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Process of ectopic tooth formation in the maxillary sinus: follow-up observation of one case

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Abstract

Objective: This study was performed to investigate the process of ectopic tooth formation.

Methods: A patient with an ectopic tooth was followed for 6 years. The tooth size and **mineralization** were evaluated by paranasal sinus computed tomography every 3 years.

Results: The ectopic tooth was present in the nasal crest of the maxilla and did not change significantly during the 6-year follow-up period. However, the patient developed a new ectopic tooth in the maxillary sinus (ETm). This tooth, located in the posterior wall of the left maxillary sinus, initially appeared as a small region of soft tissue on computed tomography. After 3 years, the area of mixed density had significantly increased, and some of it had significantly **mineralized** to form an ETm. After 6 years, the ETm had further **mineralized** and enlarged in situ. The width between the left and right sides of the ETm in 2018 (9.08 ± 2.09 mm) was significantly larger than that in 2015 (7.51 ± 2.18 mm), indicating that ETm formation is a gradual process of **mineralization**.

Conclusion: Ectopic teeth can gradually form by in situ mineralization after adolescence, suggesting that ectopic teeth are genetically regulated and result from a programmed formation process occurring at a specific time point.

Keywords

Ectopic teeth, supernumerary teeth, maxillary sinus, follow-up studies, computed tomography, mineralization

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Abbreviations

ETn, ectopic tooth in the nasal crest of the maxilla; ETm, ectopic tooth in the maxillary sinus; CT, computed tomography

Introduction

The overall occurrence rate of ectopic tooth eruption in a nondental area is not clear, but it is not uncommon. Large numbers of cases and observational case series have been reported.[1] Ectopic teeth are commonly observed in the palate and maxillary sinus[1–6]; they have also been reported in the mandibular condyle, coronoid process, orbital and nasal cavities, and skin.[7]

In most cases, ectopic teeth cause secondary conditions such as odontogenic cysts or nasal and maxillofacial symptoms.[8–10] However, with technological advances in imaging examinations, asymptomatic patients with ectopic teeth have also been reported.[7,11] Ectopic teeth affect a wide range of patients from children to advanced-age individuals.[1,12] However, the time of ectopic tooth occurrence and the mechanism of ectopic tooth formation are not clear. Are they caused by a migration disorder in tooth genesis or by in situ formation? Is ectopic tooth formation an embryonic development problem or a genetic problem? These questions have not yet been answered.

All cases of ectopic tooth formation reported in the literature to date were part of cross-sectional studies, and no studies have included follow-up observations of the process of ectopic tooth formation.[1–5,11] Therefore, previous studies provide little information on the mechanism of ectopic tooth formation. In the present study, we were fortunate to observe the process of formation of an ectopic tooth in the maxillary sinus (ETm) from soft tissue to **mineralization** during the follow-up observation of an ectopic tooth in the nasal crest of the maxilla (ETn). These observations provide valuable information regarding the mechanism of ectopic tooth formation.

Methods

Case and follow-up period

A patient with an ectopic tooth was followed for 6 years from July 2012 to September 2018. **Paranasal sinus computed tomography (CT) was performed every 3 years to observe whether the presence of the ectopic tooth led to the formation of odontogenic cysts.** The patient provided informed consent for both continuation of the follow-up examinations and publication of the examination results.

CT examination and analysis

The CT scan ranged from the superior margin of the frontal sinuses to the inferior margin of the maxillary alveolar process and was performed using a LightSpeed 64-slice spiral CT system (GE Healthcare, Chicago, IL, USA) and a bone imaging algorithm. CT scans were obtained at a 0.625-mm section thickness and 0.5-mm interval from 120 to 320 mA at 120 kV. The GE system was used for multiplanar reconstruction in the three anatomical planes. The size of the ectopic tooth and the CT values were measured using the Centricity Enterprise Web 3.0 image analysis system (GE Healthcare). Continuous-layer observations were performed by sliding the computer mouse. The CT scans were approved by the Ethics Committee of Capital Medical University affiliated with Beijing Chaoyang Hospital.

