotic or inflamed pulps. In most instances, these treatments successfully result in the resolution of apical periodontitis and continued root maturation. However, after reviewing over 180 REP cases treated in the Endodontics Department of Stomatology Hospital at Zhejiang University School of Medicine over the past seven years, we identified an unusual root development pattern in ten cases, characterized by root tips detached from the root body. We conducted a comprehensive analysis of the patients' demographic information, dental histories, and therapeutic efficacy, and identified five potential etiological factors for this rare phenomenon, including external force, prolonged extensive periapical inflammation, iatrogenic factors, traumatic history of primary teeth, and excessive tooth mobility. In our study, we observed that therapeutic failure was more likely in patients with initially separated root tips, while those with initially normal teeth demonstrated significantly better prognoses. We hypothesize that the initial root condition may exert a considerable influence on treatment outcomes.

Keywords

Regenerative endodontic procedures; Root development; Detached root tip

1. Introduction

Regenerative endodontics is defined as biologically-based procedures designed to physiologically replace damaged tooth structures, including dentin and root structures, as well as cells of the pulp-dentin complex [1]. Regenerative endodontic procedures (REPs) are widely used to treat teeth with necrotic pulps and open apexes [2]. According to the extent of treatment success, REPs can realize primary, secondary, and tertiary targets, which correspond to the bony healing and disappearance of clinical symptoms, increased root wall thickness with/without increased root length, and positive reaction to vitality testing, respectively [2]. The radiographic outcomes of immature teeth after REPs are mainly divided into five types [3]: Type 1, continued thickening of the root wall and significant root development; Type 2, arrest of root maturation with the apical foramen closed and blunt; Type 3, continued root formation with the root apex remaining open; Type 4, severe calcification, or even obliteration in the canal space; and Type 5, a hard tissue barrier developed between the coronal sealant and apical foramen (Fig. 1).

During the period of root development, Hertwig's epithelial root sheath (HERS) cells induce the dental papilla cells on its inner side to differentiate into odontoblasts. Subsequently, these odontoblasts secrete dentin and form the pulp-dentin complex. Through the interruption and perforation of HERS cells, outer dental follicle cells come into contact with the newly formed dentin on the inside, prompting dental follicle cells to become cementoblasts and secrete cementum [4]. In REPs, all the stem cells from the HERS, dental papilla, dental follicle, pulp, and periodontal ligament act as abundant sources of regenerative potential, participating in tooth root development [5]. The viability of these stem cells is dependent on many factors, including patient age, apical foramen diameter, and the severity and duration of inflammation [6]. Thus far, the "ideal outcome" of pulp-dentin complex regeneration has not been realized in REPs histologically. In reality, REPs result in the formation of cementum-like, bone-like, and periodontal ligament-like tissues [7]. Instead of tissue regeneration, REPs involve more a process of wound repair, and different wound repair types eventually lead to different root development types.

Intriguingly, of more than 180 REP cases treated in the Endodontics Department of Zhejiang University School of Stomatology Hospital between 01 November 2015 and 30 June 2022, all could be classified into one of the aforementioned root development types, except for ten cases that exhibited a completely dissimilar type, wherein the root tip was detached from the root body (Fig. 1). Concerning this atypical form of detached root apexogenesis, several questions remain unresolved:

