

Extralingival peripheral ameloblastoma arising in the pterygomandibular space: A case report with an assessment of proliferative activity

Running title: Extralingival peripheral ameloblastoma

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ABSTRACT

Background: Peripheral ameloblastoma is an extraosseous variant of ameloblastoma. We report a rare case arising in an extralingival location.

Case Presentation: The patient was a 79-year-old man with a firm nodule in the right-side buccal mucosa. Imaging examinations showed a well-demarcated mass in the pterygomandibular space. The diagnosis of ameloblastoma was made from the biopsy specimen. After conservative tumor excision, the patient had no recurrence during the follow-up period of eight and a half years. The Ki-67 labelling index indicated the non-aggressive nature of the tumor.

Conclusion: Conservative surgery is applicable to extralingival peripheral ameloblastomas.

Keywords: extralingival peripheral ameloblastoma, pterygomandibular space, proliferative activity, Ki-67, amelogenin,

INTRODUCTION

Ameloblastoma is the most common neoplasm of odontogenic epithelial origin, excluding odontomas.¹ It usually occurs inside the maxilla and mandible, and rarely occurs in the gingival soft tissue. Such gingival tumors are referred to as peripheral ameloblastomas, accounting for 2-10% of all ameloblastomas.² Moreover, tumors with similar histology are known to rarely occur in extralingival soft tissues.

We report a case of extralingival peripheral ameloblastoma in the pterygomandibular space, and discuss the surgical treatment of the lesion based on the proliferative activity of tumor cells.

CASE REPORT

A 79-year-old man was referred to our hospital with a chief complaint of pain in his right cheek. The patient had been aware of this condition for the past year and a half, and no systemic disease had been reported in the patient's medical history. A physical examination revealed a well-circumscribed nodule measuring 36 × 32 mm in the posterior region of the right buccal mucosa (Fig. 1). The lesion was firm in consistency and showed tenderness on palpation. The covering mucosa was intact and non-ulcerated. On panoramic radiographs, no apparent changes were detected in the jaw bones. Contrast-enhanced computed tomography (CT) revealed a well-demarcated lesion with muscle density in the right pterygomandibular space that showed oppressive resorption on the lateral wall of the

maxillary bone (Fig. 2A, 2B, 2C). On magnetic resonance imaging (MRI), the lesion had low- and high-intensity signals on T1-weighted imaging and on T2-weighted imaging, respectively (Fig. 3A, 3B). Fat-saturated T1-weighted imaging with gadolinium enhancement showed heterogeneously increased signal intensity with peripheral enhancement, and septa of low signal intensity inside the lesion (Fig. 3C, 3D). We performed an incisional biopsy under local anesthesia, and obtained a pathological diagnosis of ameloblastoma. The patient underwent surgical tumor excision under general anesthesia. After elevating the facial skin flap using a Weber-Fergusson incision, the right coronoid process of the mandible and a part of the zygomatic arch were resected. The tumor was then subperiosteally detached from the maxilla and extirpated with the surrounding connective tissue and buccal mucosa (Fig. 4). The surface of the maxillary bone was smooth and was not infiltrated by the tumor, and the parotid gland duct was not included. The resected zygomatic arch segment was returned to its original position and fixed with titanium plates. The postoperative course was uneventful, with no signs of recurrence during the periodic follow-up period of eight and a half years. The patient died of cardiac failure two months after his last follow-up.

Histological examination of the surgical specimens showed that the tumor was well demarcated from the surrounding connective tissue. There was no discrete capsular structure around the tumor. Large and small epithelial islands were scattered in a background of dense fibrous connective tissue (Fig. 5). The epithelial islands consisted of a central area that resembled the stellate reticulum of the

