Development of supernumerary premolars in the mandible after orthodontic extraction - A case report

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Abstract
Supernumerary premolars are relatively rare and the etiology of supernumerary tooth formation is complicated and has not yet been well known up to now. The present case documents a case of supernumerary premolars developing in the mandibular premolar region after extractions of the first premolars for orthodontic treatment in an Asian boy. What is special is that they positioned exactly where the extracted premolars used to be. Theoretical considerations for the development of them are postulated from the perspectives of tooth development and engineered tooth regeneration. Residual dental epithelial cells and mesenchyme cells in the alveolar fossas after orthodontic extraction of young permanent premolars may have the potential to proliferate, recombine and interact with each other leading to the development of supernumerary teeth under the inductive microenvironment of alveolar fossas.

Introduction
Supernumerary teeth may be defined as any teeth or tooth substance in excess of the usual configuration of twenty deciduous, and thirty-two permanent teeth [1]. They may occur in any region of the dental arch, either as isolated events or multiply, unilaterally or bilaterally, erupted or unerupted, in single or both arches, or as part of a syndrome or disease, or can be found in non-syndromic patients [2,3]. Supernumerary premolars are relatively rare and they constitute almost 10% of the total supernumerary cases, of which the prevalence reported in the literatures varies between 0.5% and 5.3% in the permanent dentition, and proximately 75% of those are in the mandible [4,5]. Yusof’s review found that mandibular premolar region was the most common site of occurrence for non-syndrome associated supernumerary teeth [6]. There also has been reported that Asian populations or males have a higher frequency in occurrence of supernumerary teeth [7,8]. Besides, among supernumeraries, supernumerary premolars are found to be more commonly developed than estimated and are special in terms of their late development and recurrence, which make treatment plans variable and complicated [7]. Some of the theories for the presence of supernumerary teeth include atavism, division of the tooth germ, hyperactivity of the dental lamina, and genetic and environmental factors [9]. Although a number of possible theories have been postulated, the exact etiology for supernumerary teeth is still uncertain.

The present case documents another case of supernumerary premolars occurring in the mandible. What is special about this case is that the supernumerary premolars were developed after the orthodontic extraction of the first premolars, and they positioned exactly at the places where the extracted premolars used to be.

Case report
The patient, an Asian boy, initially presented for orthodontic treatment with a chief complaint of irregular teeth and protrusion at age 12. Intraoral examination showed permanent dentition with severe crowding in upper arch and moderate in lower arch. Routine panoramic and lateral radiographs were taken. The panoramic showed all permanent teeth present including the third molars. At this time, there was no radiographic evidence of supernumerary teeth developing (Figure 1).

For orthodontic treatment, four first premolars were extracted. At age 14, orthodontic treatment was completed with and subsequent panoramic and lateral radiographs were taken. It was noted that early crown developments of two supernumerary teeth were in the lower premolar regions, where exactly the extracted lower premolars used to be. The left one was more developed than the right one (Figure 2). The present two supernumerary premolars were surgically removed carefully under the guidance of cone beam computed tomography (CBCT) in case of future pathological changes and damage of adjacent teeth.

Discussion
As is well known, tooth development is a complex process that takes place through reciprocal interactions between the dental epithelium and the neural crest-derived dental ectomesenchyme that forms the dental papilla and dental follicle. Epithelial-mesenchymal interaction plays important roles in tooth genesis and development [10-12]. At the initial stage of tooth development, the epithelium produces the first instructional signals to the mesenchyme. The mesenchyme then responds signals back to the epithelium [13].

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Epithelial rests of Malassez cells (ERM), which are development residues of Hertwig’s epithelial root sheath, are unique epithelial cells in the periodontal ligament. They remain in periodontal tissues throughout the adult life in cord or net-like formations or as isolated islands near the cementum [14]. It is generally acknowledged that their functional role is to maintain the homeostasis of the periodontium through reciprocal interactions with other periodontal cells [15]. In recent years, there are studies suggesting that ERM cells might contain stem cell characteristics [16,17]. The primary culture of ERM cells contains a population of primitive stem cells in which epithelial stem cell markers and embryonic stem cell markers were expressed [15]. Furthermore, there have been reports of epithelial stem cells in the periodontium might be involved in the formation of enamel-like structures. Tummers and Theistles’ study indicated that epithelial stem cells can give rise to both the ameloblast and root epithelium cell lineage which created distinct tooth patterns [18]. Another study also demonstrated that quiescent ERM can differentiate into ameloblast-like cells when subcultured and generate enamel-like tissues in combination with dental pulp cells at the crown formation stage when transplanted in vivo [19].

What’s more, beginning in 2000, several human dental mesenchymal stem/progenitor cells have been isolated and characterized, including dental pulp stem cells (DPSCs), stem cells from exfoliated deciduous teeth (SHED cells), stem cells from apical papilla (SCAP cells), periodontal ligament stem cells (PDLSCs), and dental follicle precursor, or progenitor cells (DFPCs) [20]. These mesenchymal stem cells can not only give rise to the other components of the tooth: dentin, pulp, cementum, and the periodontal ligament, but also could differentiate into at least 3 distinct lineages [21,22].

In the case presented here, there is no familial history of supernumerary teeth. The development of the first premolars had not completed yet. It was expected that the ERM as well as the dental MSCs would be more prominent in teeth with incomplete root formation [23]. After orthodontic tooth extractions, there remained ERM and dental MSCs in the alveolar fossas, especially the PDLSCs, SCAP cells, DFPCs and DSPCs (Figure 3). Dental cells are verified to have the capacity to reorganize themselves into a proper organ during the early stages of tooth development [24,25]. The classical tissue recombination experiments also indicated that either the dental epithelium or dental mesenchyme has the competence to direct tooth development depending on the stage of tooth morphogenesis [26,27]. In present case, the ERM were therefore supposed to act as an epithelial component proliferating, recombining and interacting with the dental MSCs after orthodontic extractions. Subsequently, tooth genesis and crown formation initiated under the inductive microenvironment of alveolar fossas. The ERM would differentiate into ameloblasts and give rise to enamel while the dental MSCs form the other components of the tooth. There is still an approximate 8% possibility of recurrence of supernumerary premolars even after surgical removals. Long term follow-up by taking radiographic surveys periodically is of great necessity.

Therefore, epithelial-mesenchyme recombination has been one of the strategies for bioengineered tooth regeneration in recent years [28-30]. However, tooth initiation is regulated by delicate activator-inhibitor mechanisms between the epithelial and mesenchymal cells [31]. Although researches in recent years have taught us much about the molecular mechanisms of tooth morphogenesis and differentiation [9], these intricate mechanisms underlying supernumerary tooth formation as well as the initiation of tooth formation are still unclear up to date. Consideration for the presence of supernumerary teeth in current case is theoretical based on previous studies and many questions are still doubtable and debatable. Experimental evidences are needed to illustrate these issues and more information about the molecular mechanisms of supernumerary teeth would better provide assistance in understanding of tooth genesis and development as well as engineered tooth regeneration.
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