Clinical Note

Pathological and Clinical Study of Japanese Ameloblastic Fibro-Odontomas

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Abstract: Ameloblastic fibro-odontoma (AFO) is defined as a tumor with general characteristics of an ameloblastic fibroma along with the presence of enamel and dentine. AFO is a well-encapsulated, painless, slow-growing, and expanding tumor in young patients. Histologically, it has been classified as an ameloblastic fibroma or odontoma. In the 2017 new WHO classification of odontogenic tumor, AFO is described that they in most cases represent developmental stages of either complex or compound odontoma and that retaining them as separate entities would therefore be illogical. However, there is still considerable confusion concerning the nature and histology of AFO and the surgical therapy for this lesion. Here we present a case of maxillary AFO and review the relevant literature regarding the clinical and surgical features of this lesion.

Key words: Ameloblastic fibro-odontoma, Odontogenic tumor, Japanese patients, Review

Introduction

Ameloblastic fibro-odontoma (AFO) is an uncommon mixed odontogenic tumor of the odontogenic epithelium with a mesenchyme origin. According to the World Health Organization (WHO) classification, AFO is a lesion resembling ameloblastic fibroma, which also shows inductive alterations involving both enamel and dentine. Since the introduction of the WHO classification, AFO has been recognized as a histological and clinical entity, but it is still rare among Japanese people. The purpose of this report was to describe a case of AFO and review the literature on AFO among Japanese patients between 1971 and 2016.

Materials and Methods

Case presentation

In June 2009, a 12-year-old Japanese girl presented with a chief complaint of tooth eruption disturbance in the left posterior maxilla to an orthodontic clinic. Because an asymptomatic posterior left maxillary lesion was discovered on panoramic radiography performed for routine evaluation, the patient was referred to the Division of Oral and Maxillofacial Surgery at Kagawa Prefectural Central Hospital. The medical, social, and family histories of the patient were unremarkable.

An extraoral examination revealed no obvious abnormality, without swelling or facial asymmetry. An intraoral examination showed slight tenderness at the left upper molar area. Despite eruption of the right first and second upper molars, there was no eruption of the left first and second molars of the first dentition (Fig. 1A, B). A panoramic radiograph revealed a radiolucent lesion (20 × 15 mm in diameter) with irregular borders around the unerupted first and second molars.

In addition, there was a radiolucent area containing punctate calcified components (Fig. 2A). Computed tomography (CT) images revealed a radiolucent lesion containing punctate calcifications scattered throughout the center of the lesion in the left maxillary area, with constriction of the maxillary sinus (Fig. 2B). Buccopalatal expansion and perforation of the involved cortices were not observed. Considering the clinical and radiological findings, the possible differential diagnoses were calcifying epithelial odontogenic tumor, adenomatoid odontogenic tumor, and AFO.

Treatment and outcomes

Under local anesthesia, enucleation of the lesion with careful curettage involving the first and second molars was performed using a transoral surgical approach. No bone augmentation was needed. There was no penetration into the maxillary sinus. Wound closure was performed with a trapezoidal flap. There has been no recurrence during the two-year follow-up.

Histopathological and immunohistological studies

The resected specimen was examined by hematoxylin and eosin (HE) staining and immunofluorescent (IF) staining. The target proteins assessed included the following: Wnt1 (Abcam, Cambridge, UK), a signal transduction protein acting on epithelial-mesenchymal interaction. Wnt signaling is implicated in cell proliferation and differentiation., β-catenin (E274, Abcam, Cambridge, UK), a maker of nuclear localization of β-catenin. Wnt signaling involves in the nuclear localization of β-catenin.

Search strategy of the literature

An electronic search without time or language restrictions was conducted in 2016 using the PubMed, Medline, and ScienceDirect databases. The following terms were used in the search: ameloblastic...
Figure 1. A: Extraoral examination revealed no obvious abnormality., B: Intraoral examination shows unerupted upper left first and second molars despite eruption of the upper right first and second molars.

Figure 2. Panoramic radiograph and CT image. A: A panoramic radiograph shows a radiolucent lesion (20 × 15 mm in diameter) with irregular borders around unerupted first and second molars., B: CT images revealed a radiolucent lesion containing punctate calcifications in the left maxillary area.

