

Clinical Case Report

Congenital granular cell tumor: an unusual case report



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ABSTRACT

Congenital granular cell tumor is an uncommon benign oral lesion of uncertain histogenesis that affects the alveolar ridge region of newborns. The present study aims to report an unusual congenital granular cell tumor case, emphasizing clinical, morphological, and immunohistochemical aspects. A 10-day-old newborn patient attended the stomatology service with a nodular pedunculated lesion of normal color located in the anterior region of the superior alveolar ridge. Thus, the diagnostic hypothesis was congenital epulis, and an excisional biopsy was performed. Histopathological analysis revealed features consistent with the diagnosis of congenital granular cell tumor. In addition, we performed immunohistochemical staining for vimentin, Ki-67, and S100. The patient has been under follow-up with no clinical signs of recurrence. Due to its rarity, the analysis of congenital granular cell tumor's clinicopathological characteristics enables an adequate diagnosis and treatment. (Rev Port Estomatol Med Dent Cir Maxilofac. 2022;63(3):159-166)

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Tumor congênito de células granulares: um relato de caso incomum

R E S U M O

Palavras-chave:

Epúlide congênita
Recém-nascido
Patologia oral
Pediatria

O tumor congênito de células granulares é uma lesão oral benigna incomum de histogênese incerta que afeta a região de rebordo alveolar de recém-nascidos. O objetivo do presente estudo é relatar um caso incomum de tumor congênito de células granulares, com ênfase nos aspectos clínicos, morfológicos e imuno-histoquímicos. Paciente recém-nascida, 10 dias de vida, compareceu ao serviço de estomatologia apresentando lesão nodular, pedunculada e de coloração semelhante à mucosa, em região anterior do rebordo alveolar superior. Assim, a hipótese diagnóstica foi de epúlide congênita, sendo realizada biópsia excisional. A análise histopatológica evidenciou características consistentes com o diagnóstico de tumor congênito de células granulares. Associado a isso, a coloração imuno-histoquímica foi realizada para vimentina, Ki-67 e S100. A paciente está em acompanhamento, sem sinais clínicos de recorrência. Portanto, devido à raridade dessa lesão, a análise das suas características clinicopatológicas permite a obtenção de um diagnóstico e tratamento adequados. (Rev Port Estomatol Med Dent Cir Maxilofac. 2022;63(3):159-166)

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Introduction

Congenital granular cell tumor (CGCT) is an uncommon benign lesion that affects fetuses and neonates. It shows a predilection for females, and the anterior alveolar mucosa of the maxilla is the most affected intraoral site.^{1,2} As for its histogenesis, hypotheses include odontogenic, neural, histiocytic, pericytic, fibroblastic, muscular, and even undifferentiated mesenchymal cells. However, the CGCT's histogenesis remains unknown, and there is no consensus in the literature.^{1,3,4}

Clinically, CGCT presents as a single circumscribed growth with sessile or pedunculated implantation, color ranging from pink to reddish, and size ranging from a few millimeters to about 10 centimeters in diameter.² Multiple lesions involving the maxilla and mandible have also been described in 10% of cases.^{4,5-7} Histopathological images reveal rounded voluminous cells with abundant eosinophilic granular cytoplasm and slightly basophilic oval nuclei. CGCT's microscopic appearance is very similar to granular cell tumors, and the differential diagnosis between the two is based on etiological, clinical, and immunohistochemical aspects.^{1,3,6,8}

Surgical excision is recommended immediately upon detection of the lesion, and spontaneous regression is rare. Large lesions can cause feeding difficulties and airway obstruction in the neonate.^{5,6,9} This study reports a case of CGCT and discusses clinical and histopathological characteristics, as well as differential diagnoses from other lesions, while emphasizing a multidisciplinary approach.

Case report

A 10-day-old Black female newborn was presented at a Stomatology Service with a nodular lesion in the oral cavity. Intraoral physical examination revealed a pedunculated exo-

phytic nodular lesion of firm consistency and coloring similar to the mucosa, located in the anterior region of the left upper alveolar ridge and measuring approximately 3.0 x 2.0 cm in diameter (Figure 1). This mass was causing breastfeeding problems but no airway obstruction. The infant's mother did not mention any adverse perinatal event, and the lesion was detected only at birth.