1. What causes a detached root tip, and what shared etiolog-

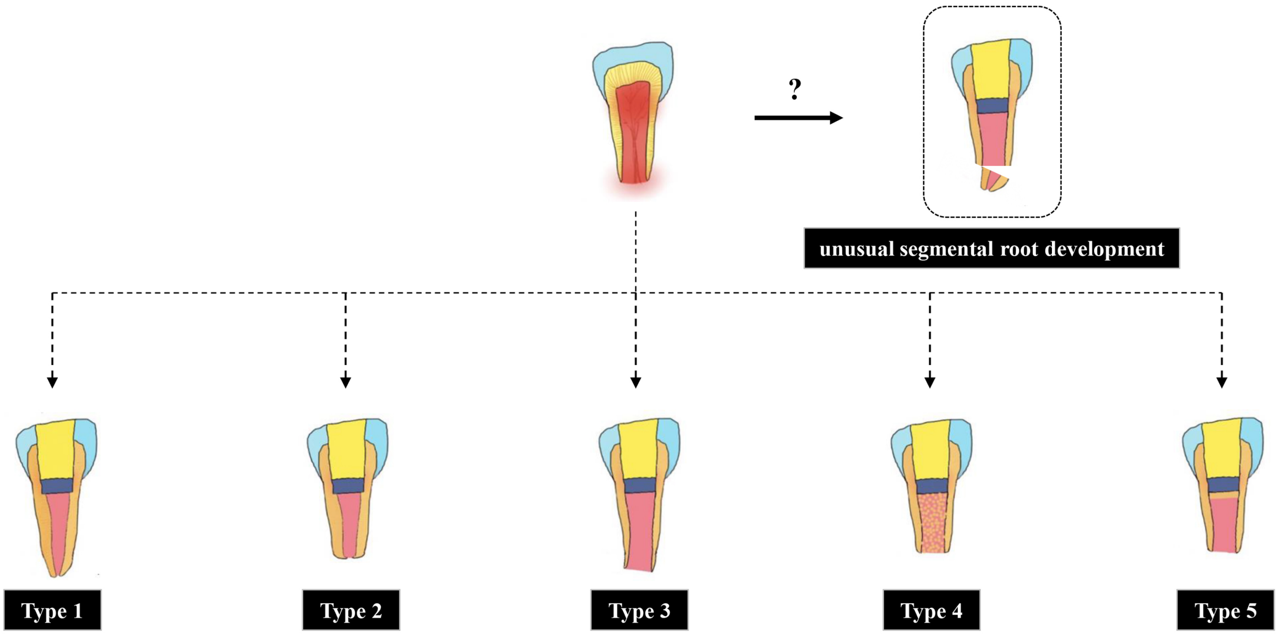

FIGURE 1. Five conventional types and one unusual type of tooth root development after REPs. Type 1: continued thickening and extension of tooth root; Type 2: closure of apical foramen without root length increased; Type 3: increase of root length with the apex open; Type 4: severe calcification inside the root canal; Type 5: a calcified barrier formed between the coronal sealant and apical foramen; the unusual type: a root tip formed separate from the body of root.

ical factors exist among these teeth?

2. What is the long-term stability and prognosis for these teeth? Are they more prone to failure compared to conventionally healed teeth?

3. If REPs fail, what alternative treatment options are available for these teeth? Additionally, does the detached root tip impact subsequent dental treatments?

To date, nearly no studies have been reported about the uncommon root development type of detached root tips after REPs, making it difficult to answer the abovementioned questions. Hence, in this study, we investigated these ten cases of abnormal segmental root development after REPs with the goal of offering valuable insight for further treatments.

2. Case series

The ten patients were treated in the Department of Endodontics, Affiliated Stomatology Hospital, Zhejiang University School of Medicine. The patients' demographic information, dental histories, clinical symptoms, physical examinations, and therapeutic efficacy are provided in detail in Tables 1 and 2. Informed consent for REPs was obtained from caretakers.

The case series comprised five males and five females, aged between 7 and 13 years. The ten immature teeth, including four anterior and six premolar teeth, underwent REP treatment. Of these, six cases presented a broken central cusp, and four cases had a history of dental trauma, with partial luxation observed in case 7. Two patients were diagnosed with acute apical abscess due to gingival swelling, percussion hypersensitivity, and grade 2 mobility of the affected tooth. Six patients were diagnosed with chronic apical abscess, with cases 2 and 8 also exhibiting root fractures. The remaining two patients were diagnosed with asymptomatic apical periodontitis, as the teeth appeared clinically normal, but periapical radiolucencies were observed on dental radiographs. Furthermore, the initial root tip condition was separate in half of the teeth and normal in the others.