Data collection and statistical analyses

The three sets of follow-up data were matched according to anatomical markers to ensure that the measured planes of the ectopic tooth were consistent. The anteroposterior width and lateral width of the ectopic tooth were measured in 15 continuous axial planes from the bottom up. The overall soft tissue density and bone tissue density areas of the ectopic tooth were measured in each plane. Finally, three sets of follow-up data regarding the size of the ectopic tooth were obtained. The size of the ectopic tooth is presented as mean $\pm$ standard deviation. Differences in the width of the ectopic tooth between the different CT scans were evaluated using the paired samples t-test, with significance defined as a P value of 0.05. All statistical analyses were performed using SPSS version 17 (SPSS Inc., Chicago, IL, USA).

Results

Overview of case at first visit in 2012

In July 2012, a 16-year-old male patient was admitted to the Department of Otorhinolaryngology/Head and Neck Surgery with complaints of mild and intermittent nasal congestion. The patient had sustained a nasal injury while playing basketball 1 month previously, resulting in only a small amount of transient epistaxis and no nasal deformity. He did not exhibit a runny nose, blood in his nasal mucus, or olfactory changes. No neurological or ophthalmological disorders were observed. No evidence of developmental disorders was found, and no systemic diseases were recorded. He exhibited a normal maxillary-mandibular growth pattern with no perceivable/obvious facial deformity. However, endoscopic examination showed nasal stenosis, bilateral inferior turbinate hypertrophy, and obvious deviation of the nasal septum. Therefore, paranasal CT was performed to further understand the structure of the paranasal sinuses and nasal cavity.

Special findings on CT (2012). CT showed deviation of the nasal septum, an ETn, and hyperaeration of the bilateral maxillary sinus (Figure 1(a)). A slight bone defect was observed in the posterior wall of the left maxillary sinus (1.89×1.80 mm) accompanied by a small soft tissue shadow ($4.81 \times 3.80 \times 2.82$ mm) (Figure 2(a)).

Treatment strategy (2012). The patient was treated with a steroid nasal spray (mometasone furoate aqueous nasal spray) at 200 mcg/day (two sprays per nostril, once a day) and followed up because the ectopic tooth was causing no obvious symptoms and he had only mild and intermittent nasal congestion.

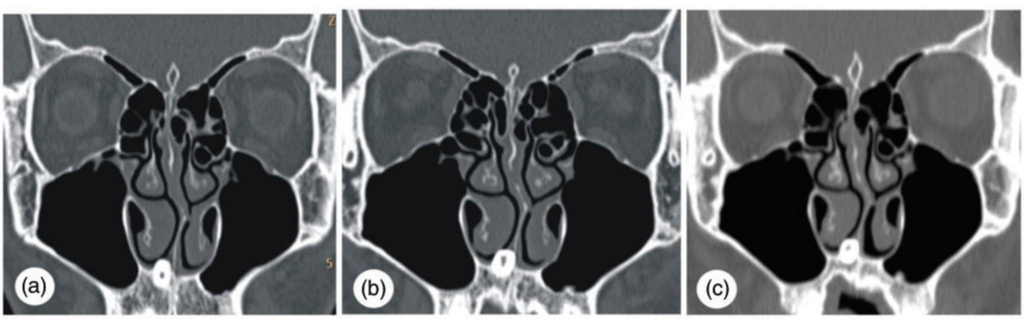

Figure 1. Coronal computed tomography images obtained at three time points showing an ectopic tooth in the nasal crest of the maxilla. (a) 2012, (b) 2015, (c) 2018. There were no significant differences among the three scans (ranging from 2012 to 2018).

