Congenital Epulis: A Case and Review of the Literature

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Abstract

Congenital epulis is an unusual benign oral mucosal lesion in newborns with no tendency to recur after excision. The histogenesis of the lesion is unknown, but it is believed to be of mesenchymal origin. We describe a case of congenital epulis (20 × 10 mm) in the mandibular gingiva of a newborn. The mass, which was smooth-surfaced and pedunculated with a healthy color, was surgically removed at 5 months post-birth. Histologically, the tumor consisted mainly of large eosinophilic granular cells. Immunohistochemical studies revealed intense staining for vimentin, STRO-1, and CD44, suggesting that it was derived from mesenchymal cells. The literature and immunohistochemical profile of congenital epulis are also discussed.

Key words: Congenital epulis — Granular cell — Immunohistochemistry — Mesenchymal cell — Origin

Introduction

A congenital epulis is a benign localized mass occurring in the alveolar region of newborns. It is extremely rare, accounting for only approximately 0.2% of all types of epulis in Japan. Only 108 domestic cases have been reported in the Japanese literature since 1935, with that number including the present case also. Various histopathological characteristics of congenital epulis have been reported, including the fibrous and granulomatous appearance of the tissue. In the majority of cases, the tissue also contains granular cells. Although several hypotheses regarding the origin of congenital epulis have been proposed, including its derivation from myocytes, neurocytes, fibroblasts, histiocytes, and mesenchymal cells, a consensus has yet to be reached. We recently treated a newborn patient with congenital epulis. This paper describes a statistical analysis of patients with this condition treated at our institution between 1967 and 2016. The literature regard-
Case Report

The patient, a girl, was first examined at the Chiba Hospital of Tokyo Dental College at the age of 1 day. Her family and medical histories showed nothing remarkable, and the birth weight was 3,575 g. She was brought to our hospital for a detailed examination following the detection of a mass in the anterior region of the mandible at birth. A general physical examination revealed no suckling disorder that would hinder appropriate feeding. An intraoral examination revealed an elastic, smooth-surfaced, pedunculated mass with a healthy color and measuring $20 \times 10$ mm (Fig. 1a).

The mass was completely resected under general anesthesia at 5 months after birth (Fig. 1b). The area under the periosteum was separated and the mass resected and extracted en bloc. The resected mass was smaller ($7 \times 5$ mm) than that observed at the initial examination (Fig. 2a). The cross-sectional surface of the mass, which was surrounded by a semitransparent, mucous-like substance, was white near the center (Fig. 2b).

Hematoxylin and eosin staining revealed that the mass comprised fibrous connective tissue covered by a parakeratotic, stratified, squamous epithelium. It also showed elongated rete ridges and thickening of the stratum spinosum (Fig. 3a). A magnified image of the center of the mass showed the proliferation of large cells with granular or clear cytoplasm (Fig. 3b). Based on these findings and the fact that the mass was present at birth, the lesion was diagnosed as congenital epulis.

The results of immunohistochemical staining were positive for vimentin, STRO-1, cluster of differentiation (CD) 44, and CD68 (Fig. 4a–d). The staining was negative, however, for S-100, neuron-specific enolase (NSE), desmin and CD34 (data not shown).

Discussion

Congenital epulis is a unique and rare benign lesion arising in the mucosa of the alveolar ridges of the jaw in newborns. It has
been described under a number of different names in the recent literature, including congenital epulis, congenital epulis of the newborn, congenital granular cell tumor, congenital granular cell lesion, and gingival granular cell tumor of the newborn. This type of mass is relatively rare, and our own review of the literature identified only 108 such cases in Japan since 1935, including the present case. Yuwanati et al. stated that approximately 250 cases have been reported overseas. Four patients with congenital epulis were treated at our institution between 1967 and 2016: 1 male and 3 female infants (maxilla, 1 patient; mandible, 3 patients). Congenital epulis commonly develops in the anterior gingiva, and has been reported to develop more frequently in the maxilla. An investigation of sex-related differences revealed that the condition occurred more frequently in girls than in boys.

The diameter of the mass varies, ranging from 3 to 80 mm, but is usually only approximately 10 mm. In some reports, however, the size of the mass showed a decrease over follow-up observations in comparison with at the initial examination performed at 1 day after birth. It has been suggested that such a reduction in size may result from the fetus being released from the influence of excessive estrogen produced in response to maternal stimulation upon birth. Characteristic histological findings shown by congenital epulis include large round cells with granular, eosinophilic cytoplasm, and small eccentric nuclei. Thus, histopathological findings have also suggested that while congenital epulis first appears as a granular cell tumor, it can subsequently change into a fibrous mass due to stimulation by the tongue during the embryonic period or during suckling after birth, and that the presence of a large number of macrophages related to this change can cause spontaneous remission. In the present case, cells positive for CD68, a macrophage marker, were recognized in the connective tissue, thereby confirming the infiltration of macrophages. This further supports the theory that the presence of macrophages plays a role in the spontaneous remission of congenital epulis.