enamel organ and a peripheral layer of columnar or cubical cells, which showed palisading nuclei (Fig. 6A). Basaloid cells with round or ovoid nuclei were predominant in some tumor islands (Fig. 6B). A few mitotic figures of tumor cells were detected in the basaloid cell proliferation area (Fig. 6B inset). In addition, anastomosing cords of columnar epithelial cells with palisading nuclei, polarized away from the basement membrane, were observed (Fig. 6C). The tumor showed no connection with the epithelium of the covering mucosa, and was also separated from the maxilla by the periosteal fibrous connective tissue (Fig. 6D). Tumor cells were positive for amelogenin by immunostaining with an anti-amelogenin antibody (rabbit anti-amelogenin antibody serum, Sangi Co., Tokyo, Japan, 1:100 dilution) (Fig. 7A). The distribution of Ki-67 positive tumor cells was varied among tumor components by immunostaining with an anti-Ki-67 antibody (MIB-1, Biomeda Co., Foster City, CA, USA, 1:50 dilution) (Fig. 7B, 7C, 7D). The Ki-67 labelling index of tumor cells, which was obtained by calculating the rate (percentage) of positive nuclei in relation to the total number of tumor nuclei in randomly selected medium-power ($\times 200$) fields, were 1.15 ± 0.80 , 3.71 ± 3.02 and 3.66 ± 3.51 (mean \pm SD) in the stellate reticulum-like cell area, basaloid cell area, and peripheral layer of tumor islands, respectively (Table 1). The mean index in all the areas examined was 3.10 ± 3.02 .

DISCUSSION

Peripheral ameloblastoma is a rare odontogenic tumor that accounts for 2-10% of all

ameloblastomas.² It usually occurs in the gingiva overlying the tooth-bearing areas of the maxilla and mandible. Tumors with similar histologies rarely occur in extralingival soft tissues, and those that do are referred to as extralingival peripheral ameloblastomas. To date, 24 extralingival lesions have been reported in the English and Japanese literature.³⁻²⁶ Philipsen et al.² reported that buccal and oral floor lesions are most likely basal cell adenomas of the salivary gland, because some extralingival cases have developed around major salivary gland duct orifices. The tumor in our case was localized in the pterygomandibular space, and showed no connection with Stensen's duct. The presence of stellate reticulum-like areas and palisading nuclei in the tumor nest periphery, and definite expression of amelogenin, which is a marker of odontogenic origin,²⁷ indicate that the present case was a peripheral ameloblastoma arising in an extralingival location.

The differential diagnoses of extralingival peripheral ameloblastoma include basal cell carcinoma of the oral mucosa and basal cell adenoma of the salivary gland. Currently, there is general agreement that peripheral ameloblastoma and oral basal cell carcinoma are the same lesion and should be regarded as a single entity.² Basal cell adenoma forms epithelial nests with a solid, trabecular or tubular pattern, and sometimes shows nuclear palisading of the peripheral cells in the tumor nests, with an absence of stellate reticulum-like cells.²⁸

On CT and MRI, extralingival peripheral ameloblastomas have sometimes been demonstrated as masses with an unclear margin, and were clinically diagnosed as malignant lesions.^{4,18,22,23} Most

extralingival peripheral ameloblastomas showed well-demarcated masses with weak enhancement on contrast-enhanced CT and heterogeneous signal intensity on T2-weighted MRI images.^{21,25} Moreover, some tumors have multinodular structures that are separated by intervening septa,^{18,26} as seen in the present case. The identification of ameloblastomas by image examinations is not easy due to the lack of specific features, and pathological examination is essential for a definitive diagnosis.

The origin of peripheral ameloblastoma in tooth-bearing locations is considered to be either from extraosseous remnants of the dental lamina or pluripotent cells in the basal cell layer of the oral mucosa.²⁹ Hovorakova et al.³⁰ traced a cell population that expressed Sonic Hedgehog, which was limited to the odontogenic areas, in embryonic mice, and demonstrated that odontogenic cells contributed to the development of the oral vestibule. This finding indicated that the vestibular epithelium possessed odontogenic potential and could be a possible source of odontogenic lesions in the vestibular area. The sites of previously reported 24 cases of extralingival peripheral ameloblastomas³⁻²⁶ and the present case are the buccal mucosa in 17 cases and the pterygomandibular space in three, and the subzygomatic space, infratemporal fossa, oral floor, tongue, and parapharyngeal space, in one case each. There is a clear tendency that extralingival peripheral ameloblastomas occur on the buccal side of the jaw. We hypothesized that the vestibular epithelium or vestibular lamina remnants could be the origin of extralingival peripheral ameloblastomas.