To avoid repeated statement of REPs, the treatment procedures can be summarized as follows:

First appointment. Local anesthesia, utilizing 4% articaine (containing 1:100,000 epinephrine), was administered for cases where the pulp was not entirely necrotic. Subsequently, under rubber dam isolation, an access cavity was prepared using a dental operating microscope (DOM (Carl Zeiss, Jena, Germany)). After determining the working length, the root canal was cleaned with a #25 file in an ultrasonic unit, while simultaneously being irrigated with an ample 1.5% sodium hypochlorite (NaOCl) (20 mL/canal, 5 min) followed by saline (20 mL/canal, 5 min). The root canal was then dried and filled with Multi-Cal calcium hydroxide paste (Pulpdent, Watertown, MA, USA). The open access was temporarily sealed using a sterile cotton pellet and glass ionomer cement (GIC (Fuji 2 LC; GC Corp, Tokyo, Japan)).

TABLE 1. Demographics of patients and clinical signs, diagnosis, and treatment procedures of ten teeth.

Case No.	Gender	Age (yr)	Tooth position	Nolla's stages	Dental history	Clinical tests	Gingival condition	Radiologic examination		Diagnosis	Scaffold in the canal
								Periapical lesion	Root tip condition		
1	F	10	45	8	Fracture of central cusp	e (−), pc (++), mb (II)	Swelling	+	Normal	AAA	Create bleeding by over-instrumenting +biomembrane +iRoot BP Plus
2	F	7	21	7	Dental trauma	e (−), pc (−), mb (I)	Sinus tract	+	Separate	CAA; Root fracture	Venous blood +biomembrane +iRoot BP Plus
3	M	10	35	8	Fracture of central cusp	e (−), pc (−), mb (−)	Sinus tract	+	Normal	CAA	Venous blood +biomembrane +MTA
4	M	11	35	8	Fracture of central cusp	e (−), pc (±), mb (−)	Sinus tract	+	Separate	CAA	Create bleeding by over-instrumenting +MTA
5	M	12	22	8	Dental trauma	e (−), pc (±), mb (−)	Sinus tract	+	Separate	CAA	Venous blood +iRoot BP Plus
6	M	9	35	7	Fracture of central cusp	e (−), pc (−), mb (I)	Normal	+	Separate	AAP	Venous blood +iRoot BP Plus
7	F	8	11	8	Dental trauma (partial luxation)	e (−), pc (±), mb (II)	Sinus tract	+	Normal	CAA	Venous blood +biomembrane +iRoot BP Plus
8	M	10	12	8	Dental trauma	e (−), pc (±), mb (I)	Sinus tract, pyorrhea	+	Normal	CAA; Root fracture	Venous blood +biomembrane +iRoot BP Plus
9	F	13	35	8	Fracture of central cusp	e (−), pc (−), mb (−)	Normal	+	Separate	AAP	Create bleeding by over-instrumenting +MTA
10	F	11	45	8	Fracture of central cusp	e (−), pc (++), mb (II)	Swelling	+	Normal	AAA	Create bleeding by over-instrumenting +MTA

F: female; M: male; e: electric pulp test; pc: percussion; mb: mobility; AAA: acute apical abscess; CAA: chronic apical abscess; AAP: asymptomatic apical periodontitis; MTA: mineral trioxide aggregate.

TABLE 2. Treatment outcomes of ten teeth.

