Content available at: https://www.ipinnovative.com/open-access-journals

Journal of Oral Medicine, Oral Surgery, Oral Pathology and Oral Radiology

Journal homepage: www.joooo.org

Case Series

Congenital granular cell epulis – Unraveling the histogenesis

Vaishali Anil Nandkhedkar[1,*], Jyoti Dilip Bhavthankar[1], Mandakini Subhash Mandale[1], Jayanti Govind Humbe[1], Savita Prashant Wagh[1], Poonam Rajendra Zanwar[1]

[1] *Dept. of Oral Pathology and Microbiology, Government Dental College and Hospital, Aurangabad, Maharashtra, India*

ARTICLE INFO

Article history:
Received 24-03-2023
Accepted 11-04-2023
Available online 02-06-2023

Keywords:
Congenital epulis
Granular cell
Histogenesis
Neumann's tumor

ABSTRACT

Congenital Granular cell epulis is a rare benign tumor of the newborn. It also known as granular cell tumor of the newborn or Neumann's tumor. It originates exclusively on the alveolar ridge, most commonly seen in maxillary anterior region, typically seen as a mass protruding out of the mouth, which may interfere with respiration or feeding. Despite its striking appearance, the lesion is ultimately benign. However, immediate surgical treatment is required if there is a risk of airway obstruction or feeding difficulties. Here, two cases were reported to reveal the histological findings and reassess the immunohistochemical characteristics that may hint towards the histogenesis of the congenital epulis. Histopathology of both masses composed of diffuse sheets and clusters of polygonal cells containing small round to oval nuclei and abundant coarsely granular cytoplasm. The immunoreactivity of the granular cell was examined by immunohistochemical markers such as S100 protein, CD68, CD1a and Neuron specific enolase (NSE). In the present case tumour cells were positive for NSE and CD68 and negative for S100 and CD1a. Although the exact nature of its histogenesis still remains a mystery.

1. Introduction

Congenital epulis is a very rare intra oral soft tissue benign growth of the new born. The first case of congenital epulis was reported in 1871 by Neumann.[1] Hence, this lesion is also known by the term Neumann's tumor. It is tumor commonly affect the anterior region of the maxillary arch of newborns.[2] Female preponderance was noticed the ratio found to be 10:1.[1] Alveolar ridge is the most common site.

Literature reveals different nomenclature for Congenital epulis such as congenital granular cell tumour, gingival granular cell tumour of newborn and congenital granular cell epulis. The WHO classification of head & neck tumours (2017) introduced the term congenital granular cell epulis. Loyola et al. 1997 suggested that congenital epulis is not restricted to the alveolar ridge but also occurs on the other sites such as the tongue, Buccal mucosa etc. Currently, most accepted terminology is congenital granular cell epulis (CGCE) which is widely acknowledged in the literature.

CGCE presents as solitary lesion which was predominantly occurring on the anterior maxillary alveolar ridges. A MEDLINE search conducted by Kayiran et al revealed 8 reported cases of CGCE on the tongue either in isolation or along with the gum lesion.[3] Although etiology behind CGCE remains unknown in the literature, many literature have been proposed in an attempt to explored the histogenesis of the tumor include odontogenic epithelium, fibroblasts, histiocytes, smoothmuscle, nerve related cells, endothelial cells and undifferentiated mesenchymal cells. Multiple immunohistochemical studies have been

* *Corresponding author.*
E-mail address: vaishalipatho72@gmail.com (V. A. Nandkhedkar).

https://doi.org/10.18231/j.jooo.2023.020

conducted in order to explore the enigma of the histogenesis of CGCE.[3]

Here, two cases are reported to reveal the histological findings and reassess the immunohistochemical characteristics that may hint towards the histogenesis of this lesion.

2. Case Report 1

A 2 days old female infant which was referred with the chief complaint of mass protruding from the anterior alveolar ridge of the oral cavity. The infant was born on 36^{th} week of gestation. There was no other obvious medical history pertaining to hereditary diseases. Maternal and paternal medical history was found to be non-contributory. Intraoral examination revealed soft, smooth reddish pink, pedunculated mass extending from the maxillary alveolar ridge, from the canine region of 8mm X 6mm in size (Figure 1 A). On palpation it has soft consistency and absence of pulsation. Based on clinical examination provisional diagnosis was congenital epulis. Surgical excision was advised and was done under local anaesthesia with all aspectic precautions.