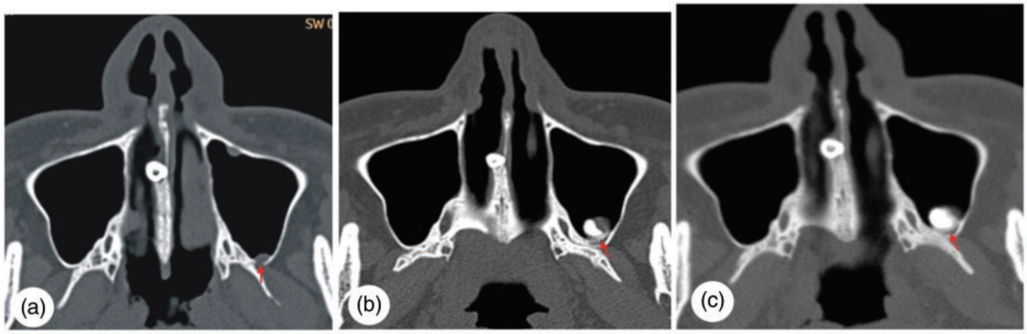

Figure 2. Axial computed tomography (CT) images showing the process of ectopic tooth formation in the posterior wall of the left maxillary sinus (ETm). (a) The first CT examination (2012) showed the ETm as only an area of soft tissue density in the posterior wall of the left maxillary sinus accompanied by a slight bone defect. (b) The second CT examination (2015) clearly showed the ETm, but mineralization was not complete, and half of the area remained an area of soft tissue density. However, the posterior wall of the left maxillary sinus showed complete ossification. (c) The third CT examination (2018) showed complete mineralization of the ETm in situ.

Second follow-up examination in 2015

At 19 years of age, the patient had no significant aggravation of nasal congestion, and there were no new symptoms of discomfort compared with those reported during the previous visit 3 years prior (2012). Paranasal sinus CT was recommended at the second follow-up visit (July 2015).

Special findings on CT (2015). No significant changes in the ETn were observed by CT in 2015 compared with the previous CT observations in 2012 (Figure 1(a) and (b)). Unexpectedly, however, a new ETm had appeared in the posterior wall of the left maxillary sinus, where a thickened area had been present in the previous CT images obtained in 2012 (Figure 2(a) and (b)). The ETm consisted of an area of soft tissue density and bone density, indicating that **mineralization** of the ETm was still in progress (Figure 2(a) and (b)). The slight bone defect in the posterior wall of the left maxillary sinus shown in the previous CT images (2012) exhibited complete ossification in the (2015) follow-up CT images (Figure 2(a) and (b)).

Treatment strategy (2015). Considering the lack of clinical discomfort resulting from the ETn and ETm and the fact that the ETm appeared to still be in the process of formation, no surgical intervention was carried out. The patient was asked to continue regular follow-up examinations to provide an understanding of the occurrence and evolution of ectopic teeth and reveal the pathophysiological process.

Third follow-up examination in 2018

At 21 years of age, the patient's nasal congestion was more severe than before, but he still had no new symptoms of discomfort compared with those reported during the previous visit (2015).

Special findings on CT (2018) and comparison with previous CT findings (2012 and 2015). There were still no significant differences in the **mineralization** or dental follicle formation of the ETn between the third CT examination (2018) and the previous CT examinations (2012 and 2015) (Figure 1 (a)–(c)). In contrast, the third follow-up CT scan showed an increase in the degree

Table 1. Measurement of the ossified area of the ETm on axial computed tomography images.

	n	2015	2018	r	P value
Entire range of the ETm (including soft tissue density)					
Anteroposterior width, mm	15	7.19 ± 1.95	7.05 ± 1.90	0.942*	0.454
Lateral width, mm	15	7.51 ± 2.18	9.08 ± 2.09	0.858*	0.000
Ossified area of the ETm, mm					
Anteroposterior width, mm	15	7.03 ± 2.51	7.05 ± 1.90	0.896*	0.957
Lateral width, mm	15	6.54 ± 2.87	9.08 ± 2.09	0.926*	0.000

Data are presented as mean ± standard deviation. ETm: ectopic tooth in the maxillary sinus, r: correlation coefficient.
*Statistically significant.

of **mineralization** of the ETm, as reflected by an increase in the ossified area compared with that shown by the previous CT scans (Figure 2). In 2012, the ETm was still an area of soft tissue density. By 2015, it had obviously ossified. By 2018, the soft tissue density was essentially gone and the ETm had completely **mineralized** (Figure 2).