Case No.	Follow-up time (mon)	Clinical tests	Gingival condition	Radiologic examination			Outcome	Remedy
				Root tip condition	Root body condition	Periapical lesion		
1	12	e (−), pc (−), mb (−)	Normal	Increase in length and thickness; drift in the mesial and coronal direction	Increase in thickness, but no obvious change in length	Disappeared	Successful	/
2	26	e (−), pc (−), mb (I)	Sinus tract	Increase in thickness, but no obvious change in length; drift slightly in the coronal direction	No obvious change in length and thickness	No change	Failed	Apical barrier technique
3	48	e (+), pc (−), mb (−)	Normal	Increase in length and thickness; drift in the distal and coronal direction	No obvious change in length and thickness	Disappeared	Successful	/
4	16	e (−), pc (−), mb (−)	Normal	Increase in length and thickness; drift in the coronal direction	Calcification in the canal space, but no obvious change in length	Disappeared	Successful	/
5	32	e (+), pc (−), mb (−)	Normal	Increase in length and thickness; drift in the coronal direction	No obvious change in length and thickness	Disappeared	Successful	/
6	24	e (+), pc (−), mb (−)	Normal	Increase in length and thickness; drift slightly in the coronal direction	No obvious change in length and thickness	Disappeared	Successful	/
7	17	e (+), pc (−), mb (−)	Normal	Increase in length and thickness; drift slightly in the coronal direction	Calcification in the canal space, but no obvious change in length	Disappeared	Successful	/
8	40	e (−), pc (−), mb (−)	Normal	Increase in length and thickness; drift in the coronal direction	No obvious change in length and thickness	Disappeared	Successful	/
9	42	e (−), pc (−), mb (−)	Normal	Increase in length, but no obvious change in thickness; drift in the distal and coronal direction	No obvious change in length and thickness	Decreased at first and then increased	Failed	Apical barrier technique
10	26	e (−), pc (−), mb (−)	Normal	Increase in length and thickness; drift in the coronal direction	No obvious change in length and thickness	Disappeared	Successful	/

e: electric pulp test; pc: percussion; mb: mobility.

Second appointment. Two weeks later, the signs/symptoms of each patient were carefully examined. If signs/symptoms persisted, additional intracanal medication with calcium hydroxide was provided. If the signs/symptoms disappeared, the procedure moved to the next step, as follows. Under local anesthesia of 3% mepivacaine (without vasoconstrictor) and isolation of a rubber dam, access was re-entered using the DOM. After removal of the cotton pellet, the canal was gently irrigated with 1.5% NaOCl (20 mL/canal, 5 min) and 17% ethylenediaminetetraacetic acid (EDTA) (20 mL/canal, 5 min) and then dried with sterilized paper tips. In four cases, bleeding was successfully induced into the canal up to the cemento–enamel junction level by rotating a precurved #25 K-file 2 mm past the apical foramen. However, in the other six cases, bleeding was not sufficient. As a substitute, a blood sample obtained from the median cubital vein was transferred into the canal. In addition, half of the cases involved use of a biomembrane (ZH-Bio, Shandong, China) due to a wide canal orifice. The biomembrane was placed over the blood clot to avoid collapse of the coronal sealing material. In this case series, mineral trioxide aggregate (MTA (Dentsply, Tulsa, OK, USA)) was used for only four premolar teeth as a coronal sealing material because it had a high risk of tooth discoloration. iRoot BP Plus (Innovative Bioceramix, Vancouver, BC, Canada) as an alternative was used for the other two premolars and all the anterior teeth. Finally, the access cavity was closed with a moist cotton pellet and GIC.

Third appointment. One week later, after reopening the access cavity, MTA or iRoot BP Plus was confirmed to have hardened by using an endodontic explorer. The cotton pellet and GIC were then replaced with nanofilled composite Filtek-Z350-XT (3M ESPE, Seefeld, Bayern, Germany).

Follow-up. Follow-up assessments (Fig. 2) of ten cases spanned a period of 12 to 48 months. Remarkably, all root tips became detached, and the majority migrated in the coronal direction. Additionally, both dentin thickness and length increased in root tips, while exhibiting no noticeable alterations in most root bodies. Concerning treatment outcomes, eight cases remained asymptomatic, with four of them even demonstrating restored pulp vitality. However, the remaining two cases were unsuccessful due to the reemergence of a sinus tract or persistence of periapical radiolucent lesions. The apical barrier technique was applied for these cases, and notably, the secondary treatment proved effective.

