

## Clinical and imaging features and treatment of Calcifying Odontogenic Cyst in a patient with Autistic Spectrum Disorder – case report

Características clínicas, imaginológicas e tratamento do Cisto Odontogênico Calcificante em paciente com Transtorno do Espectro Autista – relato de caso

Características clínicas, imagenológicas y tratamiento de Quiste Odontogénico Calcificante en paciente con Trastorno del Espectro Autista – reporte de caso

Received: 03/27/2022 | Reviewed: 04/02/2022 | Accept: 04/09/2022 | Published: 04/15/2022

**Ellen Maiany Ribeiro Santana**

ORCID: <https://orcid.org/0000-0001-5547-2417>

Federal University of Sergipe, Brazil

E-mail: [ellenmaianyrs@gmail.com](mailto:ellenmaianyrs@gmail.com)

**Manuela da Silva Oliveira**

ORCID: <https://orcid.org/0000-0001-9578-2970>

Federal University of Sergipe, Brazil

E-mail: [manu.silvaoliveira23@gmail.com](mailto:manu.silvaoliveira23@gmail.com)

**Mônica Christine Alves Cabral Cardoso**

ORCID: <https://orcid.org/0000-0001-9030-4726>

Private practitioner, Brazil

E-mail: [monica\\_chriscabral@hotmail.com](mailto:monica_chriscabral@hotmail.com)

**Álvaro Bezerra Cardoso**

ORCID: <https://orcid.org/0000-0002-6725-1547>

Federal University of Sergipe, Brazil

E-mail: [alvarobcardoso@yahoo.com.br](mailto:alvarobcardoso@yahoo.com.br)

### Abstract

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder of multifactorial etiology involving genetic and environmental factors. This population is more susceptible to develop problems such as dental caries and periodontal disease; however, it is very rare in relation to the involvement of oral cysts and neoplasms. Calcifying odontogenic cyst (COC) is an uncommon lesion, accounting for 1% to 3% of all odontogenic cysts. In most cases, its location is intraosseous, but the peripheral form may be present. Clinically, it presents as asymptomatic swelling and is usually diagnosed on routine radiographs. Due to the low risk of recurrence and favorable prognosis, conservative treatment with local excision through enucleation followed by curettage is recommended. In extensive lesions, methods such as marsupialization or decompression are indicated prior to complete removal in order to preserve adjacent noble structures. The purpose of this paper is to report a COC case in an 18-year-old patient with ASD. The lesion was removed under general anesthesia. The patient has been on follow-up for one year and there is no recurrence. This seems to be the first report in a patient with ASD.

**Keywords:** Calcifying odontogenic cyst; Autistic spectrum disorder; Gorlin's cyst; Odontogenic cysts.

### Resumo

O Transtorno do Espectro Autista (TEA) é uma desordem do neurodesenvolvimento, de etiologia multifatorial com envolvimento de fatores genéticos e ambientais. Esta população apresenta maior suscetibilidade para desenvolver problemas como cárie dentária e doença periodontal, entretanto, é bastante rara em relação ao acometimento por cistos e neoplasias bucais. O cisto odontogênico calcificante (COC) é uma lesão incomum, responsável por 1% a 3% de todos os cistos odontogênicos. Na maioria dos casos, sua localização é intraóssea, porém a forma periférica pode estar presente. Clinicamente, apresenta-se como um edema assintomático e, geralmente, são diagnosticados em radiografias de rotina. Devido ao baixo risco de recidiva e ao prognóstico favorável, o tratamento conservador com excisão local, através da enucleação seguida de curetagem, é recomendado. Em lesões extensas, métodos como marsupialização ou decompressão são indicados, previamente a remoção completa, com intuito de preservar estruturas nobres adjacentes. O objetivo desse trabalho é relatar um caso de COC em um paciente portador do Espectro do Transtorno Autista (TEA) com 18 anos de idade. A lesão foi removida sob anestesia geral. O paciente está em acompanhamento há 1 ano e não há recidiva. Este parece ser o primeiro relato em um paciente com TEA.

**Palavras-chave:** Cisto odontogênico calcificante; Transtorno do espectro autista; Cisto de Gorlin; Cistos odontogênicos.

## Resumen

El Trastorno del Espectro Autista (TEA) es un trastorno del neurodesarrollo de etiología multifactorial que involucra factores genéticos y ambientales. Esta población es más susceptible a desarrollar problemas como caries dental y enfermedad periodontal, sin embargo, es bastante raro en relación a la afectación por quistes y neoplasias orales. El quiste odontogénico calcificante (COC) es una lesión poco común, que representa del 1% al 3% de todos los quistes odontogénicos. En la mayoría de los casos su localización es intraósea, pero puede presentarse una forma periférica. Clínicamente, se presenta como una inflamación asintomática y generalmente se diagnostica en radiografías de rutina. Debido al bajo riesgo de recurrencia y al pronóstico favorable, se recomienda el tratamiento conservador con escisión local, mediante enucleación seguida de curetaje. En lesiones extensas están indicados métodos como la marsupialización o la descompresión, previa a la extirpación completa, para preservar las estructuras nobles adyacentes. El objetivo de este trabajo es reportar un caso de AOC en un paciente de 18 años con Trastorno del Espectro Autista (TEA). La lesión se extirpó bajo anestesia general. El paciente ha sido seguido durante 1 año y no hay recurrencia. Este parece ser el primer informe en un paciente con TEA.