3. Case Report 2

7 days old female infant who was a full term, normal delivered baby. On clinical examination revealed soft, smooth, pale pink, pedunculated mass of 5 mm x 3 mm (Figure 1 B) present in the anterior region of the maxillary arch. Provisional diagnosis was made as congenital epulis. Surgical excision was carried out with all aseptic precaution.

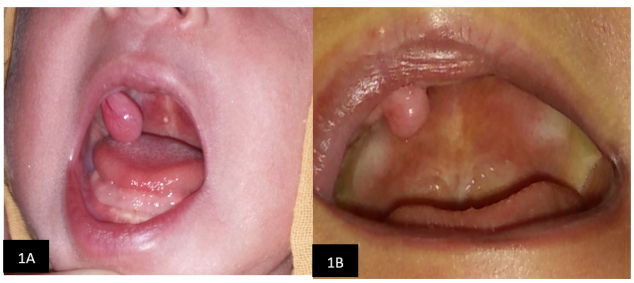

Fig. 1: A): Pedunculated mass extending from the maxillary alveolar ridge from the canine region (Case 1); **B**): Pedunculated present in the anterior region of the maxillary arch (Case 2)

Histopathologic examination of both lesions revealed a normal epithelium and underlying lesional tissue composed of large polygonal cells with granular cytoplasm and small nucleus. The connective tissue stroma was scanty. On the basis of histopathological finding, diagnosis was given as Congenital Granular Cell Epulis. (Figures 2 and 3 under 10X and 40X).

For the further exploring the nature of the lesion, granular cells were studied for IHC findings. The histogenesis of granular cell was scrutinised by IHC markers such as S100 protein, CD68, CD1a and Neuron specific enolase (NSE). In the present case report granular cells of the tumour cells were positive for NSE and CD68 and negative for S100 and CD1a. On the basis of histopathological & immunohistochemical analysis, congenital granular cell epulis was confirmed. (Figure 4)

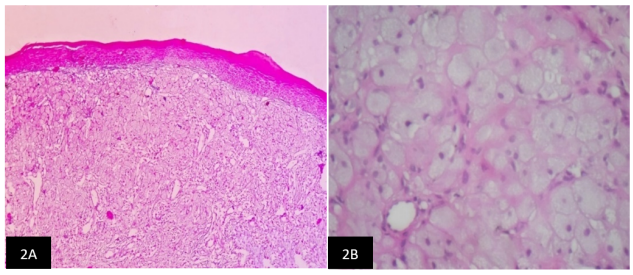

Fig. 2: (Case 1): **A):** Lesion lined by stratified squamous epithelium devoid of rete ridges granular cells are tightly packed with abundant pale granular cyto plasm (100X); **B**): Large tumor cells with darkly stained nucleus with dialated blood vessels (400X)

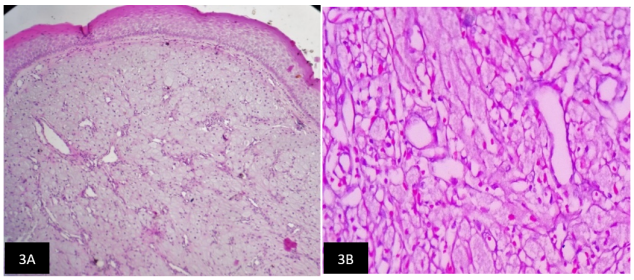

Fig. 3: (Case 2): **A**): Lesion lined by stratified squamous epithelium devoid of rete ridges granular cells are tightly packed with abundant pale granular cytoplasm (100X); **B**): Large tumor cells with darkly stained nucleus with dialated blood vessels (400X)

4. Discussion

Previously CGCE was termed as congenital epulis. An Epulis is a Greek term which means as “of the gums”. This terminology was used to describe a wide variety of gum lesions irrespective of their pathological origin.[4]

CGCE is a rare tumour of neonates. It was first designated by Neumann in 1871.[2] So, alternatively termed as Neumann’s tumour. These lesions usually present at birth with protruding soft tissue mass from the anterior region of maxilla or mandible, which is peduncalated & colour varies from pink to red. The maxillary alveolar ridge is more commonly involving site than mandibular ridge (maxillary arch and mandibular arch ratio 3:1.)[5] Simultaneous involvement of both maxillary and mandibular alveolar ridges is reported approximately in 10% of the cases. These