3. Discussion

Recently, REPs have become prevalent in the treatment of immature permanent teeth with infected necrotic pulp and/or apical periodontitis. With the help of REPs, elimination of clinical symptoms, resolution of apical periodontitis, and continued root development can be achieved for most affected teeth. Besides the conventional five types of root development [3], an unusual type in which a segmental root tip forms detached from the body of the root may occur after REPs. To date, only three pertinent reports, encompassing six cases, have documented this phenomenon [8–10].

Little is known about the cause of detached root apexogenesis, and it is not clear what specific roles REPs might play. According to the present cases, the affected teeth were either anterior or premolar teeth. No molars have been reported thus far [8–10]. That is, the phenomenon of segmental root development is more likely to be related to trauma or fracture of the central cusp and less likely to be related to dental caries. The external force causing fracture of the central cusp or caused by trauma is responsible for this phenomenon. Owing to the weak connection of the root end, the stem cells of the HERS, dental papilla, and periodontal ligament can readily be detached from the calcified end by an external force, and then a separate root tip might develop [9, 11]. Previous evidence suggests that luxation injuries of trauma will not influence the robustness and functional ability of the HERS [11–13]. When a tooth is avulsed, the HERS remained in the socket and retained vitality. The HERS continued to develop separately from the body of the root after replantation, which was consistent with the radiographic appearance of case 7. In extreme conditions, such as in cases 2 and 8, if the external force becomes increasingly stronger, root fracture may eventually occur, leading to intuitive detachment of the root and allowing for formation of a dilacerated root tip.

Apart from the factor of external force, a long-standing and extensive periapical lesion may also be associated with unusual root apexogenesis. Seven patients in this study underwent long-term and large-scale periapical pathology. It has been demonstrated that stem cells from the apical papilla (SCAP) can not only survive but also thrive in an inflammatory environment [14]. The angiogenesis and osteogenic potential of the SCAP are also significantly increased [14, 15]. Such a long duration of extensive periapical inflammation causes detachment of the SCAP and other related stem cells from the root body without damaging their vitality, eventually leading to formation of a segmental root tip.

Overall, the unusual root development caused by the above two reasons can occur prior to REPs. Based on the present case series, a dilacerated root before REPs formed in five cases, whereas the other five formed after completion of the treatment. We speculate that some iatrogenic factors might also have an effect in such an occurrence. For example, canal instrumentation or filling beyond the apical foramen in apexification intervention would lead to separation of the HERS and SCAP apically of the root end [9, 16]. In the field of REPs, only two reports have revealed the appearance of independent root tips after therapy [8, 17], and the phenomenon was attributed to the process of bleeding induction. In our study, six cases employed venous blood rather than over-instrumentation-induced bleeding; however, all participants had initially attempted to puncture periapical tissues using a rotating K-File. Indeed, the procedures in these cases tended to be more aggressive due to inadequate intracanal bleeding.

As mentioned by Cho *et al.* [18], a traumatic history for primary teeth is associated with segmental root development. The authors claimed that subluxation of a primary incisor would cause serious consequences on its permanent successor tooth, accelerating its premature exfoliation and, more interestingly, resulting in formation of a root tip despite exfoliation of the tooth body. Continued activity of the HERS or pulp remnants may account for this unusual phenomenon [18].