**Palabras clave:** Quiste odontogénico calcificante; Desorden del espectro autista; Quiste de Gorlin; Quistes odontogénicos.

## 1. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impairments in communication and social relationships. The prevalence in the world population is roughly 1%, affecting more males than females, and the presence of associated comorbidities is common (> 70% have concomitant disorders) (Lai, Lombardo, & Baron-Cohen, 2014). Although its etiology is still uncertain, the current trend is to consider it of multifactorial origin, involving genetic and environmental factors (Lai, Lombardo, & Baron-Cohen, 2014). The literature suggests that individuals with this disorder have a higher risk and susceptibility to develop chronic non-transmissible oral health problems, such as dental caries and periodontal disease (Ferrazzano et al., 2020). However, incidence of oral cysts and neoplasms is uncertain, as the respective relationship with ASD is quite rare in the scientific literature.

Calcifying Odontogenic Cyst (COC) is a pathology that has undergone changes in its classification and terminology over the years. In 1917, Thoma reported a COC case associated with odontoma, providing the first clinical and radiographic evidence of this lesion, but only in 1962 its characteristics were described in detail by Gorlin et al. (Ide et al., 2015). Since then, there has been much debate on whether COC is a developmental cyst or a neoplasm (Gorlin et al., 1962; Ide et al., 2015). Currently, according to the latest 2017 WHO classification, COC is included in the group of odontogenic cysts (Speight & Takata, 2018).

Clinically, COC is a mostly intraosseous lesion; however, the peripheral variant can be found. They are usually asymptomatic diagnosed by routine radiographs. Commonly, it presents as a unilocular, well-defined radiolucency with the presence of radiopaque structures within the lesion (José Alcides A. de Arruda et al., 2018; de Arruda et al., 2018; Neville et al., 2009). The radiographic features of COC can be related to some distinct pathologies that should be considered in the differential diagnosis. In the presence of radiopaque masses, it should be considered the possibility, mainly, of ossifying fibroma, adenomatoid odontogenic tumor, calcifying epithelial odontogenic tumor, and odontoma (Rodrigues Fregnani et al., 2003; Souza et al., 2007). When fully radiolucent, other cystic lesions should be included, such as: odontogenic keratocyst, dentigerous cyst, root cyst, residual cyst, or even tumors, such as ameloblastoma, ameloblastic fibroma, and myxoma (Rodrigues Fregnani et al., 2003; Uzun & Çinpölat, 2019).

Due to the low risk of recurrence, conservative treatment with local excision by enucleation followed by curettage is recommended prior to complete removal. Methods such as marsupialization or decompression are indicated for extensive lesions, mainly to preserve adjacent noble structures (Daniels, 2004; José Alcides A. de Arruda et al., 2018; de Moraes et al., 2020).

This paper aims to report a COC case in an ASD patient surgically treated under general anesthesia, addressing the

diagnostic process and surgical method, as well as the relationship with ASD patients.

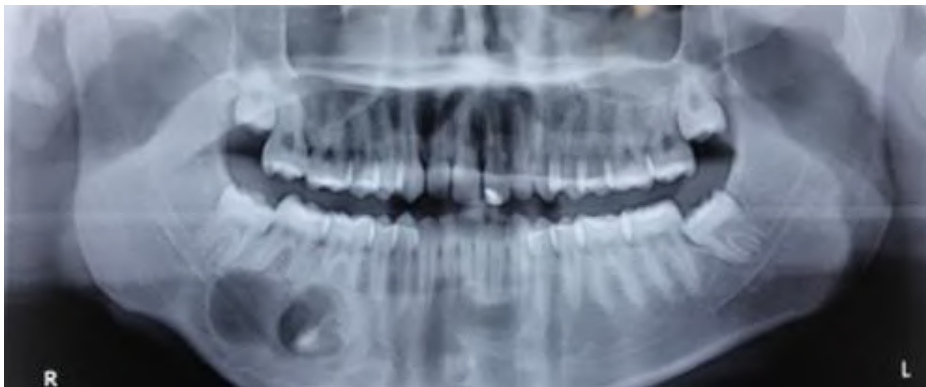
## 2. Case Report

The appropriate consents statement for publication and participation was provided for the authors. And the ethics approval was obtained from the local ethics committee under number 4.544.848.

