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Congenital granular cell epulis: case report and differential diagnosis

Epúlide de células granulares congênita: relato de caso e diagnóstico diferencial

Katianne S. Rodrigues; Caio César S. Barros; Ondina Karla M. S. Rocha; Luiz Arthur B. Silva; Marina B. Paies; Márcia Cristina C. Miguel

Universidade Federal do Rio Grande do Norte (UFRN), Natal, Rio Grande do Norte, Brazil.

ABSTRACT

A 16-days-old female patient exhibiting an exophytic nodular lesion located at anterior maxilla on the alveolar ridge since birth. The clinical hypothesis of congenital granular cell epulis (CGCE) was established, and the patient underwent excisional biopsy. Microscopically, a sheet-like proliferation of eosinophilic cells with granular cytoplasm was observed in a stroma of vascularized fibrous connective tissue. The immunohistochemical analysis for S100 evidenced the absence of immunostaining. The CGCE hypothesis was confirmed and, after six months, the patient showed no signs of recurrence of the lesion.

Key words: congenital; gingival diseases; granular cell tumor; differential diagnosis.

RESUMO

Paciente do sexo feminino, 16 dias de idade, exibiu lesão exofítica de aspecto nodular localizada em região anterior do rebordo alveolar maxilar desde o nascimento. A hipótese clínica de epúlide de células granulares congênita (ECGC) foi estabelecida, e a paciente foi submetida à biópsia excisional. Microscopicamente, observou-se a proliferação em lençol de células eosinofílicas com citoplasma granular em meio a um estroma de tecido conjuntivo fibroso vascularizado. A análise imuno-histoquímica para S100 evidenciou ausência de imunomarcação. A hipótese de ECGC foi confirmada e, após seis meses, a paciente não apresentou sinais de recidiva da lesão.

Unitermos: *congênito; doenças da gengiva; tumor de células granulares; diagnóstico diferencial.*

RESUMEN

Niña de 16 días de edad, presentaba una lesión exofítica de aspecto nodular ubicada en la región de la cresta alveolar maxilar anterior desde su nacimiento. Se estableció la hipótesis clínica de épulis congénito de células granulares, y la paciente se sometió a una biopsia por escisión. Microscópicamente se ha observado una proliferación laminar de células eosinofílicas con citoplasma granular en medio de un estroma de tejido conectivo fibroso vascularizado. El análisis inmunohistoquímica para S100 reveló ausencia de inmunomarcación. La hipótesis de épulis congénito ha sido confirmada, y, después de seis meses, la paciente no mostró señales de recidiva de la lesión.

Palabras clave: *congénito; enfermedades de las encías; tumor de células granulares; diagnóstico diferencial.*

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INTRODUCTION

Congenital granular cell epulis (CGCE) is an uncommon benign lesion of unknown etiology that mainly affects the alveolar mucosa of fetuses and neonates, which may cause respiratory and feeding difficulties[1]. The clinical diagnosis can be performed during intrauterine life from the 27th week, by three-dimensional ultrasound and magnetic resonance imaging (MRI), or just at birth, depending on the size of the lesion[2, 3].

The CGCE has a predilection for Caucasian females, with ratio of 10:1[1, 4]. Clinically, in most cases it presents as a solitary, pedunculated nodule, firm in consistency, located mainly at anterior maxilla region[5]. However, in extremely rare cases, it may also involve the underside of the tongue or present as multiple lesions[3, 6].

It is mandatory to perform the clinical differential diagnosis of CGCE with other lesions affecting the oral cavity, such as teratoma, hamartoma, choristoma, fibroma, hemangioma, lymphangioma, rhabdomyoma, rhabdomyosarcoma and granular cell tumor[2, 3]. Microscopically, it is similar to the granular cell tumor, both of which are composed of a proliferation of large eosinophilic cells with granular cytoplasm. However, the knowledge of some clinical, structural and immunohistochemical differences guarantees its definitive diagnosis[4, 7-9].

The objective of the present report is to describe the clinical, pathological and immunohistochemical characteristics of CGCE, as well as to perform its clinical and histopathological differential diagnosis.

CASE REPORT

Newborn Caucasian female patient, 16 days of age, showing lesion at birth. In the intraoral examination was observed a nodular exophytic lesion of pink to red color and smooth surface, firm in consistency, located at the alveolar ridge of the anterior maxilla region (**Figure 1**). The clinical hypothesis of CGCE was suggested, and performing an excisional biopsy under local anesthesia was the procedure of choice. The surgical specimen was sent to anatomopathological examination.

The histopathological analysis revealed the presence of a benign lesion fragment characterized by a sheet-like proliferation of large eosinophilic cells with granular cytoplasm merged in a stroma of richly vascularized fibrous connective tissue. In addition, areas of ulceration and atrophy of the crests of the lining epithelium were also observed (**Figures 2A**, **2B** and **2C**). To confirm the diagnosis, immunohistochemistry was performed for S100, which was negative (**Figure 2D**). Therefore, the diagnosis of CGCE was established. The patient currently is under medical followed up, presenting weight gain and normal oral mucosa.

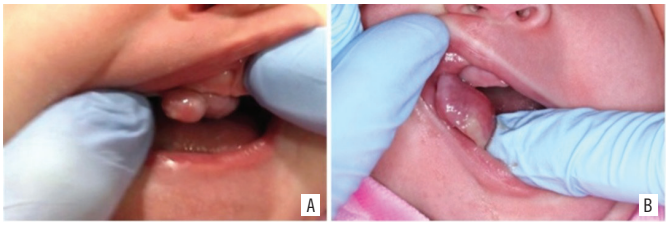

FIGURE 1 – *Clinical aspect*

A and B) clinical aspect of the lesion evidencing a nodule in the alveolar ridge of the anterior maxilla region.