Moreover, in the present study, tooth mobility was catego-

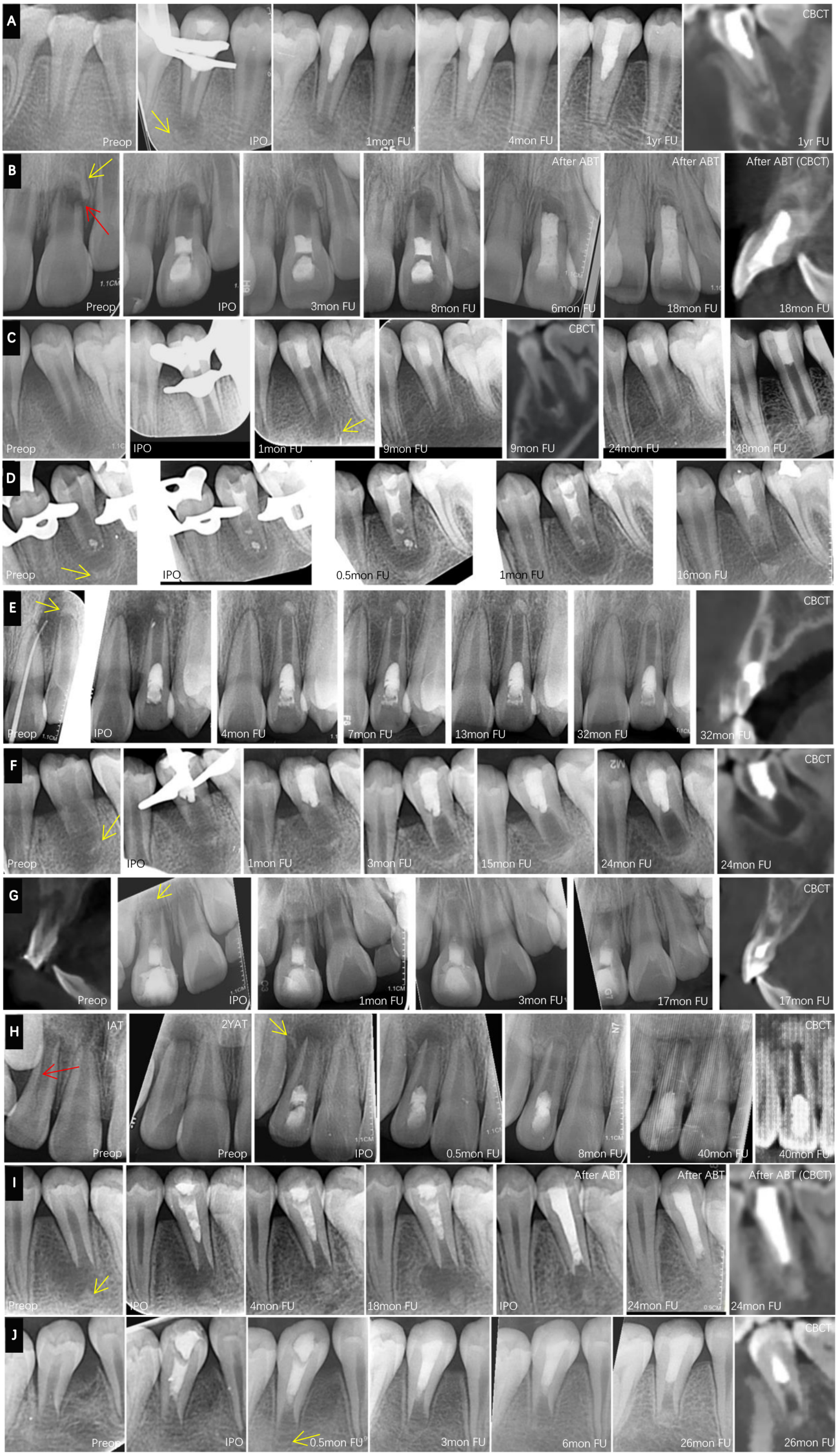

FIGURE 2. Periapical radiograph of ten cases. (A) Case 1, (B) Case 2, (C) Case 3, (D) Case 4, (E) Case 5, (F) Case 6, (G) Case 7, (H) Case 8, (I) Case 9, (J) Case 10. The red arrow in (B) and (H) indicates the presence of a fracture line. The yellow arrow in (A-J) indicates the initial occurrence of apical radiopaque tissue. Preop, preoperative; IPO, immediate postoperative; FU, follow-up; ABT, apical barrier technique; IAT, immediately after trauma; 2YAT, two years after trauma.

rized as grade 2 in three cases and grade 1 in another three cases. Given that severe mobility may act as a detachment force, we considered increased mobility as an additional factor contributing to separated root apexogenesis [9]. Taken together, we identified five possible causes of segmental root development, including external force, long duration of extensive periapical inflammation, iatrogenic factors, traumatic history of primary teeth, and excessive tooth mobility.

