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## A patient with Camurati-Engelmann disease presenting bilateral TMJ ankylosis: A case report

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## ABSTRACT

Camurati-Engelmann Disease (CED), also known as progressive diaphyseal dysplasia, is a rare congenital disorder inherited in an autosomal-dominant pattern, most commonly affecting the skull and diaphysis of long tubular bones. Clinical symptoms start in early age and include ostealgia, muscle atrophy and weakness in the lower limbs, generalized fatigue in addition to gait disturbances (Garcia Armario and Lebron, 2011; Andreu-Arasa et al., 2019; Fyrgiola et al., 2017; Damiá and García Gómez, 2017; Mwasamwaja et al., 2018). CED is believed to be caused by mutation in the gene coding for Transforming Growth Factor  $\beta$ -1 (TGFB-1) (Fyrgiola et al. 2017). This article presents a rare clinical case of CED, with bilaterally hypertrophic articular apparatus and subsequent ankylosis. A 33-year-old male is reported with temporomandibular joint (TMJ) ankylosis, bone pain, generalized muscle weakness, abnormal gait and bulging eyes. Diagnosis of CED was based on genetic mapping performed by geneticist. Upon clinical and radiological examination, a massive bony mass in the condyloid and coronoid was discovered and treatment of choice was surgical resection and installation of bilateral stock articular prostheses.

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## 1. Introduction

Camurati-Engelmann Disease (CED), a rare autosomal dominant congenital disorder, also known as progressive diaphyseal dysplasia was first described by Camurati in 1922 and then by Engelmann in 1929 [4–9]. Caused by mutation to the gene coding for Transforming Growth Factor  $\beta$ -1 (TGFB-1) [1–4]. TGF- $\beta$ 1 plays an important role in controlling the immune system, as well as bone remodeling (formation and resorption) [4]. In addition to physical presentations like osteopathy, craniomegaly, bulging eyes, fatigueness, muscular atrophy and gait disturbances [1–6], several systemic implications may be occasionally noted in CED patients such as hepatosplenomegaly, hypothyroidism and hypogonadotrophic hypogonadism [10–12]. Also, hematologic alterations have been reported like anemia, leucopenia, raised alkaline phosphatase and raised erythrocyte sedimentation rate (ESR) [1–6]. This case has been reported in line with the SCARE criteria [34].

## 2. Case report

A 33-year-old-male presented to our clinic of oral and maxillofacial surgery in December 2018 referred by gastric surgeon who reported difficult intubation to undergo a surgical procedure (cholecystectomy) under general anesthesia. The patient reported gradual decrease in mouth opening that started 3 years ago, reaching a minimal range of 2 mm on the date of primary exam. He also described extremely difficult alimentation and mastication with consequent weight loss and general health deterioration. The patient, who presented using a wheelchair and is otherwise healthy, has been diagnosed with CED after genetic mapping performed by geneticist in his childhood. No relevant family history was noted. Primary physical examination revealed well pronounced craniomegaly, bulging eyes, disproportionate body-to-head ratio, generalized muscular atrophy and difficulty to maintain standing posture and perform hand motions (Fig. 1). Upon maxillofacial examination, severe limitation of mouth opening due to bilateral ankylosis of the TMJ was noted, with subsequent limited masticatory and speech functions. Cranial nerves integrity showed to be preserved, with no visual or hearing alterations. The patient shows normal cognitive and intellectual development, with good language and computer command. A computerized tomography examination revealed abnormal bony growths in the cranium and face bones, with the formation of large bony masses in the condyloid and coronoid processes in addition to the medial surface of

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Fig. 1. Facial characteristics suggestive of CED.

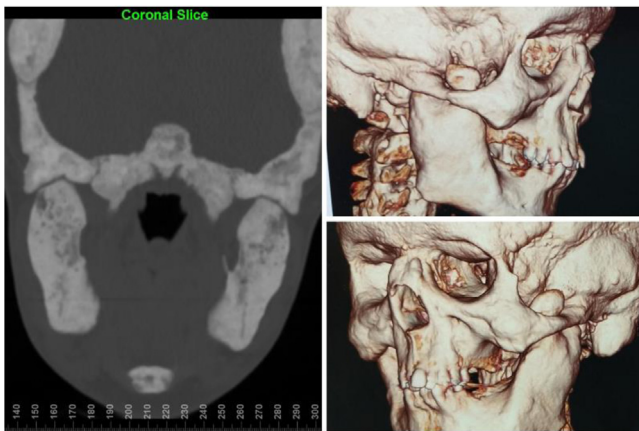


Fig. 2. Pre-operative CT scan, a: coronal view, b: 3D reconstruction of right TMJ, c: 3D reconstruction of left TMJ.

the ascending mandibular ramus bilaterally (Fig. 2). General laboratory exam and cardiologic check-up results were within the normal limits, without any significant pathology.