Figure 3. Histological findings (HE: A-D). A: Dentin like hard tissues (*) located in the tumor tissue. The background is composed of fibrous stroma and epithelial tumor nests. Scale bar= 100μm., B: Epithelial islands and mesenchymal fibrous components. Scale bar= 20μm., C: Enamel organ like epithelial tumor nests supported by dental papilla like tumor tissue. Scale bar= 20μm., D: Dentin (arrow), enamel matrix (arrowhead) and enamel (*) formation in the intermediate zone between epithelial and mesenchymal components. Scale bar= 20μm.,
fibrodentinoma OR ameloblastic fibro-odontoma OR ameloblastic fibroodontoma OR ameloblastic fibroodontoma. Moreover, Google Scholar and Web Japan Medical Abstracts Society were checked. The titles and abstracts of all publications identified through the electronic searches were read by the authors. The clinical aspects and the histological description of the lesions were thoroughly assessed to confirm the diagnosis of AFO. 

Ethics statement and confirmation of patient permission

The authors confirm that the patient undergoing the procedure described in this clinical note was fully informed about the condition and consented to the clinical and surgical procedures, which included taking photographs of the lesion and the procedure. The authors confirm that personal details of the patient included in any part of the paper and in any supplementary material have been removed before submission.

Results

Histopathological findings (HE)

Microscopically, the lesions were composed of soft tissue components and calcified components (Fig. 3A). The soft tissue included tooth bud like nest and exhibited mainly strands and cords of odontogenic epithelium that resembled the dental lamina. The stromal components were consisted of fibroblast like cell with plump nucleus which proliferating with produce dense collagen fibers (Fig. 3B). The lesion also contained epithelial islands that consisted of a peripheral layer of columnar palisading cells, which enclosed loosely arranged cells resembling the enamel organ. The epithelial elements were supported by loose connective tissue containing randomly oriented fibroblasts that resembled the dental papilla of a developing tooth (Fig. 3C). The calcified elements showed the characteristic component of irregular dentin (Fig. 3D arrow). The dentin contained entrapped epithelial and mesenchymal cells. Near the dentin like structures, enamel matrix and hollow spaces with mature enamel that was removed during decalcification (Fig3. D star). The spaces also contained enamel matrix (Fig. 3D arrowhead).

Immunohistochemical findings (IF)

Wnt1 was detected in almost epithelial and mesenchymal components. The peripheral columnar cells of epithelial tumor nest were strongly positive to Wnt1 (Fig. 3E). Although β-catenin was clearly localized on the cell membrane of tumor cells, nuclear translocation was observed in stellate reticulum cells and in many papilla-like mesenchymal cells (Fig. 3F). Wnt1 and β-catenin were present in the tumor nests mainly. The both positive area were almost merged (Fig. 3G).

Results of the literature review

The results of the literature review and our case are summarized in Table 18-56).

<table>
<thead>
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<th>Patient characteristics</th>
<th>Mean</th>
<th>Standard Deviation</th>
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<th>Median</th>
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<td>Female</td>
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<td></td>
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<tr>
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<td>26</td>
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<tr>
<td>Location</td>
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<td>Right</td>
<td></td>
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<td>Mandible</td>
<td></td>
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<td>%</td>
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<tr>
<td>%</td>
<td>91.2</td>
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<td>Exclusion</td>
<td>Exclusion of the tumor (Retention of the involved teeth)</td>
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<tr>
<td>%</td>
<td>31.6</td>
<td>68.4</td>
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Table 1. Summary of the literature review of Japanese patients with ameloblastic fibro-odontoma

Discussion

AFO belongs to the family of mixed odontogenic tumors. The term AFO was first used by Hooker and was originally termed ameloblastic odontoma. It can be defined as a neoplasm composed of proliferating odontogenic epithelium embedded in cellular ectomesenchymal tissue
that resembles dental papilla at varying degrees with regard to inductive change and dental hard tissue formation. In 1971, WHO suggested that this term was inappropriate as it encompasses two types of odontogenic tumors that share different histology and biological behavior. Therefore, it was definitively separated from other benign odontogenic tumors in 1971 by Pindborg and Kramefi. However, despite numerous efforts, there was still considerable confusion concerning the nature and relationship between mixed odontogenic tumors and related lesions.

According to the 2005 WHO classification, it is a benign tumor without invasive growth in contrast to ameloblastoma. AFO represents approximately 1% of all odontogenic tumors in Japan. To the best of our knowledge, the cases of only 58 Japanese patients, including our case, have been reported in the literature. Most of these tumors occurred in the first two decades of life, with a mean age at diagnosis of 11.5 years. There is almost no predominance of male patients. AFO is usually found in the molar area, with roughly equal distribution between the maxilla and mandible, and it does not show significant gender predilection. In our review, the mean age was 11.5 years, and there was no difference between the left and right sides for the site of occurrence (left, 56.1%; right, 43.9%). In addition, it occurred more frequently in the mandible than in the maxilla (mandible, 66.7%; maxilla, 33.3%). Moreover, occurrence was more common in the posterior than in the anterior area (posterior area, 78.9%; anterior area, 17.5%). The findings of our literature review of Japanese patients did not differ much from the findings of past reports from patients around the world.