Considering a diagnostic hypothesis of congenital epulis, pediatric and anesthetic evaluations were performed to plan the surgical excision of the lesion, which occurred under general anesthesia with orotracheal intubation, as usually recommended in such cases.^{1,3,10} The lesion was completely excised using electrocautery, bleeding was minimal, and the infant recovered with no complications, achieving normal breastfeeding.

Histopathological examination revealed a benign, well-circumscribed lesion characterized by a proliferation of polygonal cells amid a sparse stroma (Figure 2). The cells exhibited rounded morphology and abundant eosinophilic granular cytoplasm. Some of the rounded-to-oval-shaped basophilic nuclei appeared as expelled toward the cell's periphery. The dense fibrous connective tissue stroma was sparse, with a mild infiltrate of mononuclear inflammatory cells and blood vessels. The epithelium lining exhibited atrophy of its epithelial ridges at its greatest extent, with an area of focal ulceration (Figures 3, 4, and 5). In order to better characterize the lesion under study, immunohistochemical staining for vimentin (Figure 6), Ki-67 (Figure 7), and S100 (Figure 8) was performed.

The clinical, histopathological, and immunohistochemical aspects led to a diagnosis of CGCT. The patient has been under follow-up for 3 years, with no clinical signs of recurrence.

The child's parents signed a free informed consent form explaining and authorizing data usage for academic reasons. The institution's Research Ethics Committee approved this study.



Figure 1. Clinical aspect. Pedunculated nodular lesion on the anterior upper alveolar ridge of a newborn.

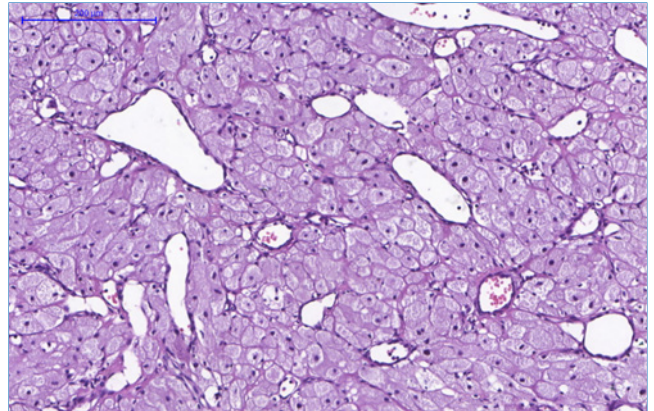


Figure 4. Histopathological features of CGCT. Blood vessels of varied shapes and sizes amid the granular cells (H&E; 400x magnification).

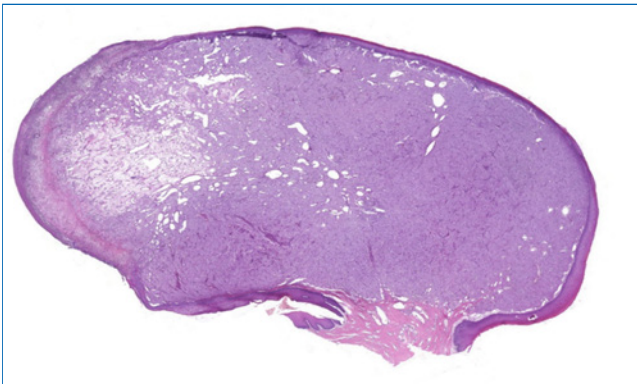


Figure 2. Histopathological features of CGCT. Well-circumscribed lesion characterized by the proliferation of polygonal cells amid a sparse stroma (H&E; 40x magnification).

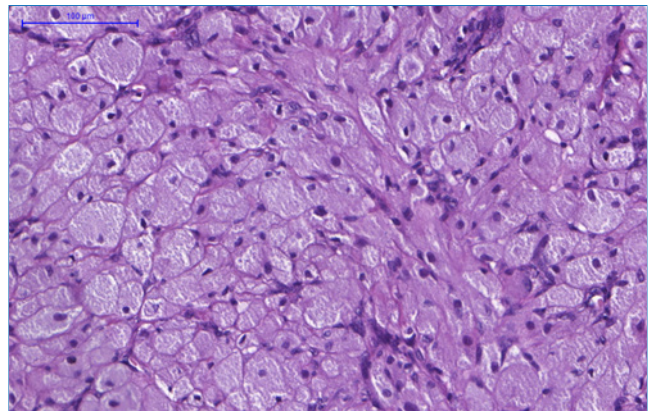


Figure 5. Histopathological features of CGCT. In detail, the cells show a rounded morphology and an abundant and eosinophilic cytoplasm with granules. The basophilic nuclei, with a rounded-to-oval shape, are positioned at the cell periphery (H&E; 400x magnification).