An 18-year-old male melanodermic patient with ASD, without associated comorbidities, was referred to the Oral and Maxillofacial Surgery and Traumatology Department of the University Hospital of Sergipe (HU/UFS) due to the presence of an intraosseous lesion in the posterior region of the right mandible, identified by routine radiographic examination.

No facial asymmetry was perceived on extraoral physical examination. However, the intraoral examination revealed the presence of a bulging bottom of the vestibule in the posterior region of the right mandible, with normal coloring, smooth surface, and asymptomatic. Radiographic examination (Fig. 1) revealed a well-defined, multilocular radiolucent intraosseous lesion with radiopaque structure inside, apical to teeth 45 to 47.

**Figure 1:** Panoramic radiograph showing a well-defined, multilocular radiolucent intraosseous lesion with a radiopaque structure in the posterior region of the mandible, apical to units 45 to 48.



Source: Authors.

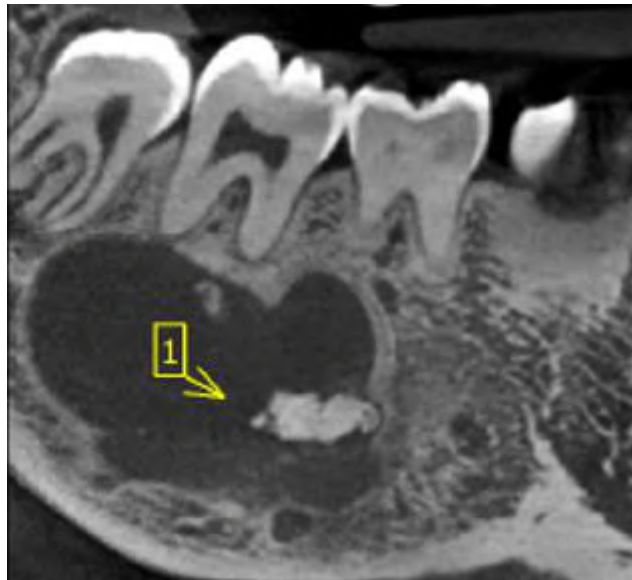
Cone Beam Computed Tomography (CBCT) was requested (Figs. 2 and 3) and it showed the presence of a hypodense image, with defined limits and festered borders, located in the posterior right mandible region (DUs. 45 to 48). The lesion had approximately 38.0 x 21.8 mm in its largest diameter and the presence of hyperdense images inside, suggesting calcification. Moreover, expansion of the buccal cortical bone, resorption of the root apices of dental units 45, 46, and 47, along with close contact with the mandibular canal were observed.

**Figure 2:** Cone Beam Computed Tomography. Transversal view showing expansion of the buccal cortical bone.



Source: Authors.

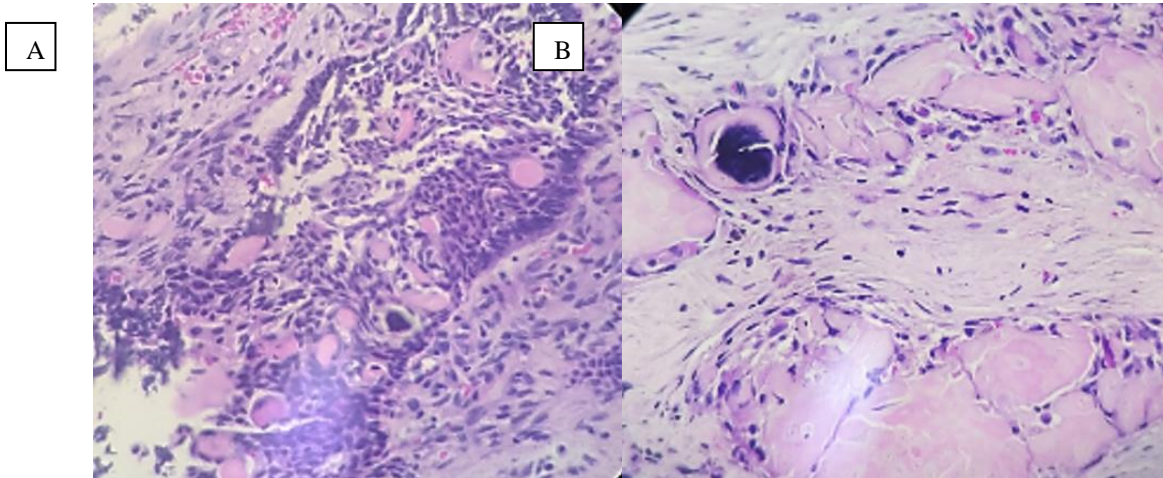
**Fig. 3** Cone Beam Computed Tomography. Sagittal view. 1- presence of hyperdense images inside, suggesting calcification.



