A Case of Congenital Granular Cell Epulis in the Maxillary Anterior Ridge: A Study of Cell Proliferation Using Immunohistological Staining

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Abstract Congenital granular cell epulis (CGCE) is a very rare benign tumor that preferentially develops in female infants. The histopathological characteristics of CGCE are very similar to a granular cell tumor, but the histological genesis is unknown. We report a case of a four-day-old female neonate who had a tumor mass in the region of the left maxillary anterior teeth. The rate of cell proliferation was determined by immunostaining with Ki-67 and PCNA, which showed labeling indexes of 16.7 and 15.1%, respectively.

Keywords Congenital granular cell epulis · Labeling index · Ki-67 · PCNA

Introduction

Congenital granular cell epulis (CGCE) is a rare benign tumor that develops in the gingiva of newborns and is synonymous with congenital granular cell tumor and congenital epulis [1]. In this paper, we describe the case of a neonate with congenital granular cell epulis in the region of the left maxillary anterior teeth. We discuss the

histogenesis and generation of this tumor and determine the rate of cell proliferation using an immunostaining procedure.

Case Report

Patient Female neonate of age 4 days after birth.

Chief complaint A mass in the left maxillary anterior ridge.

Past/familial medical history None in particular.

History of present illness The patient was born at 40 weeks and 4 days of gestation by normal labor at another hospital. She had a birth weight of 3,180 g. A mass was present in the left maxillary anterior ridge immediately after birth and the patient was referred to our department for close examination of a possible suckling disorder.

Present status

Systemic findings No respiratory or suckling disorder was noted and the nutritional condition was favorable.

Local findings An elastic slightly hard pedunculate mobile mass of size 21 × 16 mm was present in the maxillary anterior ridge of the edentulous jaw (Fig. 1). The surface of the mass was smooth with a mucosal color.

Imaging findings On MRI, a homogenous low-intensity signal due to the lesion was present on T1-weighted imaging and a mixed signal of moderate and low intensity was present in the corresponding region on T2-weighted imaging (Fig. 2).

Clinical diagnosis Congenital epulis in the left maxillary anterior ridge

Treatment and course The mass was excised under general anesthesia 6 days after birth. After oral intubation, an incision was made in the mucosa around the basal region of the pedunculate mass, and the mass was excised

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Fig. 1 Photograph of the oral cavity on the first examination. A mass was present in the maxillary anterior ridge

with the periosteum en bloc. The mass was not continuous with alveolar bone. The cross-sectional surface had a homogenous yellowish-white color (Fig. 3).

Histopathological findings Outgrowth of granular cells surrounded by stratified squamous epithelium, lymphocyte infiltration, and vascular outgrowth were noted, but there were no malignant findings (Fig. 4).

Immunohistochemical findings Samples were positive for NSE, a marker for nerve tissue and neuroendocrine cells, and for vimentin, a mesenchymal cell marker; but negative for S-100, a neuroectoderm-derived cell marker. Histochemically, positive staining was found for PAS, a glycogen marker. The Ki-67 labeling index, which reflects the level of cell proliferation, was 16.7% (Fig. 5), and the PCNA labeling index was 15.1% (Table 1). Based on these findings, we made a final diagnosis of congenital granular cell epulis.

Fig. 3 The excised specimen was a solid lesion

Since the postoperative course was excellent with no recurrence etc. recognized, and 2 years have already passed after the operation at this time point, the follow-up observation was finished.

Discussion

Congenital granular cell epulis (CGCE) is a tumor that is mainly localized in the gingiva. The tumor was initially reported by Neumann [2] in 1871, and is also referred to as congenital granular cell tumor or congenital epulis. The histological classification of lesions in the neck and head region established by the WHO in 2005 [1] positioned

Fig. 2 MRI images. The lesion gave homogenous low-intensity signals on T1-weighted imaging (a), and mixed signals of moderate and low intensity on T2-weighted imaging (b)

Fig. 4 Histopathology showing outgrowth of granular cells (H-E, ×150)

Table 1 Histochemical and immunohistological staining

	Result of histochemical staining
PAS	+
Antibody	Result of immunohistological staining
NSE	+
Vimentin	+
S-100	—
Antibody	Labeling index
Ki-67	16.7%
PCNA	15.1%

CGCE as a benign tumor consisting of eosinophilic cells containing granules in the cytoplasm and mainly present in the alveolar region. Based on this definition, masses showing the histological features of granular cell tumors are regarded as congenital epulis in many countries. However, in Japan masses showing fibrous or granular

Fig. 5 Images of immunohistochemical staining. NSE (a), vimentin (b) and PAS staining (c) were positive, and the Ki-67 labeling index (d), which shows cell proliferative ability, was 16.7%

histology are also reported as congenital epulis, in addition to those showing the features of granular cell tumors, as in this patient. This is because clinically ‘epulis’ is used to represent a small benign tumor localized in the gingiva in Japan, thereby confusing the definition of the disease.