Once the diagnosis of bilateral TMJ ankylosis was confirmed, the treatment of choice was surgical resection of hypertrophic bony masses and installation of bilateral medium stock articular prosthesis (Engimplan Ind e Com. Ltda, Rio Claro, Brazil). Elective tracheostomy was performed under local anesthesia pre-operatively to facilitate tracheal intubation during general anesthesia induction. Placing the patient in horizontal dorsal decubitus position, general anesthesia was induced and tracheal intubation accomplished via tracheostomy. Bilateral trichotomy performed, and surgical access obtained via bilateral preauricular and Risdon surgical incisions. Then condylectomy and coronoidectomy was performed, with simultaneous resection of the bony mass formed on the medial surface of the ascending ramus bilaterally (Fig. 3). Eminectomy was not necessary, and zygomatic arches were left intact. Bilateral medium stock TMJ prostheses (Engimplan Ind e Com. Ltda, Rio Claro, Brazil) were installed and adapted into position. After adequate irrigation and mobilization of the mandible to achieve satisfactory opening, the incisions were carefully closed by deep dermal and epidermal sutures. Transfusion of two bags of packed red blood cells was necessary post-operatively and the patient was maintained at the ICU for 3 days due to reduced corporal mass and extensive postoperative edema. He had an uneventful recovery, with the tracheostomy removed within 3 weeks post-operatively. No neurologic deficiency of the facial nerve



Fig. 3. Bony fragments resulting from resection of the hypertrophic condyle and coronoid processes bilaterally.

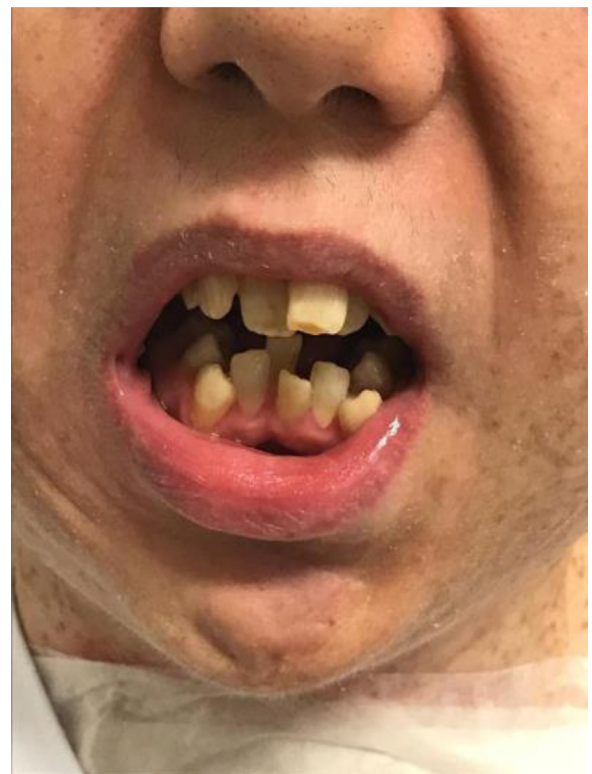
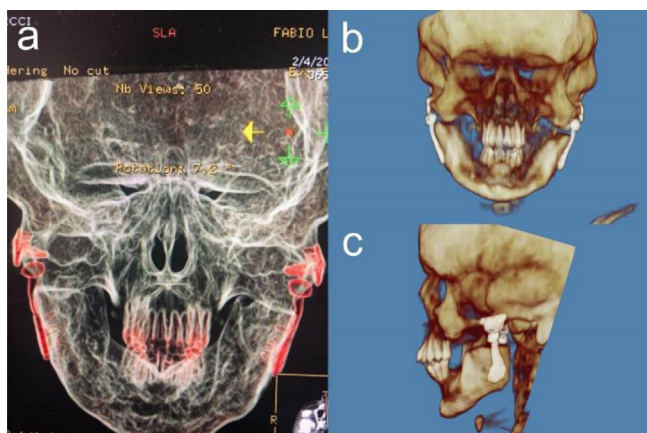


Fig. 4. Post-operative mouth opening range.

branches was observed. Immediate post-operative mouth opening ranged between 15 and 20 mm (Fig. 4). Post-operatively, aggressive immediate physiotherapy treatment for mouth opening was indicated (Fig. 5). Computerized tomography exam was performed at



**Fig. 5.** Post-operative physiotherapy for mouth opening.



**Fig. 6.** Post-operative CT scan, a: coronal view, b: frontal view of 3D reconstruction, c: lateral view of 3D reconstruction.

1 month post-operatively, showing satisfactory positioning of the mandibular and fossa components of the TMJ prostheses (Fig. 6). Periodic follow-ups were scheduled with periodic CT scans to keep track of the healing process.