Since peripheral ameloblastomas usually manifest non-aggressive behavior, the treatment for this

tumor is conservative surgical excision with tumor-free margins.^{2,29} The recurrence rate of peripheral ameloblastomas of the tooth-bearing locations has been reported to be 16-19%,^{29,31} while no recurrence has been documented in any reported cases of extralingival peripheral ameloblastomas during follow-up periods from one month to six years.³⁻²⁶ The postoperative course of the present case was also uneventful without recurrence. We examined the Ki-67 labelling index of the present case, and obtained a mean index of 3.10, which was lower than those of non-recurrent intraosseous ameloblastomas in previous studies (Ki-67 labelling index: 4.042-8.29).^{32,33} Taken together, these findings indicated the non-aggressive nature of the present case. We thus consider that conservative excision with tumor-free margins is applicable to extralingival peripheral ameloblastomas, if the tumor shows neither aggressive clinical growth nor histological features of malignancy in biopsy specimens. However, further studies are needed to better understand the pathophysiological nature and clinical behavior of extralingival peripheral ameloblastoma.

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LEGENDS

Fig. 1. Intraoral finding at the first visit. A well-circumscribed nodule was palpated in the posterior region of the right buccal mucosa.

Fig. 2. Contrast-enhanced computed tomography. There was a well-demarcated lesion with muscle density in the right pterygomandibular space (A, B). Oppressive resorption was observed on the lateral wall of the maxillary bone (C). A,B: soft tissue window, C: bone window.

Fig. 3. Magnetic resonance imaging. The lesion had low- and high-intensity signals on T1-weighted imaging (A) and T2-weighted imaging (B), respectively. It showed heterogeneously increased signal intensity with peripheral enhancement on fat-saturated T1-weighted imaging with gadolinium enhancement (C, D). There was a septa of low signal intensity inside the lesion (D).

Fig. 4. Intraoperative finding. The tumor was subperiosteally detached from the maxilla and extirpated with the surrounding connective tissue and buccal mucosa.

Fig. 5. Histological findings of surgical specimens. The tumor was well demarcated from the surrounding connective tissue. There was no discrete capsular structure. Large and small epithelial islands were scattered in dense fibrous connective tissue.

Fig. 6. Histological findings of surgical specimens. The epithelial islands consisted of a stellate reticulum-like cells and a peripheral layer of columnar or cubical cells (A). Basaloid cells were predominant in some tumor islands (B). A few mitotic figures were detected in basaloid cell proliferation area (B, inset). Anastomosing cords of columnar epithelial cells with palisading nuclei were also observed (C). The tumor was separated from the maxilla by the periosteal fibrous connective tissue (D, arrow heads: periosteum).

Fig. 7. Immunostainings for amelogenin and Ki-67. Tumor cells were positive for amelogenin (A). The distribution of Ki-67 positive tumor cells was varied among tumor components (B: stellate reticulum-like cell area, C: basaloid cell area, D: peripheral layer of tumor islands).

Table 1. Ki-67 labelling index according to tumor components of extralingival peripheral ameloblastoma