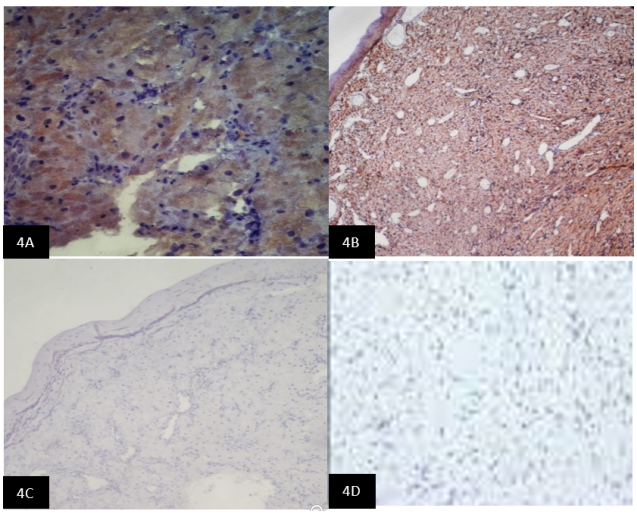

Fig. 4: A & B): Granular cells CGCG shows positive for NSE and CD68. **C & D):** Granular cells CGCG shows negative for CD1a and S100

lesions commonly interfere with the feeding. The most common location was within the future canine or lateral incisor teeth. There is a marked female preponderance as compared with male (10:1). All the clinical findings of the present case reports were supported with the literature such as Kuper et al (2009) and Milobes and Smith Famburg (2011).[6]

Classically CGCE is a soft pedunculated or sessile, lobulated nodule of normal color & texture. Generally the average diameter of CGCE was 1cm.[4] Few literatures reveal the variation in size extending from few milimeter to 9 cm in diameter. In the present case, the size of the lesion varied from 5mm X 3 mm to 8mm X 6mm. The diagnosis usually done on the clinical basis.

Microscopically congenital granular cell epulis is composed of large polyhedral cells arranged in sheets with rich granular cytoplasm and darkly stained nucleus with scanty connective tissue. On the histopathological finding, diagnosis was given as congenital granular cell epulis. (Figures 3 and 4) Different theories on the origin of the lesion have been concerning its uncertain histogenesis. Odontogenic epithelium, fibroblast, histiocytes, smooth muscle, nerve related cells, undifferentiated mesenchymal cells have been implicated in the pathogenesis of CGCE which however, remain undefined.[5]

Lack et al. (1981) believed it to be reactive in origin.[7] Zarbo et al (1983) has found smooth muscle differentiation, ultra structurally in CGCE which exihibited S100 negativity on immunohistochemical analysis.[8] He concluded that the granules were derived from a primitive gingival perivascular mesenchymal cell with the potential for smooth muscle cytodifferentiation. Takahashi et al (1990), studied immunophenotype of congenital epulis as it has biphasic pattern and interpreted as interstitial cells as to have exhibited neuroendocrine differentiation.[9] Sideny et al (2014) studied CD34 which is marker for haempoietic stem cells and progenitor cells and was found negative in CGCE thus ruling out vascular lesion.[10] However, numerous reports have shown no evidence of either estrogen or progesterone receptors towards an alternative histogenesis for CGCE.[7]

Electron microscopic study showed granular cells comprising heterogeneous electron dense granules representing lysosomes and cytoplasmic lipid droplets. The tumoral cells showed irregular cytoplasmic borders with small extension.

Histogenesis of granules present in the cytoplasm was examined by IHC markers such as S100 protein, CD68, CD1a and NSE. Neuron specific enolase is a dimeric glycolytic enzyme that is composed of three subunits (α, β & γ). The α subunit only in muscle whereas γ is expressed in neurons both normal & neoplastic neuroendocrines. CD68 is a macrophage marker which is associated with phagolysosome. The granules which are present in the cytoplasm are derived from the lysosomes. This may infer that the interstitial cells contain an intracytoplasmic accumulation of phagolysosomes.[11] S1OO protein serves as marker for neural cell origin. There is a possibility that they represent an earlier stage of the granular cells and loss of reactivity to S100 protein and frequently also to CD68 during transition to an entirely granular morphology.[2,4] Therefore, with this finding, we can suggest that neuroectodermal differentiation may play a role in the histogenesis of CGCE. The analysis was positive with CD68 AND NSE but negative for S100 protein and CD1a. In the literature, Ottoman et al[12] (2015) concluded similar findings, that granular cells were positive for vimentin and most of the cases were positive for the NSE & negative for S100 protein.[12] Vered et al. (2009) observed that 93% & 48% of the cases were positive for vimentin and NSE respectively.[4]