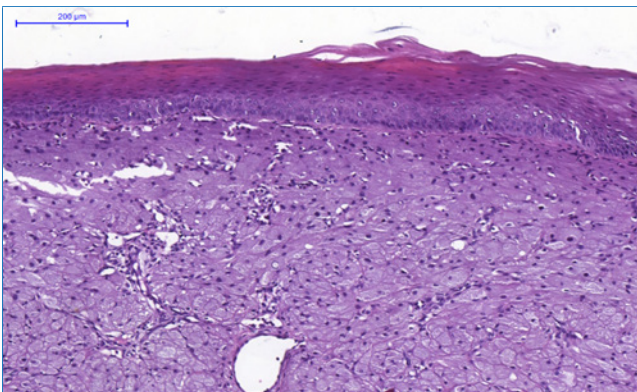


Figure 3. Histopathological features of CGCT. The lesion is lined by a parakeratinized stratified squamous epithelium exhibiting atrophy. There are lesion cells in the lamina propria (H&E; 100x magnification).

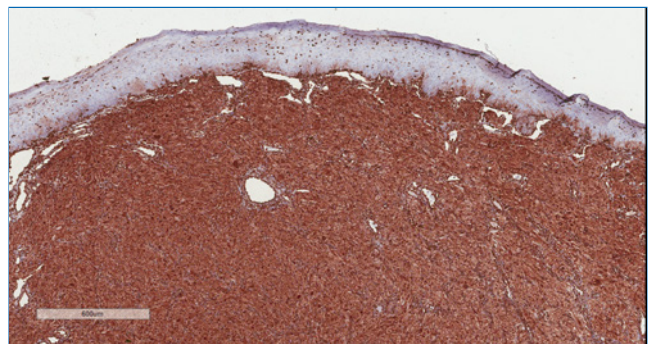


Figure 6. Immunohistochemical features of CGCT. Diffuse immunoreactivity for vimentin (400x magnification).

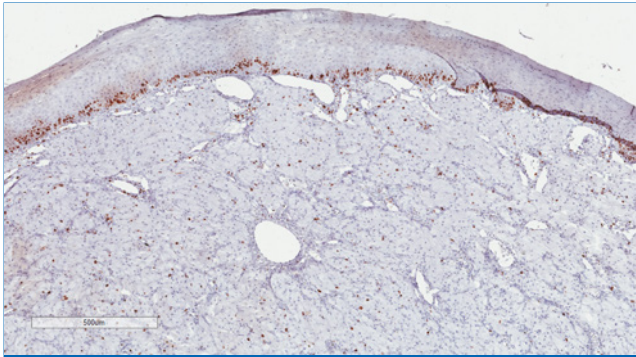


Figure 7. Immunohistochemical features of CGCT. Low proliferative index through analysis of Ki-67 immunoreactivity (400x magnification).

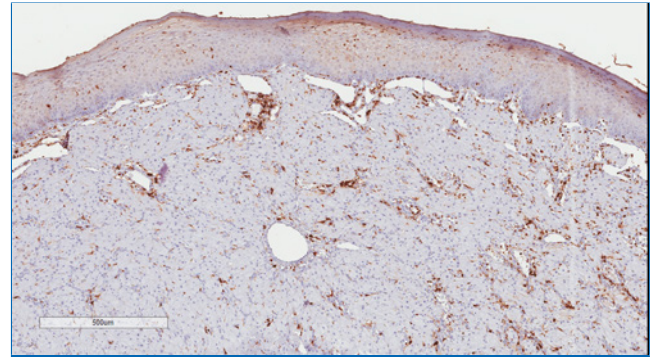


Figure 8. Immunohistochemical features of CGCT. Granular cells exhibit immunonegativity for S100 (400x magnification).