Fig.1

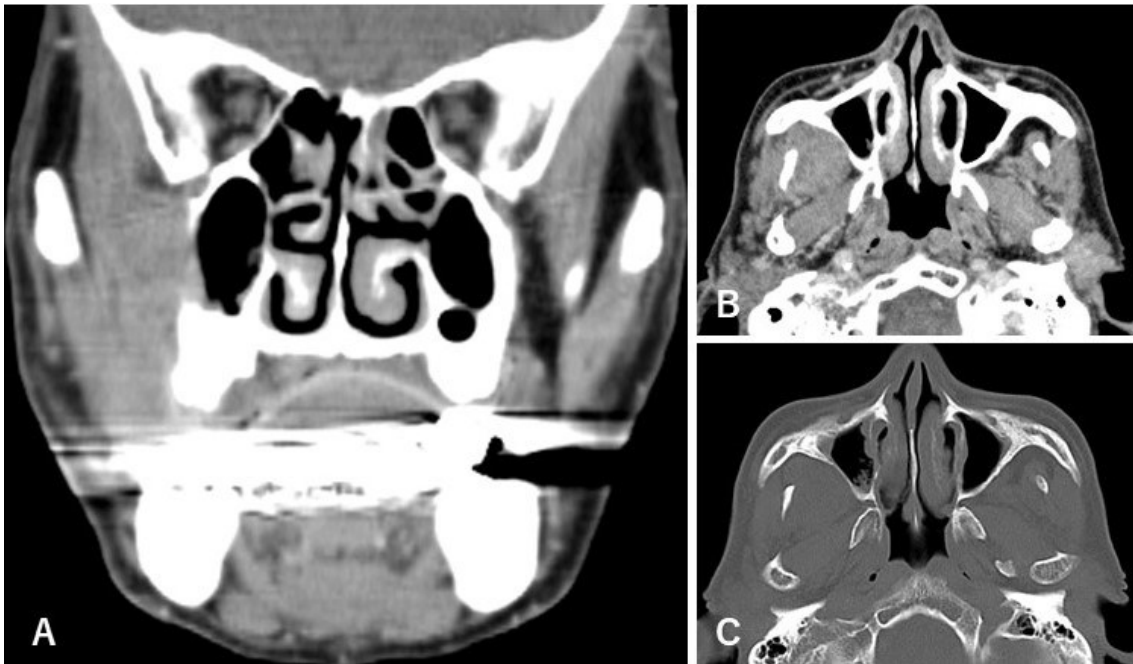


Fig.2

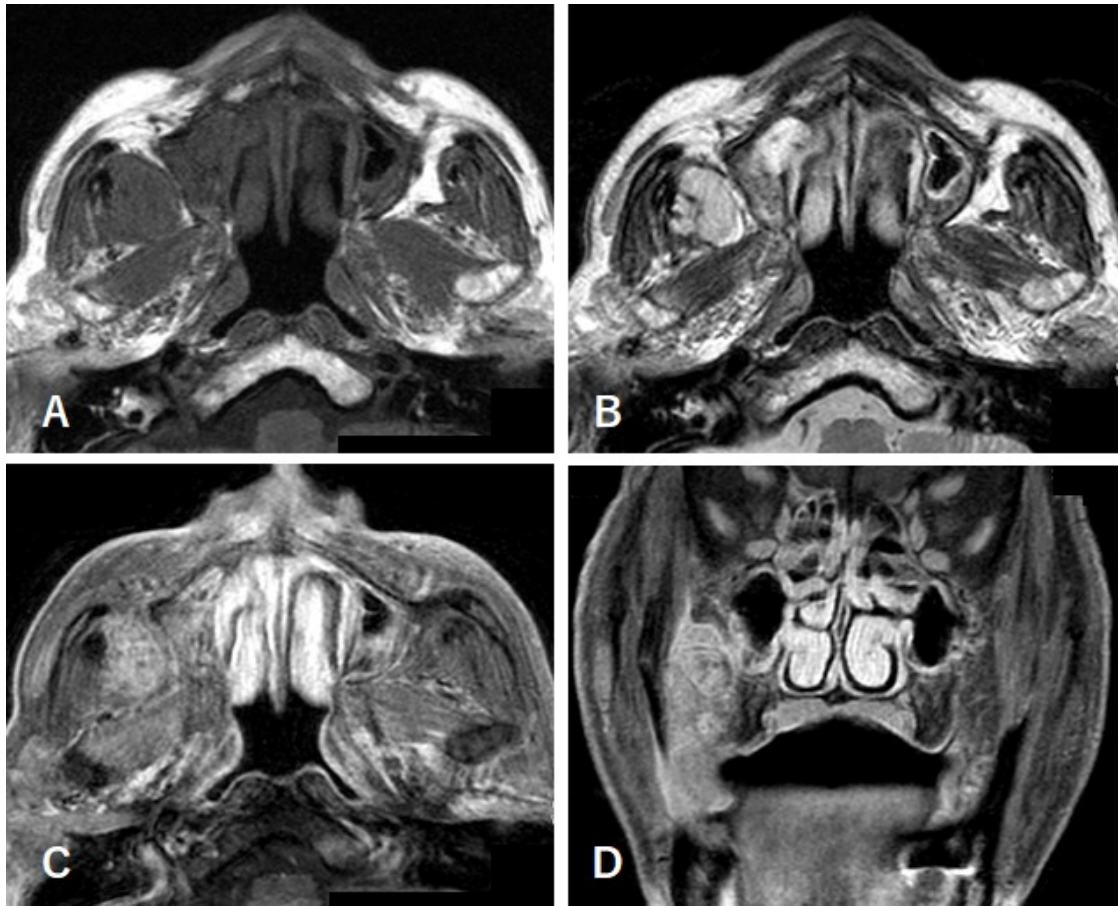


Fig.3

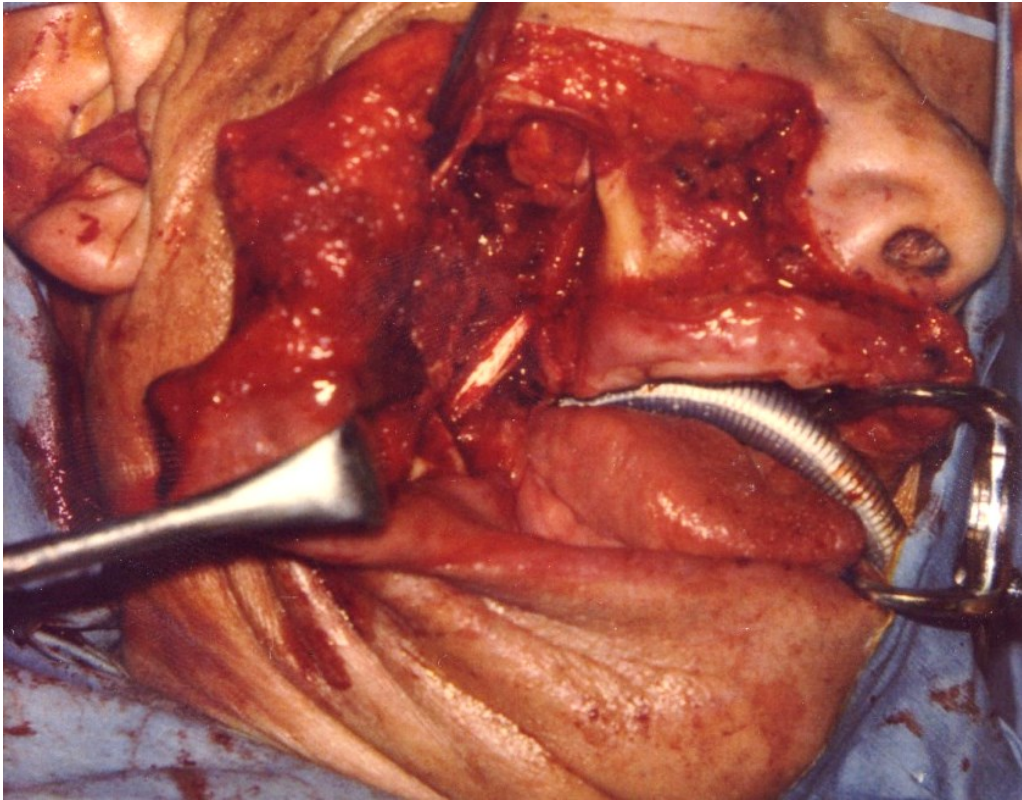


Fig.4

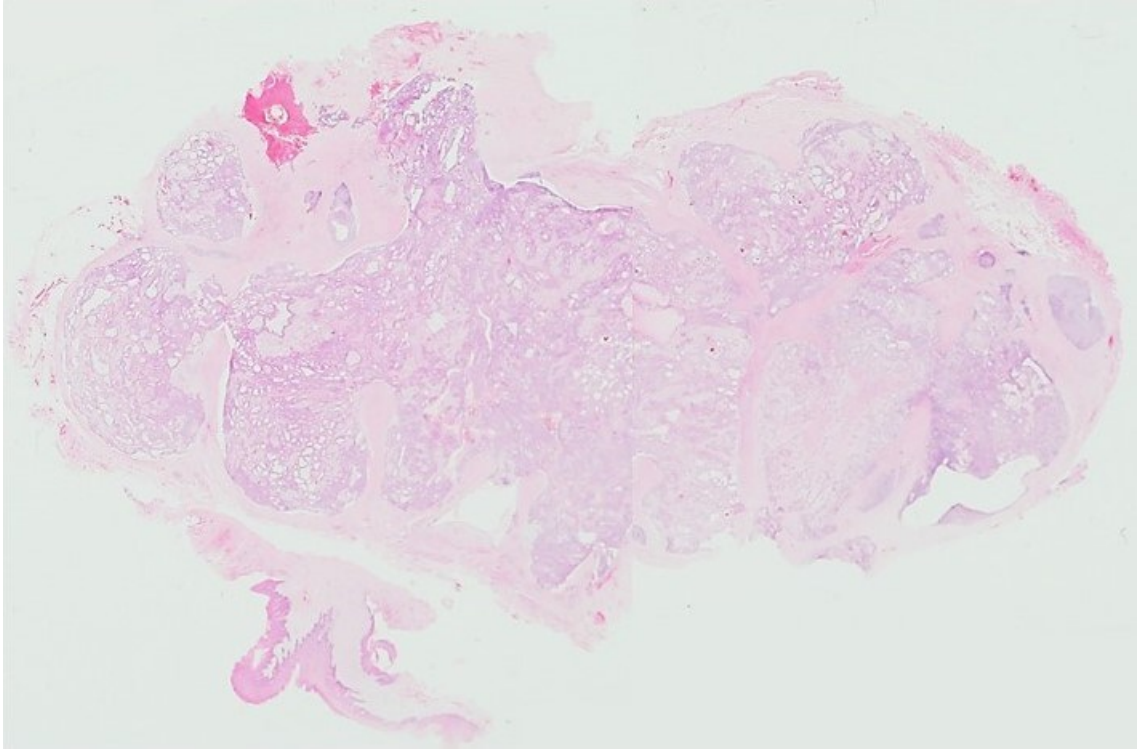