Source: Authors.

Incisional biopsy was performed under local anesthesia in an outpatient clinic and the specimen was sent for histopathological analysis. The report revealed a fragment of a cystic odontogenic lesion with a fibrovascular capsule characterized by formations of eosinophilic dentinoid material. The lining epithelium showed variable thickness, presence of clear cells and ghost cells. The microscopic picture was compatible with COC (Fig.4).

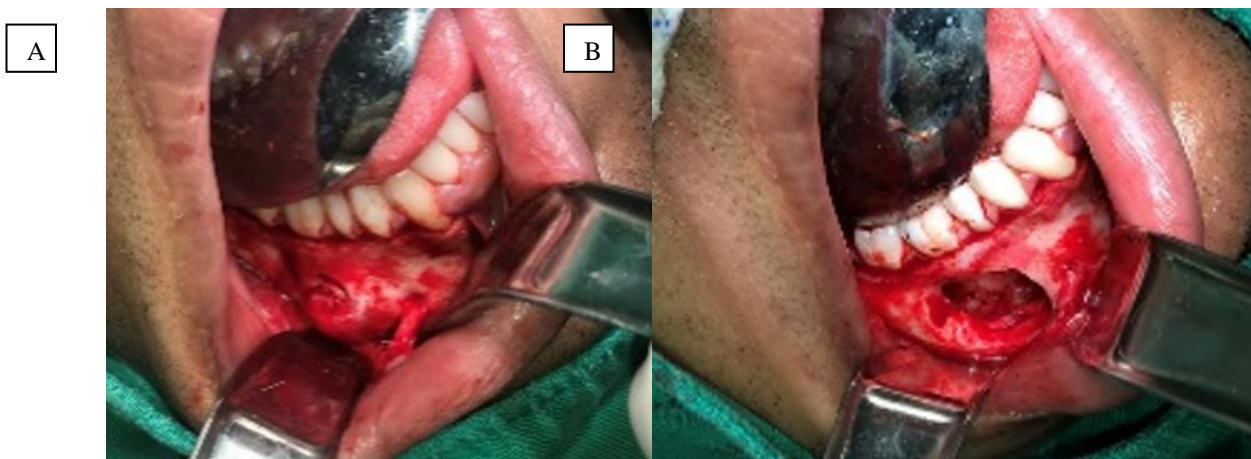
**Figure 4:** Microscopic picture. A – Presence of ghost cells within the epithelial component of the cyst (HE – 100x). B – Calcifications are observed within the ghost cells present in the capsule of the lesion (HE – 400x).



Source: Authors.

According to the established diagnosis, the excision of the intraosseous cyst (Fig. 5) was planned by enucleation, followed by curettage, under general anesthesia. The surgical specimen (Fig. 6) was sent again for histopathological analysis that confirmed the COC diagnosis. In the immediate postoperative period, the patient presented numbness in the lower lip on the right side due to paresthesia of the inferior alveolar nerve, but with complete remission in the 02-week postoperative period. Currently, the patient is being clinically and radiographically followed up for one year with no signs of recurrence (Fig.7).

**Figure 5:** Transoperative. A – Intraoral aspect of the lesion during cyst excision by enucleation and curettage under general anesthesia. B – Intraoral aspect after cyst excision by enucleation and curettage under general anesthesia.



Source: Authors.

**Figure 6:** Surgical specimen.



Source: Authors.

**Figure 7:** Panoramic radiograph of 1-year postoperative control, with no signs of recurrence.



Source: Authors.

### 3. Discussion

COC is a rare lesion with an estimated incidence of 1-3% of all odontogenic cysts and tumors. Currently, according to the 4th edition of the 2017 WHO classification, it is classified as an odontogenic cyst that has a solid variant called a dentinogenic ghost cell tumor (DGCT) with neoplastic features (Speight & Takata, 2018; de Arruda et al., 2018; Neville et al., 2009; Ledesma-Montes et al., 2008). The prevalence of the cystic form is 86% to 98%, while the neoplastic form is less common and constitutes 2% to 16% of cases (Neville et al., n.d.; Uzun & Çinpolat, 2019). Ledesma-Montes et al. (2008) showed that more than 85% of ghost cell lesions are simple, isolated cysts (65%) or associated with odontoma (22%), and only 5% of lesions were solid and can be considered true neoplasms (Ledesma-Montes et al., 2008). In another study where 52 COC cases were analyzed, Irani and Fouroghi (2017) were able to identify that 82.7% of the lesions were of the cystic type with four types of variants: 1) simple; 2) proliferative; 3) associated with odontoma and 4) ameloblastomatous (Irani & Foroughi, 2017). Still on this analysis, 17.3% were of the neoplastic type (Irani & Foroughi, 2017). In this clinical case, the lesion showed a cystic, multilocular form, with dentinoid material inside, but without association with the odontoma.

