



## Unusual Presentation of Cystic Lesions of the Jaws in a Patient with Pascual-Castroviejo Syndrome: A Case Report

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### ABSTRACT

Pascual-Castroviejo syndrome or Cerebro-facial-thoracic dysplasia is an autosomal recessive inherited disorder characterized by mental retardation, typical facies, brachycephaly, calcified clinoid ligaments, and deformities of the superior rib arches. Its etiology is not entirely clear, but an association with a mutation in the TMC01 gene has been reported. On the other hand, the dentigerous cyst is the odontogenic cyst of the most common development in the jaws. It results from the accumulation of fluid between the reduced epithelium of the enamel and the crown. They are generally solitary lesions, rare to find them bilaterally and multiple, and not reported in the literature about this syndrome. This article presents a bilateral dentigerous cyst description in the mandible of a patient with Pascual-Castroviejo syndrome. A 14-year-old male patient with a diagnosis of cerebro-fascio-thoracic dysplasia (Pascual-Castroviejo syndrome), presenting a bilateral lesion in the posterior mandible, with a year of evolution. An incisional biopsy was performed in the larger lesion, and the diagnosis was a dentigerous cyst. Subsequently, under general anesthesia, enucleation and curettage of the lesions associated with the second and third molars of the first, second, and third quadrant were performed, along with the involved teeth' extraction. Periodic postoperative controls were carried out, and after six months, there were no signs of recurrence. The appearance of cystic lesions of the jaws associated with the Pascual-Castroviejo syndrome is rare. Further genetic studies are crucial to determine the association between both entities.

### 1. Introduction

Cerebro-facio-thoracic dysplasia (CFTD) is an autosomal recessive genetic disorder first reported in 1975 by Pascual-Castroviejo et al.<sup>[1]</sup> Characterized by multiple alterations in mental development and a typical facies presenting narrow forehead, synophrys, hypertelorism, wide nasal bridge, long filtrum, micrognathia, triangular-shaped mouth, and low hair insertion line. Other features can also be found, including brachycephaly, calcified clinoid ligaments, and deformities of the superior rib arches.<sup>[2]</sup> The pathophysiology of this syndrome is not entirely clear. However, genetic studies have determined its association with the TMC01 gene mutation, which plays a critical role in the development of human cells, which could explain the multisystemic clinical involvement of this syndrome.<sup>[3]</sup> Among cystic lesions of the jaws, the dentigerous cyst is the most common developing odontogenic cyst, representing 24% of these entities. It develops most frequently in the mandible, representing 70% of cases. They usually appear in the second or third decade of life without gender predisposition.<sup>[4, 5, 6]</sup> The dentigerous cyst is formed due to an alteration in the reduced epithelium of the enamel, enclosing the crown of a non-erupted tooth at the cementum-enamel junction.<sup>[7]</sup> It is most commonly associated with an impacted mandibular third molar, followed by the maxillary third molars and canines.<sup>[8]</sup>

On the other hand, bilateral cystic lesions of the jaws have not been reported about this syndrome. Based on the above, the present study's objective is to describe the unusual appearance of bilateral cystic lesions of the jaws in a 14-year-old male patient with cerebro-fascio-thoracic dysplasia (Pascual-Castroviejo syndrome).

### 2. Case presentation

A 14-year-old male patient who was referred to the Surgical Unit of the Dentistry School of the University of Zulia, Venezuela for presenting a lesion in the posterior mandibular region on the right side, asymptomatic, with a year of evolution, without previous treatment. His medical history was notable for the genetic diagnosis of Pascual-Castroviejo syndrome and the psychological disorder of the autism spectrum. Clinical evaluation revealed scoliosis, laterodeviation of the thoracolumbar spine's longitudinal axis in the form of an italic S. On examination of the head and neck, eyebrows with a tendency to synophrys were observed, along with malar hypoplasia, long and triangular lip philtrum, micrognathia, and dental crowding (Figure 1).