The histogenesis of granular cells in congenital epulis has remained enigmatic, in spite of a vast number of immunohistochemical and ultrastructural studies. Several hypotheses have been proposed regarding the origin of the tissue constituting the mass, including one in myocytes, neurocytes, fibroblasts, histiocytes, pericytes, and undifferentiated mesenchymal cells. A consensus has yet to be reached, however. Reports have shown that granular cell tumors that develop on the lingual edge in adults originate in Schwann or mesenchymal cells. Because the clinical course of congenital epulis varies, however, with some patients exhibiting a reduction of the mass over the course of follow-up, it remains unclear whether these masses can be considered the same lesion. Abrikossoff proposed that these lesions develop from myoblasts due to aberrant muscle tissue development during the embryonic period. Ultrastructural studies have failed to support this theory, however, and the
absence of desmin and myoglobin in congenital epulis also does not support the theory that these masses are derived from muscle cells. The results of the present immunohistochemical analysis were negative for desmin. The hypothesis that the tissue of such lesions is derived from nerves is based on the fact that granular cell populations resemble peripheral nerves, and that axon-like structures are visible by electron microscopy. This led to the suggestion that the tissue arises from Schwann cells. Immunohistochemical positivity for NSE also supports the hypothesis that the tissue originates in nerve cells, with positivity for NSE being reported in 40% of such cases. Because NSE is known to lack specificity for tumor cells, however, these observations should be interpreted carefully. The results of the present immunohistological analysis were negative for NSE. The hypothesis that the tissue originates in fibroblasts is supported by the following: shifts were noted between fibroblasts with granules and granular cells; electron microscopy has revealed that granular cells lack a fibroblast-like basement membrane; and some collagenous fibers are engulfed within the protoplasm. According to the histiocyte origin theory, granular cells develop from phagocytic histiocytes that store an abnormal metabolite. From an immunohistochemical aspect, however, the absence of lysozyme and alpha-1 antichymotrypsin in congenital epulis does not support a histiocytic origin. A pericytic origin had previously been suggested by Rohrer and Young, who described cells that exhibited the fine structural details of pericytes and were juxtaposed to small vessels in the position of pericytes. As in earlier studies, the accumulation of these cells was also noted around vessels, but it was not clear whether they were hyperplastic or neoplastic in nature. The results of the present immunohistological analysis were negative for CD34, a hematopoietic stem cell marker. Most investigators agree that granular cells are derivatives of undifferentiated mesenchymal cells. The presence of vimentin and the lack of cytokeratin, desmin, neurofilaments, and glial fibrillary acidic protein suggest a mesenchymal non-muscular, non-neural, and non-glial nature of granular cells. The positivity for vimentin can be explained by the large amount of collagen and collagen precursors found with the tumor cells. Damm et al. noted that tumor cells exhibited active production of extracellular collagen. Occasionally, banded collagen fibrils were seen among the cytoplasmic granules. A limiting membrane surrounded some of these intracellular collagen fibrils, while others appeared to lie free within the cytoplasm.

A vast array of immunohistochemical studies has been undertaken in an effort to determine the immunohistochemical profile of congenital epulis. The results of the present immunohistological analysis were negative for the nervous system marker S-100. S-100 protein antigen staining has shown negative results in previous studies, which excludes a neurogenic etiology and thereby differentiates between a congenital epulis and a granular cell tumor. Congenital epulis is also negative for 75 kDa nerve growth factor receptor, trk gene product, and phosphotyrosine-positive cells, all confirming the lack of a neurogenic origin, in contrast to granular cell tumors. Among the traditional markers, positive immunoreactivity for vimentin was the most frequently reported (93% of cases). The congenital epulis in the present patient was positive for vimentin and mesenchymal stem cell markers STRO-1 and CD44. To our knowledge, no studies to date have investigated the expression of mesenchymal stem cell markers in congenital epulis. The positivity for vimentin observed in the present patient, however, suggests that the congenital epulis originated in mesenchymal cells. Further investigation is necessary, however, as the possibility that the tissue developed from multiple sources cannot be excluded.

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