Majority of CGCE is surgically excised, no recurrence has been reported after surgical intervention. In the literature Lack et al. stated that out of 15 cases which included 11 cases of incomplete resection showed no recurrence. In present case reports also no recurrence was observed. Overall prognosis of the CGCE is good. Whether the CGCE is a true neoplastic lesion or reactive lesion is still not clear.

5. Conclusion

A new born infant with CGCE can be remarkable sight for both parents as well as health care professionals involved in neonatal care. CGCE is a rare unique lesion, clinically presenting as lobulated mass in the oral cavity of newborn. Many theories are carried out to reveal the histogenesis with IHC studies. The present case reports were positive for CD 68 and NSE markers pointing towards a neural origin of the

lesion, still the lesion poses scope for the research for exact etiopathogenesis.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Fister P, Volavšek M, Sever MN, Jazbec J. A newborn baby with a tumor protruding from the mouth. Diagnosis: congenital gingival granular cell tumor. *Acta Dermatovenerol Alp Pannonica Adriat*. 2007;16(3):128–30.
2. Jalil AA, Auzair LM, Lau SH. Congenital epulis: Immunohistochemical findings of 12 cases. *Arch Orofac Sci*. 2015;10:1–7.
3. Kayıran SM, Buyukunal C, Ince U, Gürakan B. Congenital epulis of the tongue: A case report and review of the literature. *JRSM Short Rep*. 2011;2(7):62.
4. Vered M, Dobriyan A, Buchner A. Congenital granular cell epulis presents an immunohistochemical profile that distinguishes it from the granular cell tumor of the adult. *Virchows Arch*. 2009;454(3):303–10.
5. Ottoman BAE. Diagnosis and management of congenital epulis of new-born: a rare case report and literature review. *Int J Sci Rep*. 2015;1(1):80–2.
6. Yuwanati M, Mhaske S, Mhaske A. Congenital granular cell tumor - a rare entity. *J Neonatal Surg*. 2015;4(2):17.
7. Lack EE, Perez-Atayde AR, Mcgill TJ, Vawter GF. Gingival granular cell tumor of the newborn (congenital "epulis"): Ultrastructural observations relating to histogenesis. *Hum Pathol*. 1982;13(7):686–9.
8. Zarbo RJ, Lloyd RV, Beals TF, Mcclatchey KD. Congenital gingival granular cell tumor with smooth muscle cytodifferentiation. *Oral Surg Oral Med Oral Pathol*. 1983;56(5):512–20.
9. Takahashi H, Fujita S, Satoh H, Okabe H. Immunohistochemical study of congenital gingival granular cell tumor (congenital epulis). *J Oral Pathol Med*. 1990;19(10):492–6.
10. Sidney LE, Branch MJ, Dunphy SE, Dua HS, Hopkinson A. Concise review: evidence for CD34 as a common marker for diverse progenitors. *Stem Cells*. 2014;32(6):1380–9.
11. Lapid O, Shaco-Levy R, Krieger Y, Kachko L, Sagi A. Congenital epulis. *Pediatrics*. 2001;107(2):E22.
12. Ottoman BAE. Diagnosis and management of congenital epulis of new-born: a rare case report and literature review. *Int J Sci Rep*. 2015;1(1):80–2.

Author biography

Vaishali Anil Nandkhedkar, Assistant Professor https://orcid.org/0000-0001-9676-7182

Jyoti Dilip Bhavthankar, Professor and HOD

Mandakini Subhash Mandale, Associate Professor

Jayanti Govind Humbe, Associate Professor

Savita Prashant Wagh, Assistant Professor

Poonam Rajendra Zanwar, Post Graduate Student https://orcid.org/0000-0003-0447-9955

Cite this article: Nandkhedkar VA, Bhavthankar JD, Mandale MS, Humbe JG, Wagh SP, Zanwar PR. Congenital granular cell epulis – Unraveling the histogenesis. *J Oral Med, Oral Surg, Oral Pathol, Oral Radiol* 2023;9(2):91-94.