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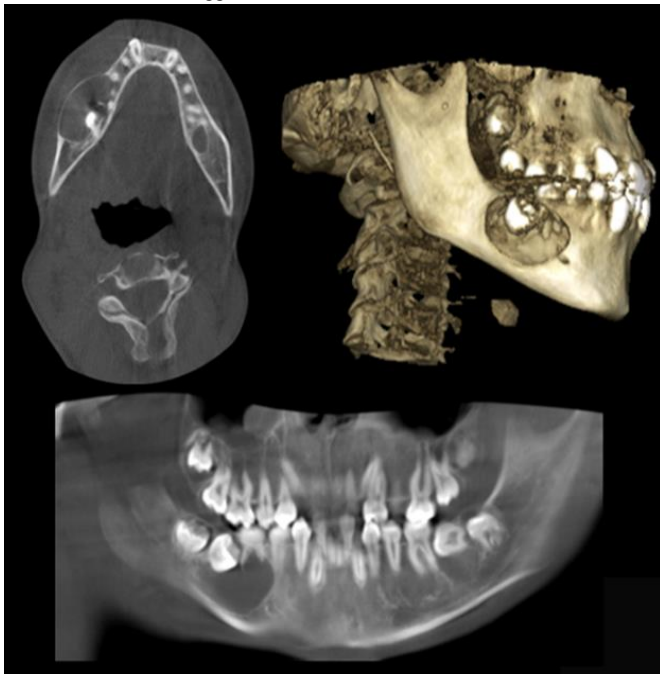
<http://doi.org/10.30485/IJSRDMS.2020.240458.1076>





**Figure 1: Extraoral imaging showed sinophrys, malar hypoplasia, long and triangular lip filtrum, and micrognathia.**

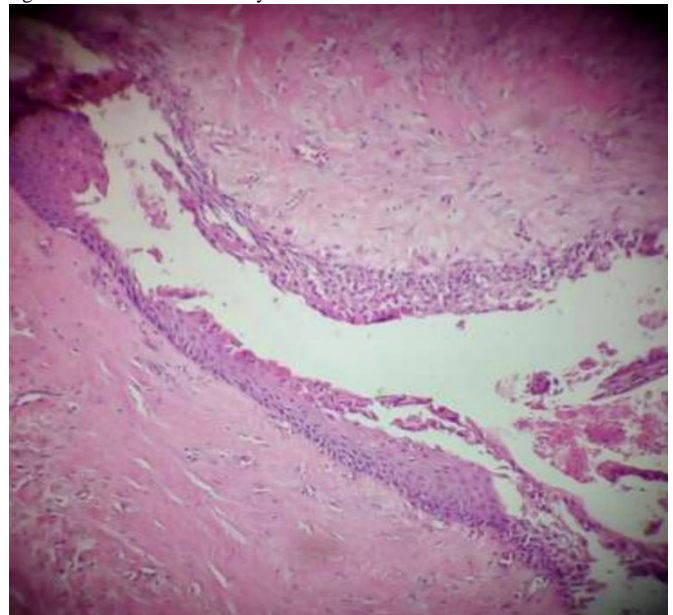
Cone-beam computed tomography showed a hypodense image associated with the left mandibular second and third molar, which caused the expansion of the adjacent cortical plates (Figure 2). In addition to hypodense, images associated with the second and third molars on the first, second, and third quadrants. Differential diagnoses of the dentigerous cyst, keratocyst, and ameloblastoma were suggested, due to their association with retained teeth.



**Figure 2: Cone beam computed tomography showed a bilateral hypodense images.**

In accordance with the protocols established in our Surgical Unit, it was decided to perform an incisional biopsy under conscious sedation monitored prior indication of preoperative studies with Midazolam 0.05mg / kg and Ketamine 0.25mg / kg as inductors and Flumazenil 0.1mg as reverser. The

sample was taken from the lesion located in the fourth quadrant since it was the largest. The specimen, sent for histopathological study, showed a cystic cavity lined by stratified squamous epithelium, thin for most length. The rest of the wall was made up of fibrous connective tissue, which contained odontogenic remains and a moderate mononuclear inflammatory infiltrate. Thus, the diagnosis of Dentigerous Cyst was obtained. Subsequently, under general anesthesia, the enucleation and curettage of the lesions located in the remaining three quadrants and the extraction of the dental organs associated with them were performed, sending the surgical samples for histopathological study, showing a cavity lined by stratified squamous epithelium. The rest of the wall was made up of underlying fibrous connective tissue. It contained abundant odontogenic remains and basophilic calcifications and hemorrhage, providing a definitive diagnosis of Dentigerous Cyst for the mandibular lesions (Figure 3) and hyperplastic dental follicles for the maxillary lesions. Periodic postoperative controls were carried out, and after six months, there were no signs of recurrence or sensory and motor neuronal changes. In order to comply with the bioethics norms and the agreements established in the Helsinki declaration, the patient's legal representative was instructed on the purposes and scope of the procedure and the investigation, requesting her written authorization for that purpose. In addition to this, an anonymity agreement was established by the bioethical criteria.