The **mineralization** area of the ETm was significantly greater at the third follow-up visit (2018) than at the previous visits (2012 and 2015) as determined by measurements on 15 continuous axial CT planes (Table 1). The mean width between the left and right sides of the ETm in 2018 (9.08 ± 2.09 mm) was significantly larger than that in 2015 (7.51 ± 2.18 mm) in 2015 (Table 1) ($P < 0.05$), indicating that ETm formation is a gradual process of **mineralization**. However, the mean width between the anterior and posterior sides of the ETm in 2018 (7.05 ± 1.90 mm) was similar to that in 2015 (7.19 ± 1.95 mm), suggesting that ETm formation involves gradual mineralization from crown to root (because the ETm has a transverse orientation in the maxillary sinus, with the crown oriented medially and the root laterally), with no changes in the width of the ETm.

The ETm was located where there had only been a small range of soft tissue density in 2012. In this same position, the area of abnormal density (including areas of bone and soft tissue density) was significantly increased in 2015, and an ectopic tooth had appeared (Figure 2). In 2015, the mean width of the soft tissue density area of the ETm between the anterior and posterior sides was 3.25 ± 2.10 mm, and that between the left and right sides was 5.64 ± 1.64 mm. However, the area of soft tissue density was almost completely gone in 2018, suggesting that the process of ETm formation consists of gradual **in situ** soft tissue mineralization into bone.

Treatment strategy (2018). Nasal cavity ventilation expansion surgery was performed in November 2018 (including septoplasty with three high-tension line resections and lateral displacement of the inferior turbinate). ETn extraction was simultaneously performed to relieve the nasal obstruction (Figure 3). However, no intervention was performed for the ETm; instead, the follow-up observations were continued to observe whether this ectopic tooth would form dental cysts or other pathological structures and because the ETm was asymptomatic. Additionally, the advantages and disadvantages of surgery still needed to be weighed at that time.

Discussion

In recent years, many cases of ectopic teeth have been reported in various locations,[5] most of which were found because of conditions such as odontogenic cysts and

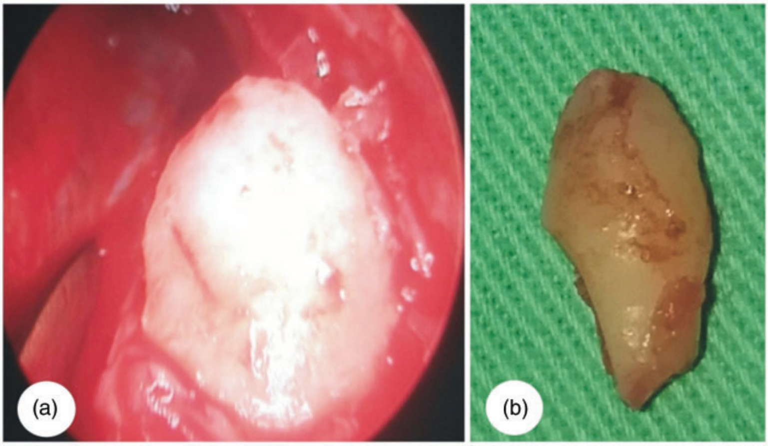

Figure 3. The ectopic tooth in the nasal crest of the maxilla (ETn) was extracted during nasal cavity ventilation expansion surgery. (a) Intraoperative observation of the ETn. (b) The extracted ETn.

odontogenic sinusitis.[1,9] Asymptomatic ect opic teeth are also found during routine radiologic examinations.[11] The diagnosis and treatment of ectopic teeth are not difficult. Endoscopic methods have been widely used in the management of ectopic teeth in the nasal cavity or sinuses.[2,8,10] Currently, nasal cavity ventilation expansion surgery and ETn extraction can be performed at the same time (Figure 3). However, the etiology of ectopic teeth remains unclear.