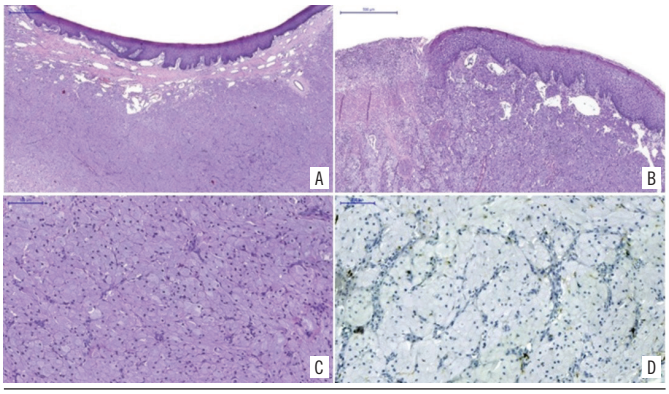

FIGURE 2 – *Microscopy*

A and B) 500 µm; histopathological aspects evidencing a benign lesion fragment characterized by sheet-like proliferation of large/bulky eosinophilic cells; C) 100 µm; with granular cytoplasm and round, basophilic nucleus (HE); D) 100 µm; immunohistochemical expression for S100.

HE: hematoxylin and eosin.

DISCUSSION

The CGCE is a relatively rare lesion, presenting only about 250 cases registered in the literature since its first description in 1871 by Neumann[10]. The term CGCE was established by the World Health Organization (WHO) in 2005 and is still the same since its last classification in 2017[11, 12]. However, this lesion is also found in the literature with other terms, such as congenital epulis, congenital epulis of the newborn, congenital granular cell lesion, congenital gingival granular cell tumor, congenital myoblastoma, and Neumann's tumor[4, 5, 13, 14].

The pathogenesis and histogenesis remain unclear, although some authors believe that this lesion is a reactive or degenerative process, and not a true neoplasm[7]. Furthermore, many authors suggest that lesion growth due to maternal hormones effects during pregnancy, such as increased levels of estrogen and progesterone, especially in the third trimester, which is the period in which there is a greater development of the lesion. This hypothesis corroborates the fact that the CGCE growing ceases after birth[15, 16].

Regarding the histogenesis, several immunohistochemical and ultrastructural studies have managed to identify the origin of CGCE, which consider that this lesion may originate from the odontogenic epithelium or it may be fibroblastic, myogenic, neurogenic, histiocytic and endothelial, or from undifferentiated mesenchymal cells. This last hypothesis is the most accepted, assuming that the CGCE is a degenerative process of the cells, which are able to differentiate into several cell types[1, 2, 8, 16-18].

Some authors have evaluated the immunohistochemical profile of CGCE in order to elucidate its histogenesis. Leocata *et al*. (1999)[17] obtained positive immunostaining for vimentin and desmin, while Kokubun *et al*. (2018)[5] found positive for vimentin, CD44, CD68 and marker of undifferentiated mesenchymal stem cells (STRO-1). Therefore, it is not possible to confirm the histogenetic origin of the CGCE, but a mesenchymal origin is suggested[5, 17]. Furthermore, in the aforementioned studies, no immunopositivity was observed for S100 protein, nerve growth factor receptor (NGFR), neurotrophin receptor (P75), carcinoembryonic antigen (CEA), macrophage marker antibody (MAC 387), CD34, lysozyme polyclonal antibody, leukocyte common antigen (LCA) and muscle-specific actin (HHF-35), strengthening the hypothesis of an origin from undifferentiated mesenchymal cells.

The differential clinical diagnosis of CGCE is broad; however, characteristics related to the period of development, site of involvement, lesion size and growth potential may help in the exclusion of other lesions that perform the differential diagnosis with CGCE[2-4, 8].

Among the histopathological differential diagnoses are granular cell lesions, such as granular cell tumor (GCT), granular cell odontogenic tumor and adult rhabdomyoma, therefore, knowledge of its clinical and histopathological characteristics is crucial for performing a correct diagnosis. From these lesions, the GCT stands out[7-9].

Clinically, GCT is a true neoplasm that affects mainly adults between 30 and 60 years of age, and it is mainly found on the tongue. On the other hand, the CGCE is a non-neoplastic reactive process that manifests in fetuses and neonates, with a preference for the alveolar ridge[1, 8]. By microscopic examination, GCT exhibits large polygonal cells with granular cytoplasm and pseudoepitheliomatous hyperplasia, whereas in CGCE there is atrophy of the epithelial ridges in the lining epithelium[2, 4]. Regarding immunohistochemistry, GCT is positive for S-100 protein, which suggests that this tumor is derived from Schwann cells; while CGCE has negative expression for S-100 protein, testifying different origins between these lesions, aiding in the differential diagnosis[5, 9, 19]. In the present report, based on clinicopathological characteristics and negative immunohistochemical expression for S100 protein, the diagnosis of GCT was excluded.

The treatment of CGCE is surgical excision, since there are few reports of regression of the lesion, beyond this, it may result in mouth closing limitations and respiratory and feeding difficulties, interfering in the patient's quality of life[14, 16]. It presents an excellent prognosis, and there are no reports of recurrence in the literature[3, 19].

CONCLUSION

CGCE is a rare entity of uncertain histogenesis, which main differential diagnosis is GCT. Although these lesions are microscopically similar, both present different clinical aspects and immunohistochemical profiles, which allow the differentiation between them and help to establish the definitive diagnosis.

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CORRESPONDING AUTHOR

Márcia Cristina da Costa Miguel 0000-0002-6661-2566
e-mail: mccmiguel@hotmail.com