COC shows a slight predilection for young men in the second and third decades of life, mainly affecting the posterior mandible region (Daniels, 2004; Ledesma-Montes et al., 2008). However, some studies report no predilection for sex, age, and

location, occurring with equal frequency in the maxilla and mandible (Buchner, 1991). Clinically, intraosseous COC, in most cases, presents as a painless, and thus asymptomatic, edema and are usually diagnosed on routine radiographs (José Alcides A. de Arruda et al., 2018; Souza et al., 2007). Extraosseous presentation can occur in 13-30% of cases, with a preference for the anterior region of maxilla and mandible (Buchner, 1991; José Alcides A. de Arruda et al., 2018; José Alcides Almeida de Arruda et al., 2018). The clinical case reported is an intraosseous lesion in a young, melanodermic, male patient in the 2nd decade of life, who presented a slight increase in intraoral volume in the posterior region of the mandible. This was not identified by the patient or family members and was only observed after a routine radiographic examination by means of panoramic radiography.

COC has a variable radiographic appearance, ranging from a well-defined unilocular radiolucency to multiloculation, with the presence or absence of radiopaque structures within the lesion, or it can even be completely radiopaque (Daniels, 2004; José Alcides A. de Arruda et al., 2018; José Alcides Almeida de Arruda et al., 2018). The imaging exams of the patient showed a multilocular characteristic, of defined limits with approximately 38.0 x 21.8mm in its largest diameter and the presence of radiopaque/hyperdense images inside the lesion, suggesting calcifications. This characteristic, defined as mixed radiographic appearance corroborates with studies by Arruda et al. (2018) who suggested that the deposition and number of calcifications may be related to lesion size, i.e., as they grow, there is a greater deposition of calcified material (de Arruda et al., 2018). This was demonstrated by comparing radiolucent, mixed, and radiopaque lesions that had increasing sizes (mean: 32.0, 36.0, and 50.0 mm, respectively).

Interestingly, when COC is located near the apices of the teeth, there is a high incidence of root resorption (Rojo, Prados-Frutos et al., 2017; Souza et al., 2007). Daniels (2004) reported an incidence of root resorption in 75% to 77% of cases and concluded that COC should be included in the differential diagnosis of cystic lesions associated with root resorption of involved teeth. In addition, Yoshiura and collaborators (1998) observed features such as tooth displacement, bone expansion, cortical perforation, and association with impacted tooth by conventional radiographs and CT scans. In the present case, we observed cortical bone expansion (buccal and lingual) without perforations, external root resorption in the apices of dental units 45, 46, and 47, displacement of the mandibular canal and close contact with it.

COC can be related to other benign odontogenic tumors, mainly to odontoma in about 20% of cases (Chindasombatjaroen et al., 2012; Daniels, 2004; Gallana Alvarez et al., 2005; Rodrigues Fregnani et al., 2003), or even 26%, according to Buchner (1991) in a literature review of 200 cases, of which 52 were associated with odontoma. Chindasombatjaroen et al. (2012) demonstrated the occurrence of other lesions associated with COC, such as ameloblastoma, ameloblastic fibroma, ameloblastic fibro-odontoma, and adenomatoid odontogenic tumor. In the present case, although there was a radiopaque appearance inside the lesion, the histopathological report revealed that it was a deposition of dentinoid material without the formation of an associated odontoma.

Histologically, the COC is characterized as a cystic lesion composed of a fibrous capsule lined by an odontogenic epithelium with columnar and cuboidal cells resembling ameloblasts. In addition, it presents in the suprabasal layers structures analogous to the stellate reticulum (de Arruda et al., 2018; Santos et al., 2018). Other important findings associated with this type of lesion are: 1) the presence of a cluster of anucleated and slightly eosinophilic cells, with calcification capacity, known as ghost cells; and 2) the presence of dentinoid material in its structure (Irani & Foroughi, 2017; Santos et al., 2018). According to Khandelwal, Aditya, and Mhapuskar (2015), ghost cells have nuclear and cytoplasmic organelle remnants, and may or may not have filaments inside them. Some studies point to theories for the presence of these two elements, such as induction through granulation tissue or even the presence of ghost cells as a result of metaplastic changes (Irani & Foroughi, 2017). The clinical case reported brings as histological characteristics the presence of odontogenic cystic capsule formed by fibrovascular connective tissue, exhibiting epithelial lining with few cell layers that presented areas of deposition of dentinoid

material and ghost cells, consistent with the findings in the literature.

The indicated treatment for COC depends on issues such as location, lesion size, and histological type. In general, enucleation followed by curettage is the first choice for cystic types, while surgical resection is selected in cases of the neoplastic type (Daniels, 2004; Kim, Choi, & Ko, 2016). According to Amin, Maglioca, and Abramowicz (2020), the chosen treatment will depend on the variant and clinical behavior of the COC. Options include 1) enucleation followed by curettage, 2) decompression followed by enucleation and curettage, 3) enucleation and curettage associated with a peripheral ostectomy, and 4) segmental resection. The latter in cases where neoplastic features are present.