**Figure 3: The microscopic feature showed a cystic lesion lined by Stratified Squamous Epithelium.**

**3. Discussion**

The etiology of CFTD is unknown; the main hypothesis regarding this lies in the mutation of the TMC01 gene, which causes an excessive accumulation of calcium in the endoplasmic reticulum, interrupting the development of the brain and the structures in the head, face and torso, resulting in the characteristics of this syndrome.<sup>[9]</sup> Rufo-Campos et al.<sup>[2]</sup> described other additional clinical characteristics that include hypoplasia of the corpus callosum and the cerebellar vermis. Similarly, Smigiel et al.<sup>[10]</sup> found hypothyroidism and cleft lip and palate associated with this disorder. Other authors have described Chiari type I malformations, optic nerve colobomas, ptosis, small and conical teeth, talipes, as well as hypermobility and hypodensity of the gray matter.<sup>[11]</sup> In the present study, the patient

presented multiple clinical features characteristic of the syndrome, and additionally, bilateral cystic lesions in the jaws.

The appearance of cystic lesions of bilateral or multiple jaws is rare. It is generally associated with Maroteaux-Lamy syndrome (mucopolysaccharidosis, type VI), cleidocranial dysplasia, and basal cell nevus syndrome (Gorlin-Goltz syndrome). Likewise, other syndromes related to the appearance of multiple cystic lesions of the jaws have been described, such as Gardner's syndrome,<sup>[12]</sup> Cramer-Niederdelmann's syndrome<sup>[13]</sup> Neurofibromatosis-Noonan syndrome.<sup>[14]</sup> As in the present case, the management of this pathology implies the careful enucleation of the cyst and the extraction of the associated unerupted tooth. However, for cysts with a larger diameter, marsupialization or decompression can be used to reduce the lesion's size and subsequently perform, if necessary, surgical removal by secondary enucleation.<sup>[8, 12]</sup>

Occasionally, it is suggested that the prescription of certain drugs induce the appearance of multiple dentigerous cysts. It has been reported that the combined effect of cyclosporine and a calcium channel blocker may also be related to the appearance of bilateral dentigerous cysts.<sup>[15]</sup> Pleomorphism on chromosome 1qh + has also been reported with this condition.<sup>[16]</sup> In the present case, the patient did not present any of the syndromes or conditions previously described. Autism spectrum disorder corresponds to a heterogeneous group of clinical expressions, the leading cause of which is unknown.<sup>[17]</sup> The clinical manifestations demonstrated in autism include deficiencies and persistent deterioration in communication and social interaction, restricted and repetitive behavior patterns, as well as deficiencies in socio-emotional reciprocity, deficits in non-verbal communication behaviors, and in skills to develop, maintain and understand relationships with or without impairment of cognitive skills and abilities, the intellectual deficit being frequent. Due to the alterations in these patients' behavior, special considerations must be taken at the time of the surgical management, among which conscious sedation is described as an alternative, which is why it was used in this case.<sup>[18, 19]</sup> On the other hand, the relationship between autism spectrum disorder and Pascual-Castroviejo syndrome has not yet been described in the literature. As far as the authors know, in the world literature, there are only 23 reported cases of CFTD to date,<sup>[20]</sup> in which none of them describe the association of this disorder with cystic lesions of the jaws (bilateral dentigerous cysts in our case). Thus, the simultaneous appearance of these entities is unusual.

#### 4. Conclusion

The appearance of cystic lesions of the jaws associated with Pascual-Castroviejo syndrome is rare. It is necessary to carry out more genetic studies to evaluate the relationship between this syndrome's pathophysiology and the appearance of cystic lesions of the jaws. Similarly, it is necessary to carry out clinical and imaging controls in the short, medium, and long term to detect any sign of recurrence in early stages or some other alteration in the jaws that could also be related to this syndrome.

#### Conflict of Interest

The authors declared that there is no conflict of interest.

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