Suggested etiologies include trauma, embryological and genetic factors, and various syndromes. Trauma to the maxillofacial region may result in the displacement of a tooth bud, resulting in the crown facing toward the nasal floor and leading to ectopic tooth formation in the nasal cavity.[13] This situation can lead to the absence of teeth in the normal position. The ETn observed in the present case was a supernumerary tooth that was already present at the time of the post-traumatic examination; thus, its formation was unrelated to the trauma. Ectopic supernumerary teeth may be caused by a division or split of developing tooth buds. These divisions may occur subsequent to trauma-related aberrations.[14] However, the ETm in the present case had also begun to form at the time of the trauma and was accompanied by a bone defect in the posterior wall of the maxillary sinus, which is a characteristic of programmed development and was not related to the trauma. Furthermore, ectopic teeth in the maxillary sinus have often been reported to be ectopic supernumerary teeth[1,5,8] in patients without a clear history of trauma.[15]

Based on the follow-up data of the present case and reports in the literature, genetic and developmental abnormalities may be the most important causes of ectopic tooth formation.[1] The average age at which ectopic teeth are identified in the maxillary sinus is 28.36 years.[1] However, this age is only the age at which such ectopic teeth are clinically discovered because they cause odontogenic conditions.[16] To some extent, this reported average age only reflects the age at which ectopic teeth cause symptoms, not the age at which ectopic teeth appear. Furthermore, ectopic teeth have been widely reported in children,[3,17] with a minimum age of 3.5 years.[3] Ectopic teeth have been suggested to form at the time of deciduous tooth formation. Additionally, the abnormal development of deciduous teeth has been suggested to be an important cause of ectopic teeth.[11,12] The development of teeth occurs over the long term, from embryonic development to birth and adulthood. In the present case, the ETn was incidentally found by CT at the age of 16 years, and it was completely formed with no significant changes occurring over the next 6 years. This suggests that it was formed in the early stage of development, perhaps along with the deciduous teeth, and the mineralization of an ectopic tooth structure does not change over time after its development is complete. In contrast, some impacted ectopic teeth accompanying the formation of dental cysts and other diseases may be caused by incomplete development.

The exact age at which ectopic teeth appear is not clear. The literature indicates that ectopic teeth are found mostly in adults.[9,10,16] However, ectopic teeth might also form after permanent teeth have developed.[9] Unfortunately, all previous studies in the literature are cross-sectional observations or case reports, and no studies have focused on the process of ectopic tooth formation.[2–5,9,10,16] Fortunately, in the present study, the dynamic process of the formation of an ETm in a young person was observed for the first time through follow-up examinations (Figure 2). An obvious ectopic tooth appeared at the age of 19 years in the posterior wall of the maxillary sinus; this tooth had been observed as only an area of soft tissue density and a small bone wall defect at the age of 16 years. **Mineralization** of the ectopic tooth had increased by the age of 21 years (Figure 2 and Table 1). This study revealed two important findings. First, the present results show that ectopic teeth can still form after adolescence, supporting the hypothesis that ectopic teeth may also form after the development of permanent teeth. Second, the follow-up observations showed that the ETm formed via a process of gradual **mineralization**, with changes from soft tissue density to bone density (Figure 2 and Table 1). This revealed a mechanism of in situ **mineralization** for ectopic tooth formation.