In a case report, Moraes et al. (2020) opted for the association of marsupialization and enucleation techniques due to the dimensions of the lesion, which was located in the region of the body, angle, and ascending ramus of the mandible, measuring approximately 7 cm in its largest diameter. Clinical radiographic follow-up after marsupialization was performed for four months, observing regression of tumor size and bone neoformation, enabling the execution of enucleation and curettage without compromising important structures (de Moraes et al., 2020). In the clinical case reported, the treatment was performed through enucleation followed by curettage, under general anesthesia. Although the lesion was in close contact with the inferior alveolar nerve, no marsupialization or decompression was previously chosen. The patient had a temporary paresthesia postoperatively, but with complete remission in two weeks.

The involvement of individuals with ASD by oral cysts and tumors is practically not described in the literature. The most cited data refer to the prevalence of dental caries and periodontal disease, as well as the need to perform procedures under general anesthesia due to the lack of cooperation of these patients (Corridore et al., 2020; da Silva et al., 2017). However, there are studies on the relationship of autism with malignancies, in which the increased risk of cancer in this population was studied by Chiang et al. (2015). The authors analyzed 8,438 patients diagnosed with autism in Taiwan between 1997 and 2011. In the study group, 20 presented some type of malignant neoplasm, including 06 cases (30%) of the hematological type. Only one case occurred in the head and neck region, in a salivary gland, with no statistically significant risk (Chiang et al., 2015).

Genetics is known to play a key role in the etiology of autism. Mutations in tumor suppressor genes and oncogenes have already been identified, as well as genetic alterations associated with both cancer and autism (Chiang et al., 2015; Crespi, 2011; Lai et al., 2014). Interestingly, there is evidence in the literature about the presence of genetic mutation in COC, which between 2005 and 2017 was already considered a neoplasm (Gomes et al., 2019; Ide et al., 2015; Sekine et al., 2003; Yukimori et al., 2017). In a study by Yukimori and colleagues (2017), mutation in a tumor suppressor gene (CTNNB1) was identified in 10 of 11 COC cases. Thus, the authors argued that this pathology consisted of a neoplastic lesion caused by genetic mutations. Likewise, Sekine and collaborators (2003) had already identified the same mutation in 9 of 10 cases analyzed and concluded that it was a genetic characteristic of COC.

The constant changes in terminology and classification reflect the lack of precise knowledge on COC pathogenesis. As it is a rare lesion, its relationship with autism, mainly due to the scarcity of studies on the involvement of oral cysts and tumors in this population, lacks sufficient scientific evidence. Thus, further studies and surveys of cases correlating calcifying odontogenic cysts with ASD patients are needed.

#### **4. Conclusion**

COC is a rare lesion, usually asymptomatic and of non-aggressive clinical behavior. However, it is important to consider the diversity of the clinical-radiographic profile due to neoplastic variant and/or possibility of association with other lesions. CBCT is an indispensable tool in directing the correct diagnosis, as well as in choosing the appropriate surgical treatment.



