Clinical Report

Epithelium-Poor Type Central Odontogenic Fibroma: An Immunohistological Study and Review of the Literature

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Abstract: The object of this study was to determine the characteristics of central odontogenic fibroma (COF) in order to help achieve a correct diagnosis. Central odontogenic fibroma, which tends to be epithelium-poor, is an extremely rare type of odontogenic fibroma. The lack of data concerning COF, due to its low incidence, can make this entity difficult to diagnose. We herein report an epithelium-poor type of COF of the mandible, which we examined immunohistologically. We also provide a review of the previous English literature to expand the knowledge about this disease. Positive reactions for vimentin and negative reactions for desmin and α -smooth muscle actin (α -SMA) in COFs were common findings in the previous reports. We also noted similar immunohistological findings. Our data (vimentin positive, α -SMA and desmin negative) should contribute to correctly diagnosing epithelium-poor type COF.

Key words: Central odontogenic fibroma, Epithelium-poor type, Mandible

Introduction

Odontogenic fibroma (OF) is a relatively rare benign tumor originally derived from odontogenic ectodermal mesenchymal tissue¹⁾. These tumors are divided into central (COF) and peripheral odontogenic fibroma (POF) based on the area affected²⁾. COF is less common than POF, and the incidence of COF comprises 1.5% of all odontogenic tumors arising in the jaw bone³⁾. The anterior site of the maxilla and the posterior site of the mandible are the most common sites of COF¹⁾.

The histopathological findings of OF include dental sac-like connective tissue with scattered nests of odontogenic epithelium¹⁾. Regarding the pathological features, OF has been divided into an epithelium-rich type (WHO-type) and an epithelium-poor type (simple type) according to the amount of the odontogenic epithelium in the tumor, as reported in the WHO classification in 1992⁴⁾, and this classification was still applicable based on the latest WHO classification in 2005¹⁾. Since the epithelium-poor type COF

is an extremely rare disease, the characteristics of these tumors are still unclear.

It is important to obtain a correct diagnosis of this disease to decide on the appropriate treatment strategy. However, epithelium-poor type COF is often confused with other diseases, such as central desmoplastic fibroma (DM) and odontogenic myxoma (OM). To acquire more knowledge about the epithelium-poor type COF for its correct diagnosis, we herein describe an epithelium-poor type COF arising at the anterior site of the mandible, which we examined immunohistologically. We also provide a review of the previous English literature.

Materials and Methods

This study received ethical approval from the institution. A 74-year-old Japanese female was referred to the Department of Dentistry and Oral Surgery, University of Fukui Hospital. She had complained of an asymptomatic swelling without spontaneous pain in the anterior mandible. She had been suffering for one month prior to visiting her dental clinic, and her dentist recommended that she visited a specialist. She had no remarkable past medical history nor any family medical history. Her facial appearance was

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Figure 1. The intraoral findings. A painless swelling was observed at the anterior mandible (arrowheads).

Figure 2. Orthopantomography. A well-defined radiolucent area was observed at the anterior mandible (arrowheads).

Figure 3. CT imaging. The lingual cortical bone of the anterior mandible was expanded and thinned (arrowheads). The lesion included the tooth roots.

Figure 4. The intraoperative findings (a) and the resected specimen (b). A marginal mandibulectomy was performed under general anesthesia.

symmetrical and her lower lip and mental region were not swollen. In her intraoral findings (Fig. 1), an elastic soft swelling was observed at the lingual gingiva from the right central incisor to the left first premolar of the mandible. The relevant teeth were mobilized as level 2.

Imaging findings

Orthopantomography (OPG) (Fig. 2): A well-defined unilocular radiolucent area was found in the anterior region of

Table 1. A list of primary antibodies for immunostaining study. These antibodies identify the mesenchymal tissue. All samples were stained by ENVISION kit (Dako).

Antibody	Immunized animal	Dilution
Vimentin	Mouse	1:10
S-100	Rabbit	Ready to use
α -SMA	Mouse	1:50
Desmin	Mouse	1:100
CD34	Mouse	Ready to use
CD68	Mouse	Ready to use
Ki-67	Rabbit	1:50

the mandible by orthopantomography. The apices of the left lateral incisor, canine and first premolar of the mandible were included in the radiolucent region, and the first two were slightly resorbed.