Fig.5

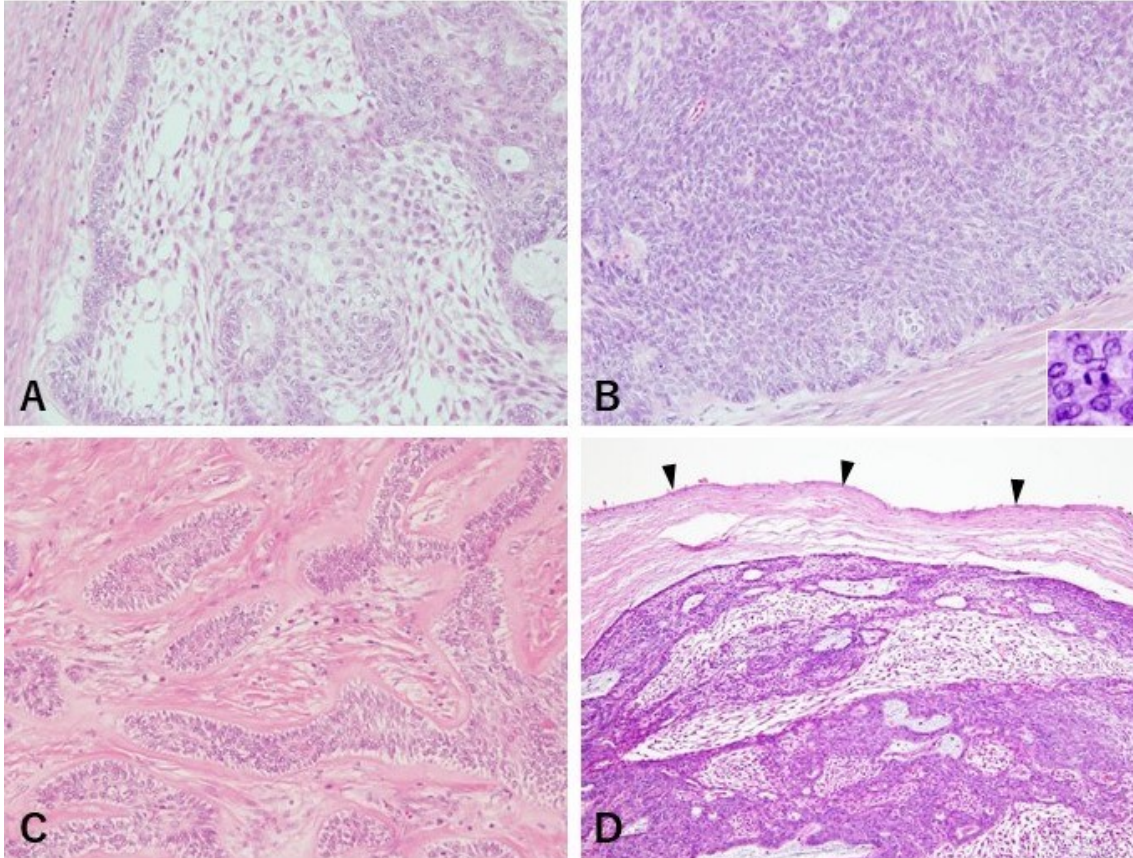


Fig.6

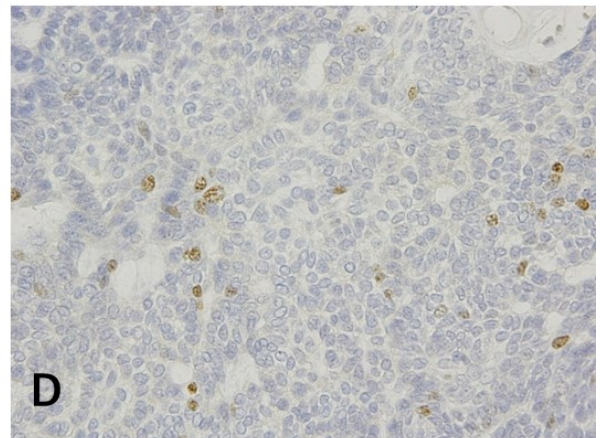
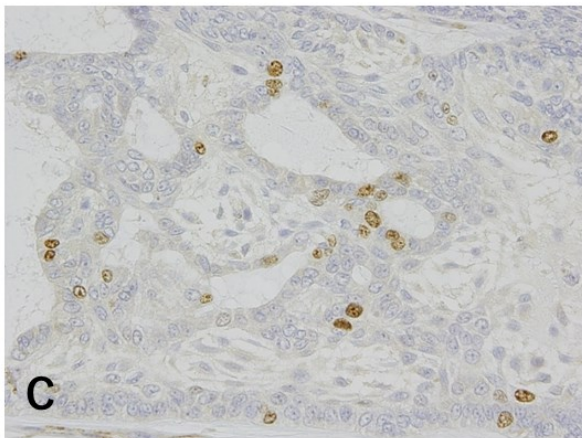
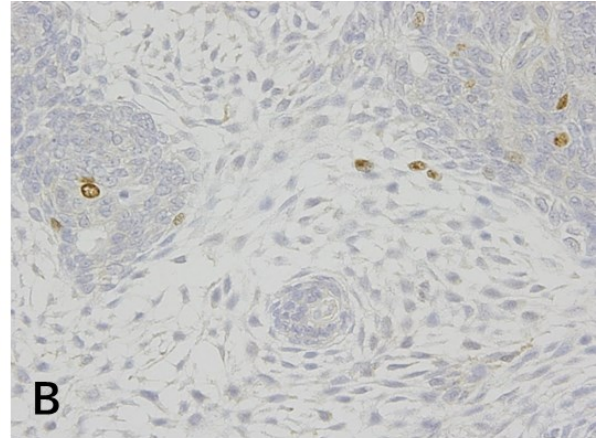