Discussion and conclusions

CGCT was originally described by Neumann, who called it “congenital epulide.”¹¹ Since then, few cases have been reported in the literature. In the last 5 years, only 22 studies^{2,7,10,12-30} reporting CGCT occurrence were published (Table 1). The Greek-derived term “epulid” means “swollen gums” and is nonspecifically used in dentistry for hyperplastic lesions in the gingival tissue. The use of more specific terminology to name CGCT has been suggested, including “congenital granular cell lesion,” “newborn gingival granular cell tumor,” “newborn congenital epulis,” “congenital granular cell myoblastoma,” and “granular cell fibroblastoma.” However, due to the occurrence of extra-gingival cases, the term “congenital granular cell tumor” is likely most appropriate.^{9,31}

CGCT is most frequently located in the anterior maxillary alveolar ridge and has demonstrated a marked predilection for female neonates compared to males at a ratio of 8:1. Clinically, CGCT presents as solitary lesions that are rarely multiple, are similar in color to the mucosa (or reddish), of firm consistency, with a smooth and non-ulcerated surface, and with sessile or pedunculated implantation. Typically, the CGCT is 1 to 2 cm in diameter, despite some reports of lesions larger than 9 cm.^{1-3,5,31} The present case report has clinical characteristics consistent with the findings shown in the literature.

Although its histogenesis is not well established, some authors believe that CGCT is a reactive entity.^{1,3} Others believe that this lesion’s cellular phenotype is related to pericytic or myopericytic cells due to the marked vascularization typically observed in its stroma, with increased pericytic proliferation around small venules.⁵ Furthermore, due to its intrauterine origin and female predominance, the development of CGCT has been suggested as closely associated with maternal hormones.^{1,3,31} Despite a possible endogenous hormone influence, this hypothesis becomes untenable when considering the absence of estrogen or progesterone receptors in the lesion cells. Thus, the reason for the female gender preference is still uncertain.^{5,8,32}

Due to CGCT’s rarity, healthcare professionals sometimes cannot clinically recognize it, leading to misdiagnoses. It is thus extremely important to perform an adequate anamnesis that, together with microscopic aspects, can facilitate diagnosis. Upon histopathological examination, CGCT is very similar to

granular cell tumors: both lesions exhibit tumor growth composed of polygonal eosinophilic cells containing cytoplasmic granules.^{5,33} However, while CGCT demonstrates atrophy of the epithelium lining, the granular cell tumor has a characteristic pseudoepitheliomatous hyperplasia in its epithelial lining. Although both lesions have a predilection for females, their location differs: CGCT exclusively affects the alveolar ridge of newborns, while granular cell tumors can affect many sites in the body, despite being more common in the tongue, and are most common between the third and sixth decades of life.^{1,3}

In differential diagnosis, other lesions that present granular cells should be considered, such as granular cell melanoma, certain fibro-histiocytic neoplasms, smooth muscle tumors, and soft-tissue alveolar sarcoma. Immunohistochemical techniques can be used as a complementary tool to characterize the lesion better and discard other histologically similar lesions. Previous studies have evaluated the immunoreactivity of proteins such as S100, smooth muscle actin (SMA), desmin, calponin, neuro-specific enolase (NSE), CD68, vimentin, cytokeratins (CKs), CD34, CD31, and Ki-67.⁵ In the present study, we observed lesion cells’ immunopositivity for vimentin, negativity for S100, and a low cell proliferation index in Ki-67 analysis. These findings reinforced CGCT’s non-neoplastic nature and suggested a mesenchymal origin. CGCT immunohistochemical profile analysis increases diagnostic accuracy and enables clinical management and treatment.

In contrast to granular cell tumors, which present granular cells immunoreactive for vimentin and S100, CGCT’s lesion cells present strong and diffuse immunostaining for vimentin, negativity for S100, and weak, focal immunostaining for Ki-67.^{1-3,29} Immunoreactivity for S100 and NSE in the granular cell tumor suggests a Schwann-cell origin. On the other hand, CGCT is usually negative for S100 and positive for vimentin, suggesting a mesenchymal origin. However, CGCT positivity for NSE has been reported, indicating a possible neural origin.^{1,2}

Although uncommon, spontaneous remission is possible because CGCT’s growth tends to cease after birth, as in cases of small lesions that do not interfere with breathing or feeding.³⁴ Yet, most studies recommend surgical excision of the lesion under local or general anesthesia.^{1,3,10} There are no reports of recurrence after surgical CGCT excision, even when there are tissue remnants of the lesion.^{4,3} In addition to surgical excision, techniques using electrocautery and carbon di-

Table 1. Summary of clinical cases reported in the literature in the last 5 years.