## References

- Amin, D., Magliocca, K. R., & Abramowicz, S. Calcifying odontogenic cyst: Report of 2 cases and review of literature, 6 Oral and Maxillofacial Surgery Cases 100153 (2020). Elsevier Inc. <https://doi.org/10.1016/j.omsc.2020.100153>
- Arruda, J. A., Silva, L. V., Silva, L., Monteiro, J. L., Álvares, P., Silveira, M., & Sobral, A. P. (2018). Calcifying odontogenic cyst: A 26-year retrospective clinicopathological analysis and immunohistochemical study. *Journal of Clinical and Experimental Dentistry*, 10(6), e542–e547. <https://doi.org/10.4317/jced.54528>
- Buchner, A. (1991). The central (intraosseous) calcifying odontogenic cyst: An analysis of 215 cases. *Journal of Oral and Maxillofacial Surgery*, 49(4), 330–339. [https://doi.org/10.1016/0278-2391\(91\)90365-S](https://doi.org/10.1016/0278-2391(91)90365-S)
- Chiang, H. L., Liu, C. J., Hu, Y. W., Chen, S. C., Hu, L. Y., Shen, C. C., ... Gau, S. S. F. (2015). Risk of cancer in children, adolescents, and young adults with autistic disorder. *Journal of Pediatrics*, 166(2), 418–423.e1. <https://doi.org/10.1016/j.jpeds.2014.10.029>
- Chindasombatjaroen, J., Poomsawat, S., & Klongnoi, B. (2012). Calcifying cystic odontogenic tumor associated with other lesions: Case report with cone-beam computed tomography findings. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, 113(3), 414–420. <https://doi.org/10.1016/j.oooo.2011.09.009>
- Corridore, D., Zumbo, G., Corvino, I., Guaragna, M., Bossù, M., Polimeni, A., & Voza, I. (2020). Prevalence of oral disease and treatment types proposed to children affected by Autistic Spectrum Disorder in Pediatric Dentistry: A Systematic Review. *Clinica Terapeutica*, 171(3), E275–E282. <https://doi.org/10.7417/CT.2020.2226>
- Crespi, B. (2011). Autism and Cancer Risk. *Autism Research*, 4(1), 302–310. <https://doi.org/10.1002/aur.208>
- da Silva, S. N., Gimenez, T., Souza, R. C., Mello-Moura, A. C. V., Raggio, D. P., Morimoto, S., ... Tedesco, T. K. (2017). Oral health status of children and young adults with autism spectrum disorders: systematic review and meta-analysis. *International Journal of Paediatric Dentistry*, 27(5), 388–398. <https://doi.org/10.1111/jpd.12274>
- Daniels, J. S. M. Recurrent calcifying odontogenic cyst involving the maxillary sinus, 98 Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology 660–664 (2004). <https://doi.org/10.1016/j.tripleo.2004.04.015>
- de Arruda, José Alcides A., Schuch, L. F., Abreu, L. G., Silva, L. V. O., Monteiro, J. L. G. C., Pinho, R. F. C., ... Mesquita, R. A. (2018). A multicentre study of 268 cases of calcifying odontogenic cysts and a literature review. *Oral Diseases*, 24(7), 1282–1293. <https://doi.org/10.1111/odi.12906>
- de Arruda, José Alcides Almeida, Monteiro, J. L. G. C., Abreu, L. G., de Oliveira Silva, L. V., Schuch, L. F., de Noronha, M. S., ... Mesquita, R. A. (2018). Calcifying odontogenic cyst, dentinogenic ghost cell tumor, and ghost cell odontogenic carcinoma: A systematic review. *Journal of Oral Pathology and Medicine*, 47(8), 721–730. <https://doi.org/10.1111/jop.12727>
- de Moraes, A. T. L., Soares, H. A., Viana Pinheiro, J. de J., & Ribeiro Ribeiro, A. L. (2020). Marsupialization before enucleation as a treatment strategy for a large calcifying odontogenic cyst: Case report. *International Journal of Surgery Case Reports*, 67, 239–244. <https://doi.org/10.1016/j.ijscr.2020.01.031>
- Ferrazzano, G. F., Salerno, C., Bravaccio, C., Ingenito, A., Sangianantoni, G., & Cantile, T. (2020). Autism spectrum disorders and oral health status: Review of the literature. *European Journal of Paediatric Dentistry*, 21(1), 9–12. <https://doi.org/10.23804/ejpd.2020.21.01.02>
- Gallana Alvarez, S., Mayorga Jimenez, F., Torres Gómez, F. J., Avellá Vecino, F. J., & Salazar Fernandez, C. (2005). Calcifying odontogenic cyst associated with complex odontoma: Case report and review of the literature [Quiste odontogénico calcificante asociado con odontoma complejo: Presentación de un caso y revisión bibliográfica]. *Medicina Oral, Patología Oral y Cirugía Bucal*, 10(3), 243–247. <https://www.scopus.com/inward/record.uri?eid=2-s2.0-18744402731&partnerID=40&md5=6bbaa8268f3d7da7a15cee5a661b50dc>
- Gomes, C. C., de Sousa, S. F., & Gomez, R. S. (2019). Craniopharyngiomas and odontogenic tumors mimic normal odontogenesis and share genetic mutations, histopathologic features, and molecular pathways activation. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, 127(3), 231–236. <https://doi.org/10.1016/j.oooo.2018.11.004>
- Gorlin, R. J., Pindborg, J. J., Clausen, F. P., & Vickers, R. A. (1962). The calcifying odontogenic cyst—a possible analogue of the cutaneous calcifying epithelioma of Malherbe. An analysis of fifteen cases. *Oral Surgery, Oral Medicine, Oral Pathology*, 15(10), 1235–1243. [https://doi.org/10.1016/0030-4220\(62\)90159-7](https://doi.org/10.1016/0030-4220(62)90159-7)
- Ide, F., Kikuchi, K., Miyazaki, Y., Kusama, K., Saito, I., & Muramatsu, T. (2015). The Early History of Odontogenic Ghost Cell Lesions: From Thoma to Gorlin. *Head and Neck Pathology*, 9(1), 74–78. <https://doi.org/10.1007/s12105-014-0552-6>
- Irani, S., & Foroughi, F. (2017). Histologic variants of calcifying odontogenic cyst: A study of 52 cases. *Journal of Contemporary Dental Practice*, 18(8), 688–694. <https://doi.org/10.5005/jp-journals-10024-2108>
- Khandelwal, P., Aditya, A., & Mhapuskar, A. (2015). Bilateral calcifying cystic odontogenic tumour of mandible: A rare case report and review of literature. *Journal of Clinical and Diagnostic Research*, 9(11), ZD20–ZD22. <https://doi.org/10.7860/JCDR/2015/15817.6776>
- Kim, Y., Choi, B. E., & Ko, S.-O. (2016). Conservative approach to recurrent calcifying cystic odontogenic tumor occupying the maxillary sinus: a case report. *Journal of the Korean Association of Oral and Maxillofacial Surgeons*, 42(5), 315. <https://doi.org/10.5125/jkaoms.2016.42.5.315>
- Lai, M. C., Lombardo, M. V., & Baron-Cohen, S. (2014). Autism. *The Lancet*, 383(9920), 896–910. [https://doi.org/10.1016/S0140-6736\(13\)61539-1](https://doi.org/10.1016/S0140-6736(13)61539-1)
- Ledesma-Montes, C., Gorlin, R. J., Shear, M., Prætorius, F., Mosqueda-Taylor, A., Altini, M., ... Meneses-García, A. (2008). International collaborative study on ghost cell odontogenic tumours: Calcifying cystic odontogenic tumour, dentinogenic ghost cell tumour and ghost cell odontogenic carcinoma. *Journal of Oral Pathology and Medicine*, 37(5), 302–308. <https://doi.org/10.1111/j.1600-0714.2007.00623.x>