Computed tomography (CT) (Fig. 3): The lesion at the anterior site of the mandible was enhanced, and a $27 \times 16 \times 19$ mm well-circumscribed mass was shown. The apices of the left lateral incisor, canine and first premolar of the mandible were included in the lesion, similar to the OPG images.

Treatment and outcomes

A marginal mandibulectomy, including the relevant teeth, was performed under general anesthesia since the intraoperative frozen section diagnosis of the lesion was a benign tumor (Fig. 4). Following the tumor resection, exposed bone at the resected site was covered with a collagen membrane (Terudermis[®], Olympus Terumo Biomaterial Corp., Tokyo, Japan). There has been no recurrence during the 4-year follow-up.

Histological and immunohistological studies

The resected specimen was examined by hematoxylin and eosin (H&E) staining and immunohistologically. The proteins assessed included the following: vimentin (Dako; Carpinteria, CA, USA); a unique intermediate filament in the mesenchymal cells, desmin (Dako); a protein existing in the skeletal monocyte and the smooth monocytes, α -smooth muscle actin (α -SMA) (Dako); a marker of myoepithelial cells, S-100 (Nichirei Bioscience; Tokyo, Japan); a marker of the neural ectoderm, CD34 (Nichirei Bioscience); a marker of endocapillary cells, CD68 (Nichirei Bioscience); a marker of histiocytes, Ki-67 (Nichirei Bioscience); an index of cell proliferation. The details of the antibodies are listed in Table 1.

Results

Histopathological findings (H&E staining)

The remaining bone tissue was replaced by the tumor (Fig. 5a). Most of the tumor cells were spindle-shaped cells. These cells proliferated intensely, and connected with the periodontal ligament

Figure 5. The histological findings of specimen under low (a) and high magnification (b-d). (a) shows the relationship between the remaining bone and the tumor. (b) shows the dentin (D), cementum (C) and periodontal ligament (P). The margin between the tumor and periodontal ligament is not clear. (c) and (d) are the high magnification findings ($\times 400$). The arrow indicates the odontogenic epithelium (d).

Figure 6. The immunohistological study for identification of mesenchymal tissue. Vimentin positivity and negative staining for S-100, desmin and α -SMA were found in the specimen.

fibers at the tooth apical region under low magnification (Fig. 5b). Eosinophilic endoplasmic reticula, orbicular nuclei and nucleoli were observed in the tumor cells under high magnification. There were minimal polymorphic and atypically-shaped cells, and collagenous fibers were mixed with the tumor cells in the stroma (Fig. 5c). A small amount of odontogenic epithelium was also observed (Fig. 5d, arrow). The surgical margins of the resected specimen were histologically tumor-free.

Immunostaining

To diagnose the lesion correctly, immunostainings for identification of mesenchymal tissue were performed. The tumor cells showed vimentin positivity, but they were S-100 and CD34 negative. The tumor cells did not give positive results for α -SMA

and desmin. There were CD68-positive cells detected occasionally, but these were considered to be histiocytes, not tumor cells (Fig. 6). The Ki-67 positive rate was 5.3%.

Discussion

WHO-type COF frequently arises at molar sites on the mandible, and the epithelium-poor type COF also seems to occur in the same region, as indicated in Table 2. In fact, five of the nine previously reported cases occurred at a molar site of the mandible⁵⁻⁷⁾. On the other hand, only one case⁹⁾ was previously reported the diagnosis of an epithelium-poor type COF at the anterior region of the mandible and the present case was second epithelium-poor type COF arising at the anterior region of the mandible. COFs are less frequently seen in this region. Since these tumors tend to gradually increase in size without any symptoms, they are usually discovered incidentally by dental radiographic examinations during general dental care⁸⁻¹⁰⁾. Bone bulging also developed gradually without pain or other symptoms in this case.

The histological features of OF include the existence of various amounts of odontogenic epithelium in the fibrous connective tissue, and OF is divided into the WHO-type and epithelium-poor type depending on the amount of the odontogenic epithelium present¹⁾. The main component of the present lesion was fibrous connective tissue, and only a little odontogenic epithelium was observed in the lesion in this case (Fig. 5). The small amount of

Table 2. The previous epithelium-poor type central odontogenic fibromas reported in the English literature.