Several theories have attributed the formation of ectopic teeth to aberrations during embryologic formation.[13,18] Such anomalies may involve different stages of tooth development, including abnormal development of the dental ridge, dental lamina, and tooth germ. First, aberrant processes related to the dental ridge have been suggested. The occurrence of ectopic teeth may be due to aberrant processes related to the dental ridge extending into regions beyond the alveolar process.[7] The palate (ETn) and maxillary sinus (ETm) are the most common sites, possibly because the jaw bones are the natural origins of teeth and the palate and maxillary sinus are anatomically proximal to the alveolus. Second, ectopic teeth are thought to be associated with abnormal development of the dental lamina and tooth germ. Supernumerary ectopic tooth buds or germs could be derived from an ectopic dental lamina and then gradually form ectopic teeth. The tooth bud is composed of dental lamina ingrowth and mesenchymal tissue concentration.[7] Mesenchymal tissue in the jaws is derived from neural crest cells that migrate from the caudal area of the mesencephalon and the cranial area of the metencephalon. Hence, it can be hypothesized that a defect in the migration of neural crest cells can lead to the formation of a tooth bud or germ located away from the normal position. Finally, developmental atavism may be another reason for the occurrence of ectopic teeth.[7,14] From a phylogenetic point of view, the ectopic tooth in the present case may be likened to the persistence of a tooth germ at an ancestral site.[7,14] A congenital bone defect was observed in the posterior wall of the maxillary sinus, which was also the location of the appearance of another ectopic tooth. Gradual **mineralization** of the ectopic tooth and bone defect in the posterior wall of the maxillary sinus subsequently occurred (Figure 2). These observations suggest that this congenital bone defect in the posterior wall of the maxillary sinus may have been the germinal center of the ectopic tooth remaining after embryonic development and may be the basis for the involvement of embryonic development in the formation of ectopic teeth. However, what kind of content is left behind in this germinal center during embryonic development remains uncertain.

Nevertheless, the ETm began to form after adolescence, suggesting that ectopic teeth are genetically regulated and that the formation process is programmed and independent from normal tooth development. This supports the theory of gene regulation activated at a specific time point. In recent years, many genes related to ectopic teeth and supernumerary teeth have been reported.[19] In 2018, Yu et al.[20] identified a new mutation in the adenomatous polyposis coli gene that results in supernumerary teeth in association with Gardner syndrome. Humans with Lrp6 mutations have supernumerary teeth, but no systemic syndrome has been reported.[21] In 2015, Blackburn et al.[22] reported that excess NF-κB induces ectopic odontogenesis in the embryonic incisor epithelium. Epithelial–mesenchymal interactions are key to the proper development of specific teeth at specific locations. Epithelial Wnt/β-catenin signaling can activate Shh, bone morphogenetic proteins, fibroblast growth factors, and Wnts in the dental epithelium, which in turn trigger the expression of odontogenic genes in the underlying mesenchyme. Expression of Shh and its downstream regulatory proteins (Ptc1 and Hhip1) is important in the initiation of tooth development at odontogenic sites. Bone morphogenetic proteins play significant roles in tooth specification, initiation, and differentiation. In 2006, Ray et al.[7] also considered that the ectopic teeth in the inferior nasal concha in their report could have been due to the ectopic expression of Shh or bone morphogenetic proteins, leading to the formation of ectopic tooth germs. However, the specific genetic and signaling pathways related to the occurrence of ectopic teeth are not clear. The current results suggest that genetic sequencing of ectopic teeth may be helpful to further clarify the related regulatory genes.

Conclusions

A congenital bone defect was observed in the posterior wall of the maxillary sinus, which was also the location of the formation of an ectopic tooth. Gradual **mineralization** of the ectopic tooth and a bone defect in the posterior wall of the maxillary sinus subsequently occurred. These observations suggest that this congenital bone defect in the posterior wall of the maxillary sinus may have been the germinal center of the ectopic tooth remaining after embryonic development, suggesting a basis for the involvement of embryonic development in the formation of ectopic teeth. The ETm began to form after adolescence, suggesting that ectopic tooth formation is a genetically regulated and programmed process independent of normal tooth development. This supports the theory of gene regulation activation at a specific time point.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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