Neville, B. W., Damm, D. D., Allen, C. M., & Bouquot, J. E. (2009). *Patologia Oral e Maxilofacial*.

Rodrigues Fregnani, E., Ramôa Pires, F., Quezada, R. D., Shih, I. M., Vargas, P. A., & De Almeida, O. P. (2003). Calcifying odontogenic cyst: Clinicopathological features and immunohistochemical profile of 10 cases. *Journal of Oral Pathology and Medicine*, 32(3), 163–170. <https://doi.org/10.1034/j.1600-0714.2003.00070.x>

Rojo, R., Prados-Frutos, J. C., Gutierrez Lázaro, I., & Herguedas Alonso, J. A. (2017). Calcifying odontogenic cysts. *Journal of Stomatology, Oral and Maxillofacial Surgery*, 118(2), 122–124. <https://doi.org/10.1016/j.jormas.2016.10.007>

Santos, H. B. de P., de Moraes, E. F., Moreira, D. G. L., Neto, L. F. de A., Gomes, P. P., & Freitas, R. de A. (2018). Calcifying Odontogenic Cyst with Extensive Areas of Dentinoid: Uncommon Case Report and Update of Main Findings. *Case Reports in Pathology*, 2018, 1–4. <https://doi.org/10.1155/2018/8323215>

Sekine, S., Sato, S., Takata, T., Fukuda, Y., Ishida, T., Kishino, M., ... Hirohashi, S. (2003).  $\beta$ -Catenin Mutations Are Frequent in Calcifying Odontogenic Cysts, but Rare in Ameloblastomas. *American Journal of Pathology*, 163(5), 1707–1712. [https://doi.org/10.1016/S0002-9440\(10\)63528-6](https://doi.org/10.1016/S0002-9440(10)63528-6)

Souza, L. N., Souza, A. C. R. A., Gomes, C. C., Loyola, A. M., Durigetto, A. F., Gomez, R. S., & Castro, W. H. Conservative Treatment of Calcifying Odontogenic Cyst: Report of 3 Cases, 65 *Journal of Oral and Maxillofacial Surgery* 2353–2356 (2007). <https://doi.org/10.1016/j.joms.2006.09.021>

Speight, P. M., & Takata, T. (2018). New tumour entities in the 4th edition of the World Health Organization Classification of Head and Neck tumours: odontogenic and maxillofacial bone tumours. *Virchows Archiv*, 472(3), 331–339. <https://doi.org/10.1007/s00428-017-2182-3>

Uzun, T., & Çinpolat, E. (2019). Calcifying odontogenic cyst associated with the impacted third molar: a case report, 8688, 1–5. <https://doi.org/10.11604/pamj.2019.33.151.17601>

Yoshiura, K., Tabata, O., Miwa, K., Tanaka, T., Shimizu, M., Higuchi, Y., ... Kanda, S. (1998). Computed tomographic features of calcifying odontogenic cysts. *Dentomaxillofacial Radiology*, 27(1), 12–16. <https://doi.org/10.1038/sj.dmf.4600305>

Yukimori, A., Oikawa, Y., Morita, K., Thi, C., Nguyen, K., Harada, H., ... Sakamoto, K. (2017). Genetic basis of calcifying cystic odontogenic tumors. *PLoS ONE*, 12(6), 1–13.