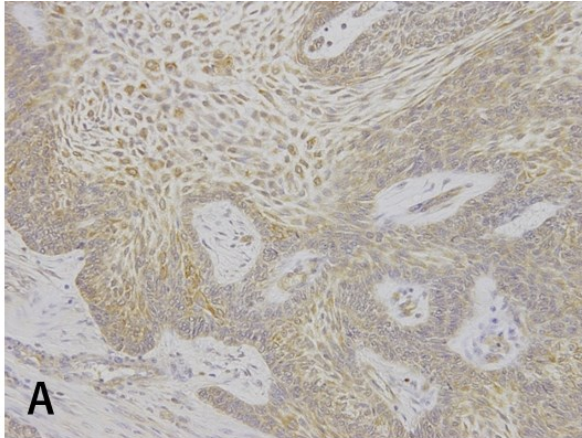


Fig.7

Table 1. Ki-67 labelling index according to tumor components of extralingival peripheral ameloblastoma

Tumor component	No of fields	Mean \pm SD (%)	Range (%)
Stellate reticulum-like area	9	1.15 \pm 0.80	0 - 2.35
Basaloid cell area	16	3.71 \pm 3.02	0.14 - 7.45
Peripheral layer	14	3.66 \pm 3.51	0 - 8.77
All areas	39	3.10 \pm 3.02	0 - 8.77