The incidence of this lesion is generally higher in female neonates than in male neonates, and the most common site is the upper frontal tooth region. Damm et al. [3] reported that the incidence was eight times higher in females than in males, and three times higher in the upper jaw compared to the lower jaw. Regarding the gender difference, Cussen [4] proposed an association with intrauterine stimulation by estrogen produced by the fetus, but the cause has yet to be identified. Although there are diseases that require clinical discrimination, such as epithelial pearl, congenital tooth, and gingival bulging accompanying congenital tooth eruption, they are easily differentiated. For example, the case in this report showed no pedicle and congenital tooth, which can be differentiated by X-ray and ultrasonic examinations.

Granular cell tumor (GCT) develops in children and adults and differs from CGCE in several ways, including the most common site, clinical findings, and immunohistochemical characteristics. CGCE frequently develops as a pedunculate mass in the upper and lower gingiva, while GCT is more common in the tongue. Clinically, GCT is an elastic hard tumor with mobility in the lower tissue and adherence to the epidermis. Immunohistochemically, GCT is usually positive for S-100 protein and NSE, suggesting that histologically many cases of GCT are derived from Schwann cells. In contrast, CGCE is S-100 protein-negative and vimentin-positive in many cases. There are various hypotheses regarding the origin of CGCE, including histiocyte, myogenic, and mesenchymal cell origins, and no consensus has been reached [3, 5–8]. In our patient, S-100 protein was negative and vimentin was positive, suggesting a mesenchymal origin, but NSE was also positive, based on which a nerve cell origin cannot be ruled out. Regarding recurrence, Lac et al. [9] found a rate of 8% for GCT, whereas CGCE has been reported not to recur even in cases with incomplete resection [10]. These observations indicate that only the histopathological findings are similar between GCT and CGCE, and that these tumors may be derived from different tissues.

Cell proliferative activity in CGCE cases has not been investigated previously. In our patient, the mass was subjected to immunostaining for Ki-67 and PCNA, and the labeling indices were 16.7 and 15.1%, respectively. Agostini et al. [11] have reported Ki-67 and PCNA labeling indices of higher than 50% in oral squamous cell carcinoma, and Barboza et al. [12] also found a mean PCNA labeling index of higher than 50% in adamantinoma and adenomatoid odontogenic tumor. In contrast, in normal tissue, the Ki-67 labeling index in mucosa is less than 10%

[13], that for PCNA in the normal gingiva is less than 5%, and that in plaque-induced gingivitis is about 10% [14]. Simple comparison of these indices is difficult, but considering the high cell activity in infants, the proliferative activity in our patient may not have been high. Cases in which size reduction and disappearance of lesions within 1 year of course observation have also been reported [15–17]. Moreover, the size has varied from several mm to 9 cm in reported cases [18–20], and large lesions in the anterior tooth region have been reported, although these may have been due to the influence of mechanical stimulation. Therefore, it is possible that these lesions were due to reactive hyperplasia, rather than a tumor.

Surgical resection is often performed for treatment of CGCE, but Welbury et al. [21] proposed that surgical resection is unnecessary when no marked disorder is present. Interference of resection with tooth eruption has also been reported [22]. When the mass is small and located in a region with little stimulation in which the tooth germ is less likely to be injured, course observation may be selected with the expectancy of size reduction and disappearance. However, when the mass is large or located in a region that is likely to be stimulated by the anterior tooth region, retention of the lesion may lead to functional disorders such as impaired suckling and respiration, and aspiration of the spontaneously dropped mass. Early treatment should also be performed to differentiate the mass from granular cell myoblastoma, for which a relatively high recurrence rate (8%) has been reported [23]. Resection of a wide alveolar gingival area affecting tooth eruption should be avoided because many cases of CGCE are pedunculated, suggesting that recurrence is unlikely.

Conflict of interest The authors declare no conflict of interest.

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