Treatment outcomes may depend on the root condition before the beginning of REPs, and therapy failure occurs more easily in those whose root tips are initially separated. In this case series, five cases presented an initially detached root; unfortunately, failure due to recurrence of the gingival sinus tract or persistence of periapical radiolucent lesions occurred in two of these cases. The cases of failure either involved a history of root fracture or a very long-term and extensive periapical lesion. We suspect that severe dental trauma might harm the blood supply of the apical area and decrease its ability to fight infection [19, 20]. A long duration of extensive periapical pathosis as well as preexisting separation of the root might render infection control difficult and challenging [21]. Any residual bacterial biofilm and its byproducts would probably affect osteogenic differentiation of SCAPs and influence further therapeutic effects [22]. For failed REPs, we chose the apical barrier technique as an additional endodontic intervention and adopted the more intensive disinfection procedure suggested by Lee *et al*. [23]. After several months, the clinical symptoms and periapical radiolucent lesion disappeared. For those whose root tip was normal initially, the prognosis was much better. All of the patients in this study achieved complete resolution of radiolucency and showed significant healing of periapical lesions. The radiopaque mass was observed apically and separate from the open end of the root body. This newly formed segment showed a similar structure to the root canal inside and appeared as a normal root tip. With time, the apical segment continued to develop both in dental thickness and root length, and its morphology became increasingly regular. Nevertheless, the body of the root had no obvious change in thickness or length, except for one case in which the thickness of the dentinal wall increased moderately. Overall, REPs are still recommended for those whose root tip is normal initially because the occurrence of segmental root development is unpredictable; even if separation appears later, there is no evidence that the failure rate will rise. However, for those whose root tips are initially separate, the apical barrier technique may be a more effective remedy than REPs because in that situation, a better antibacterial effect can be obtained by using a higher level of irrigation solution freely.

According to this case series, the separated root tip was not stationary. Most of them drifted coronally over 12 to 48 months of follow-up. The root tip was able to reach toward the body of the root with a decrease in inflammation, yet the structure was not the same as that of a normal root. Caution is warranted in subsequent dental therapies, particularly during orthodontic treatments. And care must be taken to maintain a safe distance from the root tip. When root canal therapy is necessary, we should prepare or fill the canal no further than the end of the root body, which may lead to difficulty in inflammation control in the root tip region. Postcore restorations are not recommended for these teeth, given their poor retention force and weak fracture resistance. Once periapical inflammation becomes uncontrollable, further apical microsurgery or tooth extraction should be taken into consideration. The tip of the root, not merely the root body, should also be pulled out. More studies are needed to better understand the pathogenesis, prognosis, long-term stability, and influence on subsequent dental therapies of detached root apexogenesis.

4. Conclusions

This case series revealed a new pattern of root development after REPs, characterized by the formation of a detached root tip distinct from the primary root structure. Possible etiological factors for this phenomenon encompass external force, persistent extensive periapical inflammation, iatrogenic influences, traumatic history of primary teeth, and excessive tooth mobility. Notably, root tip detachment prior to REPs may potentially affect ultimate treatment outcomes, and if REPs fail, the apical barrier technique remains an alternative option.

ABBREVIATIONS

REPs, regenerative endodontic procedures; HERS, Hertwig's epithelial root sheath; SCAP, stem cells from the apical papilla.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

MY—contributed to interpretation of data, original draft preparation and manuscript review and editing; SW—contributed to operation of REPs and interpretation of data; SD—contributed to operation of REPs, study conception and design and manuscript review and editing. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Medical Ethics Committee of Stomatology Hospital, Zhejiang University School of Medicine (No. 2019-23). All methods were carried out in accordance with relevant guidelines. Informed consent was acquired from all participants and their legal guardians.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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