AFO has the histologic features of ameloblastic fibroma in conjunction with the presence of dentin and enamels. This pathological classification was defined in the 2005 WHO classification of head and neck tumours. In the 2017 WHO classification of odontogenic tumor, AFO is described that they in most cases represent developmental stages of either complex or compound odontoma and that retaining them as separate entities would therefore be illogical. Accordingly, in the new classification of odontogenic tumors are defined AFO as immature odontoma. In the other hand, there are clinical reports of AFO recurrence, whether it is a tumor or a hamartoma is controversial. Gardner described that odontomas develop during the period of normal odontogenesis and, therefore, any apparent ameloblastic fibroma found after that time is unlikely to represent the early stage of a developing odontoma. These data suggested that AFO have true neoplastic conditions.

In our present case, immunohistochemical analysis clarified that Wnt1 and β-catenin were detected in almost epithelial and mesenchymal components. In general, Wnt signaling is responsible for cytotological regulation of cell fate, morphogenesis and/or development. In the tooth development, it controls epithelial-mesenchymal interaction. Besides that, the excessive activation of Wnt signaling induce tumorigenesis. There are some report that mentioned the epithelial-mesenchymal interaction was activated in ameloblastic fibroma. Our examination results suggest that Wnt signaling plays the tumorigenesis through activation of epithelial and mesenchymal interactions and inducing the neoplastic feature of the ameloblastic fibroma.

The most common complaints patients present with are asymptomatic swelling and delayed tooth eruption in the affected region. The lesion may displace the erupted teeth, but other symptoms, such as pain and paresthesia, are uncommon. Therefore, asymptomatic cases are usually discovered incidentally on radiography. The radiographic findings of these lesions usually show a mixed mass of a well-defined radiolucent area containing various amounts of radiopaque material of irregular size and form. The ratio of radiopaque to radiolucent areas differs from one lesion to another. Sometimes, the mineralized element in the tumor predominates, and the lesion may resemble an odontoma. Panoramic radiographs are very suitable for first-time lesion screening. For accurate localization of the tumor and for preparing a surgical treatment strategy to preserve adjacent vital structures, a CT scan is recommended.

The treatment of odontogenic tumors is based on their clinical and biological behavior. However, there is no consensus on the treatment of AFO. Many authors have reported that small lesions are not aggressive and can be adequately treated with enucleation of the lesion without removing the adjacent teeth. Enucleation remains the gold standard owing to the non-invasive advancement of the disease. This surgical method shows good results with a good prognosis. Enucleation will allow the maintenance of adequate periosteum and jawbone for spontaneous regeneration in defects among patients. Recurrences are rare and have been attributed to inadequate surgical removal at the time of initial treatment. If recurrence is accompanied by a change in the histological pattern toward a more unorganized fibrous stroma, with displacement of the epithelial component, more extensive treatment procedures are indicated. With regard to the maintenance of the involved unerupted teeth, we believe that if the teeth do not interfere with the enucleation of the tumor, there is no reason to remove them, and there is a possibility of spontaneous eruption. In the literature review of Japanese patients, 52 of the 57 tumors were associated with unerupted teeth. Treatment for the unerupted teeth was confirmed in 34 of the 52 cases. Most of the cases were treated with retention of the unerupted teeth, and the prognosis of eruption of the teeth appeared to be good. Follow-up revealed no signs of recurrence, indicating that conservative procedures associated with the related tooth removal can be successful in the treatment of these lesions if considerable bone is present.

AFO recurrence is associated with inadequate surgical removal and may occur if tumor remnants persist in the resection margins and in the tooth involved, especially for large tumors. Although malignant transformation of AFO was not found in the Japanese patient series, a few cases of malignant transformation were reported in studies from other countries. However, potential transformation alone does not justify radical treatment for this benign lesion. As noted in the literature review, not all lesions previously classified as AFO are aggressive lesions, and they are not expected to recur following conservative surgical intervention.

In conclusion, AFO is a rare benign neoplasm with low recurrence. We recommend tumor enucleation as the first step in treatment, which is consistent with the recommendation of most authors. Only in the case of repeated recurrence or evident malignancy, we recommend performing a more extensive treatment. With regard to retention of the involved unerupted teeth, if the teeth do not interfere with the enucleation of the tumor, there is no reason to remove them and there is a possibility of spontaneous eruption.

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Conflicts of interest
The authors have declared that no COI exists.

References
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