Case	Age	Gender	Site	Symptom(s)	Diagnostic Method	Treatment	Reference
1	71	M	33-35	PS	H&E	ST	4
2	36	F	23-24	PS	H&E	ST	6
3	30	F	43-47	PS	H&E	ST	7
4	24	F	22-24	No	H&E	ST	8
5	12	F	47-48	No	H&E	ST	8
6	28	M	41-46	No	IS	ST	9
7	20	F	37	No	H&E	ST	10
8	52	M	23-25	PS	H&E	ST	13
9	29	M	12-13	Pain	IS	ST	14
10	74	F	32-45	PS	IS	ST	The present case

H&E; hematoxylin and eosin staining, IS; immunostaining, PS; painless swelling, ST; surgical therapy

Table 3. The immunohistological data for mesenchymal tissue of the previous reports and this case

Case	α -SMA	Vimentin	S-100	Desmin	CD34	CD68	Ki-67	Reference
3		+	-					7
6		+	+/-	-	-	-	<1%	9
10	-	+	-	-	-	-	5.3%	The present case

Table 4. The typical immunostaining data of odontogenic fibroma, desmoplastic fibroma and odontogenic myxoma

	Vimentin	S-100	α -SMA	Desmin	CD68
Odontogenic fibroma	+	-	-	-	-
Desmoplastic fibroma	+	-	+	+/-	-
Odontogenic myxoma	+	+			

the odontogenic epithelium made it difficult to diagnose whether the lesion was an odontogenic or a non-odontogenic tumor. In particular, desmoplastic fibroma (DF) and odontogenic myxoma (OM) have similar histological findings^{4,11,12}. Therefore, it is important to distinguish epithelium-poor type OF from these diseases in order to determine the optimal treatment strategy. Since odontogenic epithelium was observed in the H&E section, the present lesion was considered to be an odontogenic tumor. In order to correctly diagnose the lesion, an immunostaining study was performed and the results were closely similar to those of previous reports (Table 3).

DF usually grows invasively into the surrounding tissue, unlike OF. In the histological findings, spindle shaped fibroblasts are observed with spindle- or oval-shaped nuclei in cases of DF. It is difficult to distinguish OF from DF because both diseases have similar shaped fibroblasts. However, an immunohistological study can differentiate these lesions. DF contains vimentin and α -SMA positive cells¹¹, but while OF also has vimentin positive cells, OF is α -SMA negative. This difference can permit the differential diagnosis between epithelium-poor type OF and DF.

OM does not have a capsule surrounding the tumor, resulting in invasive and destructive growth into the contiguous tissue. It contains connective tissue with abundant collagen fibers and mucoid tissue, and sometimes includes odontogenic epithelium. The mucoid tissue is a key component to distinguish OF from OM, but little mucoid tissue is generally contained in OM, making it difficult to differentiate between OF and OM. S-100 usually positive in OM, but negative in OF. Therefore, S-100 can be useful to distinguish OF from OM (Table 4).

Our immunohistological study showed positive staining for vimentin and negative staining for CD34, S-100, α -SMA and desmin. A small number of CD68 positive cells were observed occasionally in the field, but not in the tumor substance. These results indicated that our case was not a benign fibrous histiocytoma. On the other hand, only a few Ki-67 positive cells were observed. Mosqueda-Taylor et al.⁹ examined Ki-67 positive

cells in COF (13 WHO-type cases and one epithelium-poor type case) and all cases showed less than 1 % of Ki-67. Compared with their report, the present case had slightly high Ki-67 positive cells. However, malignant tumor such as squamous cell carcinoma showed about 20% Ki-67 positive. This suggested that the proliferative activity of this tumor was low, and that this tumor had a small likelihood of being malignant. According to the findings of a small amount of odontogenic epithelium in the H&E section, an immunohistological study and the clinical features of our case, a final diagnosis of the epithelium-poor type COF was made.

The epithelium-poor type OF generally has a small amount of odontogenic epithelium, resulting in difficulty in obtaining a definite diagnosis based on the histology. For this reason, immunohistological studies are essential to diagnose the epithelium-poor type OF correctly. There have been only a few reports describing the epithelium-poor type COF, and further examinations will be necessary in the future to provide a better understanding of this disease.

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