### 3. Discussion

More than 300 cases of CED were reported up to date, yet the exact prevalence is still unknown [13]. Clinical manifestations range from constant, dull bone pain mainly in the lower limbs to generalized muscle weakness, difficult ambulation, fatigue, headache, among others. . . Clinical examination often reveals muscle atrophy in the limbs, more evident in the lower limbs, leading to difficulty in sitting, standing and walking in addition to gait disturbances [14]. Other orthopedic alterations are noted less frequently, such as radial head dislocation, kyphosis, scoliosis, coxa valga, genu valga, and flat feet [15]. Cranial alterations in CED are observed though skull base involvement where cranial nerve palsies are caused due to sclerosis and narrowing of cranial foramina. Most common alterations are vision and hearing problems, in addition to facial nerve palsy [16]. Cranial hyperostosis is a relatively common characteristic of CED, where manifestations like hearing loss, headache, exophthalmos, frontal bossing, vision changes, headaches, vertigo, facial numbness and hyposmia are clinically observed [16]. Dental implications are less frequent, and dental eruption is normal, although alterations at the level of the condyle and coronoid process are noted [17]. Moreover, thick bony masses are noted in the paranasal sinuses leading to the loss of pneumatization, in a radiologic presentation similar to skull base sclerosis in 50 % of the patients, however only 25 % develop cranial nerve dysfunction [18].

The diagnosis is based on clinical and radiologic findings, and confirmed by genetic mapping. Radiographic examination of long tubular bones reveals uneven cortical thickening of the diaphysis with hyperostosis, most frequently in the lower limbs. Sclerosis of the skull base is also observed [19]. Bone scintigraphy can show normal results despite presence of bone lesions radiographically.

It is a useful tool for disease activity monitoring and observation [20,21].

On the molecular level, a mutation of the *TGFβ-1* gene on chromosome 19q13 is believed to be the causative factor of CED. Moreover, phenotypic expression is very variable even within the same family [22,23].

In the case presented here, the parents were not affected leading to conclude that a *de novo* mutation is likely to have occurred, though non-penetrance or germline mosaicism in one of them cannot be excluded.

Differential diagnosis of CED should consider sclerosing bone dysplasias with abnormal bone shape due to diaphyseal modeling defects. Van Buchem disease is a recessive autosomal disease characterized by mandibular enlargement, widening of short tubular bones in hands and feet, syndactyly and cranial thickening, all of which are characteristics distinguishing it from CED [23]. Radiographically, Ribbing disease has a similar presentation, but cranial nerve alterations are rare [24]. Ghosal hematodiaphyseal dysplasia can represent CED, however, less pronounced hyperostosis and more severe hematologic disorders are observed in the former [25]. Cranio-diaphyseal dysplasia is also recessive autosomal, characterized by sclerosis of facial bones and skull base, in addition to widening of the ribs, clavicles and short tubular bones in hands, which are not features of CED [26].

Treatment of CED is individualized depending on the symptoms and severity of each case. Corticosteroids, bisphosphonates and NSAIDs have been used to relieve the symptoms [27]. Several Histologic studies have shown that steroid therapy helps increase bone resorption and secondary remodeling with increased osteoblast activity and decreased lamellar bone deposition. Nevertheless, no regression of sclerosis was reported radiographically or on scintigrams in several studies [28,29]. Recently, treatment with the angiotensin II type 1 receptor antagonist *Losartan* has been reported to increase muscle strength and reduce limb pain in multiple case reports, however further studies to determine its efficacy and safety for CED patients [30,31].

Surgical treatment is indicated in certain cases. Craniotomy, which includes removal of a part of the cranium with titanium mesh cranioplasties, is the treatment of choice to reduce intracranial pressure and relieve symptoms, in case of recurrent cranial hyperostosis. Resection of hyperostosis in the condylar and coronoid process with simultaneous installation of bilateral TMJ prosthesis is indicated in severe debilitating jaw ankylosis [32]. Myringotomy, a surgical procedure in which a tiny incision is created in the eardrum (tympanic membrane) to relieve pressure caused by excessive build-up of fluid, can help improve conductive hearing loss [33].

In conclusion, clinical cranial presentation of CED involves mandibular enlargement with severely decreased mouth opening. Surgical resection with simultaneous bilateral TMJ prostheses is the treatment of choice with satisfactory long-term post-operative results.

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### Ethical approval

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).

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Author contribution

Prof. Dr. Eduardo Sant'Ana: Head of surgical team, supervision of case report manuscript writing.

Dr. Denis Piment E. Souza: Member of surgical team, revision of the manuscript.

Dr. Erika Kuriki: Member of surgical team, revision of the manuscript.

Dr. Nour Salman: Member of surgical team, writing of the manuscript, corresponding author.

## Registration of research studies

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Prof. Dr. Eduardo Sant'Ana.

Dr. Nour Salman.

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## Declaration of Competing Interest

The authors report no declarations of interest.

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