Authors	Sex / age	Predilection site	Clinical aspects	Histologic appearance	Immuno-histochemistry
Present case	F/10 days old	Maxillary alveolar ridge	Nodular appearance, healthy color, firm. Asymptomatic	Rounded polygonal cells with abundant eosinophilic granular cytoplasm and basophilic nuclei	NR
Cheung et al., 2020 [2]	F/ Newborn	Maxillary alveolar ridge	Sessile smooth pink lesion. Asymptomatic	Sheets of polygonal cells with eosinophilic granular cytoplasm and eccentric nuclei.	S-100 (-), Vimentin (+)
Pasqual et al., 2020 [13]	F/ Newborn at 38 weeks and 3 days of gestation	Right upper gingival line	Nodular appearance, measuring 1 × 0.8 × 0.6 cm	Polygonal cells with eosinophilic granular cytoplasm and eccentric nuclei.	S-100 (-), CK (-), CD68 (+)
Jain et al., 2019 [14]	F/ 13 days old	Alveolar, left maxilla Alveolar, left lower arch	Pedunculated firm smooth pink mass, 2.5 x 2 x 1.5 cm. Asymptomatic Similar type mass of size 1x1 cm	Flattening of rete ridges and tumor cells arranged in sheets in the dermis. Polygonal cells with granular cytoplasm, central-to-eccentric vesicular nucleus, vessels and lymphocytes interspersed amid them	NR
McAllister, O'Neill & Devlin, 2019 [15]	F/ 4 days old	Anterior region of the maxillary alveolar ridge	Pedunculated firm, smooth mass measuring 20 × 10mm	Sheets of large polygonal cells with eosinophilic granular cytoplasm, small central nuclei, and occasional odontogenic rests	NR
Mizutani et al., 2019 [16]	M/ newborn at 40 weeks of gestation	Maxillary alveolar ridge	Multiple nodules. Measuring 2.0 cm	Proliferation of large polygonal cells with demarcated cell membrane, granular cytoplasm, and small uniform nuclei	S-100 (-)
Rodrigues et al., 2019 [17]	F/ 16 days old	Anterior maxillary alveolar ridge	Nodular pink-to-red appearance, smooth surface, firm consistency.	Sheets of polygonal cells with eosinophilic granular cytoplasm and basophilic nuclei	S-100 (-)
Wong et al., 2019 [7]	F/ 2 months old	1. Maxillary alveolar ridge 2. Mandibular alveolar ridge.	2 sessile masses of firm consistency. Not removed.	NR	NR
Dhareula et al., 2018 [18]	F/ 2 days old	Anterior maxillary alveolar ridge	2 sessile masses of nodular appearance and smooth surface. Measuring 3.5 x 2.0 × 4.0 cm	Sheets of polygonal cells with an eosinophilic granular cytoplasm	S-100 (+)
Gardner & Rozzele, 2018 [12]	F/ 6 days old	Mandibular alveolar ridge	1.5-cm pedunculated soft-tissue mass with adjacent secondary 8-mm mass	Squamous mucosa with underlying large polyhedral cells containing granular acidophilic cytoplasm as well as small hyperchromatic nuclei	S-100 (-)
Kaminecki et al., 2018 [19]	F/ 2 days old	1. Tip of the tongue. 2. Ventral surface of the tongue.	Pedunculated multilobulated mass preventing mouth closing	Large oval granular cells with abundant eosinophilic cytoplasm and keratinized stratified squamous epithelium	S-100 (-), Vimentin (+) PAS (+)
Kokubun et al., 2018 [32]	F/ 1 day old	Anterior mandibular ridge	Pedunculated mass with a healthy color measuring 20 × 10mm	Proliferation of large polygonal cells with demarcated cell membrane, granular cytoplasm, and small uniform nuclei	Vimentin (+) CD68 (+) CD44 (+) S-100 (-) NSE (-) Desmin (-) CD34 (-)
Sasaki et al., 2018 [20]	F/ 1 day old	Maxillary alveolar ridge	Pedunculated mass with a healthy color measuring 15 × 15mm	Proliferation of large cells with granular cytoplasm under the squamous epithelium	CD68 (+)

Table 1. Summary of clinical cases reported in the literature in the last 5 years. (cont.)

Authors	Sex / age	Predilection site	Clinical aspects	Histologic appearance	Immuno-histochemistry
Anisowicz et al., 2017 [21]	F/ Newborn at 38 weeks and 4 days of gestation	Anterior maxillary alveolar ridge	Nodular pink-to-red appearance, smooth surface, firm consistency.	Many polygonal cells with eosinophilic granular cytoplasm and small round nuclei.	NR
Johnson et al., 2017 [25]	F/ Newborn at 32 weeks and 6 days of gestation	Maxillary alveolar ridge	Nodular pink-to-red appearance, smooth surface, firm consistency.	NR	NR
Podestá et al., 2017 [22]	F/ 7 days old	Maxillary alveolar ridge	Multiple pink-to-red pedunculated lesions.	Polygonal cells with eosinophilic granular cytoplasm and hyperchromatic oval nuclei	NR
Vinay et al., 2017 [10]	F/ 2 days old	Maxillary alveolar ridge	Solitary, firm pedunculated mass, measuring about 3.5 cm	Polygonal rounded cells with abundant eosinophilic granular cytoplasm and basophilic nuclei	NR
Yıldırım et al., 2017 [23]	F/ 2 days old	Right posterior region of the maxillary alveolar ridge.	Pedunculated firm smooth lesion measuring 4.0 × 7.0mm	Polygonal cells with eosinophilic granular cytoplasm and small round nuclei.	S-100 (-)
Halka et al., 2016 [24]	F/ Newborn	Maxillary alveolar ridge	NR	NR	NR
Wong et al., 2016 [27]	F/Newborn	Maxillary alveolar ridge	Pedunculated lesion measuring 5.0 x 3.0 x 3.0 cm	Polygonal cells with eosinophilic granular cytoplasm and small round nuclei	NR
Yancoskie et al., 2016 [28]	F/ 2 days old	Anterior ventral tongue	Firm, non-pulsatile pedunculated mass, measuring 2.0 x 1.5 cm	Squamous epithelium lacking rete ridges with an underlying submucosal proliferation composed almost entirely of large rounded and polyhedral cells with small oval dark nuclei and abundant eosinophilic granular cytoplasm. The granular cells abutted the overlying epithelium. The stroma consisted of minimal fibrous tissue and rare vascular channels.	CD68 (+) S-100 (-)
	F/ 2 days old	Ventral tongue	Pedunculated smooth mucosal-colored mass of 0.8 x 0.6 x 0.4 cm. Asymptomatic.	Epithelium lacking rete ridges, overlying a sheet-like proliferation of granular cells with small hyperchromatic nuclei and abundant eosinophilic cytoplasm.	Vimentin (+) CD68 (+) S-100 (-) alpha-smooth (-) muscle actin (-)
Bianchi et al., 2015 [34]	F/ neonate	1. Anterior maxillary alveolar ridge 2. Anterior mandibular alveolar ridge	Two pedunculated reddish nodules with an irregular surface, located in the mandible and maxilla, measuring about 3 cm.	Proliferation of large round granular cells with abundant cytoplasm and basophilic nuclei	S-100 (-) CD34 (-) CD 105 (-) CD 68 (+) VEGF (+) FGF (+) D2-40 (+) Ki-67 (+)
Rajendran et al., 2015 [26]	2 F/ Newborn	1. Mandibular alveolar ridge. 2. Maxillary alveolar ridge	1. Large bilobed mass of 7.0 x 7.0 x 5.0 cm 2. Firm pink sessile mass of 2.0 x 2.0 cm	1. Polygonal cells with an eosinophilic granular cytoplasm 2. Surgical removal was not performed	Vimentin (+)

F – female; M – male; SMA – smooth-muscle actin; CK – cytokeratin; NSE – neuron-specific enolase; NR – not reported

oxide laser, or even gingivoperiosteoplasty, can be used for subsequent primary alveolar reconstruction, promoting proper alignment and normal dental development.³⁰

The present study reviews CGCT's histopathological and immunohistochemical characteristics, comparing them with data reported in the literature and emphasizing the differential diagnosis from other oral lesions. Due to CGCT's rarity, studies that analyze its clinicopathological and immunohistochemical characteristics can provide greater knowledge, enabling better diagnosis and clinical management.

Conflict of interest

The authors have no conflicts of interest to declare.

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Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).





Confidentiality of data. The authors declare that they have followed their work center protocols on access to patient data and for its publication.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Yailit Del Carmen Martínez Vargas: Conceptualization, Data curation, Project administration, Visualization, Writing – original draft, Writing – review & editing; **Rani Iani Costa Gonçalves:** Conceptualization, Data curation, Methodology, Visualization, Writing – original draft, Writing – review & editing; **Danielle Machado Farias:** Data curation, Validation, Visualization, Writing – review & editing; **Lélia Maria Guedes Queiroz:** Formal analysis, Investigation, Project administration, Supervision, Visualization, Writing – review & editing.

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