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Functional and structural alterations of the craniofacial complex in the branchio-oculo-facial syndrome: case report

Alterações funcionais e estruturais do complexo craniofacial na síndrome branquio-óculo-facial: relato de caso

Alteraciones funcionales y estructurales del complejo craneofacial en el síndrome branquio-óculo-facial: relato de caso

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Abstract

Introduction: Branchio-Oculo-Facial Syndrome (BOFS) is a rare autosomal disease with variable expression, dependent on genetic mutations, whose phenotype is characterized by ocular, hearing and craniofacial alterations. **Purpose**: describe the clinical features, the functional and structural alterations in the craniofacial complex of a subject with branchio-oculo-facial syndrome. **Method:** A 13-year

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Authors' Contribution:
GRS: designed the case report, gathered and interpreted the data, and wrote the article; GJK and MBS: gathered the data and wrote the article; LRB and MSM: wrote the article and critically revised the content; MCAFC: interpreted the data, wrote the article and critically revised the content; MAPM: designed the case report, gathered and interpreted the data, wrote the article, and critically revised the content.

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and 3-month-old girl, with moderately severe conductive bilateral hearing loss diagnosed with BOFS, presented: bilateral cleft lip and palate treated by labioplasty and palatoplasty, facial asymmetry, anterior maxillary fistula, transverse maxillary atresia, imperfect dentinogenesis, negative horizontal trespass, Angle Class I bilateral, anterior and lateral open bite on both sides, severe left superior midline deviation, eruption by vestibular of the superior canine on the left side, prolonged retention of the second inferior molar right deciduous, lower dental crowding, hypotonia and inadequate tongue positioning, absence of labial resting at rest, adapted swallowing, alteration in mobility of lips, cheeks and palate with nasal air exhaust in speech, characterizing velopharyngeal dysfunction. There are few publications of BOFS, given its rarity. Subjects with cleft lip and palate may present a wide variety of changes in the production of headphones. Patient presents deficient growth of the maxilla which, as reported in the literature, may alter the development of the middle third of the face with repercussion in dental occlusion, speech and nose shape. **Conclusion:** The functional and structural clinical alterations reported are the majority of the craniofacial complex, demonstrating the importance of otorhinolaryngology, speech therapy and orthodontics in the interdisciplinary therapy of patients with BOFS.

Keywords: Branchio-Oto-Facial Syndrome; Speech, Language and Hearing Sciences; Orthodontics; Speech; Tooth.

Resumo

Introdução: A Síndrome Branquio-Óculo-Facial é uma doença autossômica rara com expressão variável, dependente das mutações genéticas, cujo fenótipo caracteriza-se por alterações oculares, auriculares e craniofaciais. **Objetivo:** Descrever características clínicas, alterações funcionais e estruturais do complexo craniofacial de sujeito com síndrome branquio-óculo-facial. **Método:** Paciente de 13 anos e 3 meses, respiradora oral com perda auditiva condutiva de grau moderadamente severo em ambas as orelhas, diagnosticada com síndrome branquio-óculo-facial, apresentou: fissura labiopalatina transforame bilateral completa corrigida por labioplastia e palatoplastia primárias, assimetria facial, fístula em região anterior de palato duro, atresia maxilar transversa, dentinogênese imperfeita, trespasse horizontal negativo, oclusão Classe I de Angle e mordida aberta anterior e lateral bilateralmente, desvio severo da linha média superior para a esquerda, incisivo lateral superior permanente semi-erupcionado por vestibular do canino superior decíduo do lado esquerdo, retenção prolongada do segundo molar inferior decíduo direito, apinhamento dentário inferior, hipotonia e posicionamento inadequado de língua, ausência de vedamento labial em repouso, deglutição adaptada, alteração na mobilidade de lábios, bochechas e palato mole com escape de ar nasal na fala, caracterizando disfunção velofaríngea. Sujeitos com fissura lábiopalatina podem apresentar grande variedade de alterações na produção dos fones. Paciente apresenta crescimento deficiente da maxila que, como relatado na literatura, pode alterar o desenvolvimento do terço médio da face com repercussão na oclusão dentária, fala e formato do nariz. **Conclusão:** As alterações clínicas funcionais e estruturais relatadas são na maioria do complexo craniofacial, demonstrando a importância da otorrinolaringologia, fonoaudiologia e odontologia na terapêutica interdisciplinar dos pacientes com a síndrome.

Palavras-chave: Síndrome Brânquio-Oculo-Facial; Fonoaudiologia; Ortodontia; Fala; Dente

Resumen

Introducción: El síndrome branquio-oculo-facial (BOFS) es una enfermedad autosómica rara con expresión variable, dependiente de las mutaciones genéticas, caracterizada por alteraciones oculares, auriculares y craneofaciales. **Propósito:** describir características clínicas, alteraciones funcionales y estructurales del complejo craneofacial de un sujeto con BOFS. **Método:** Niña de 13 años y 3 meses de edad, con pérdida de audición conductiva moderadamente grave bilateralmente diagnosticada con SBOF, presentó: paladar y labio hendido bilateral tratado por labioplastia y palatoplastia primarias, asimetría facial, fístula maxilar anterior, atresia maxilar transversal, dentinogénesis imperfecta, traspaso horizontal negativo, clase I de Angle bilateral, mordida abierta anterior y lateral bilateralmente, desviación severa de la línea media superior izquierda, erupción vestibular del canino superior del lado izquierdo, retención

prolongada del segundo molar inferior derecho deciduo, apiñamiento dental, hipotonía e inadecuada colocación de la lengua, ausencia de sello labial en reposo, deglución adaptada, alteración de movilidad de labios, mejillas y velo del paladar con escape de aire nasal y disfunción velofaríngea Hay pocas publicaciones de BOFS, dada su rareza. Los sujetos con labio y paladar hendido pueden presentar una gran variedad de cambios en la producción de auriculares. El paciente presenta crecimiento deficiente del maxilar que, según se informa en la literatura, puede alterar el desarrollo del tercio medio de la cara con repercusión en la oclusión dental, habla y la forma de la nariz. **Conclusión:** Alteraciones clínicas funcionales y estructurales la mayoría del complejo craniofacial. Eso demuestra la importancia de otorrinolaringología, fonoaudiología y odontología en la terapia interdisciplinaria de pacientes con SBOF.

Palabras clave: Síndrome Brânquio-Otorrenal**;** Fonoaudiología; Ortodoncia; Habla; Diente

Introduction

The branchio-oculo-facial syndrome (BOFS) is a rare autosomal disease with highly varying expression, depending on the existing genetic mutations[1], of which 81 cases are described in literature[2]. The TFAP2A gene, localized at the chromosome 6, may appear deleted or mutated in people with BOFS[3]. The phenotype of the syndrome is characterized by ocular, auditory and craniofacial alterations[1].

The craniofacial alterations frequently found in people with BOFS are: false cleft lip; cleft lip either associated or not to cleft palate[4]; narrow and ogival palate; asymmetric and malformed nose, with wide bridge and flat tip[4,5]. The bilateral post-auricular cervical branchial defects with hemangiomatous lesions covered with an abnormal portion of skin, either associated or not with preauricular or auricular pits, hearing loss and low-set ears are also characteristic of the syndrome[4,5].

Ocular alterations, such as microphthalmia, coloboma, cataract, nasolacrimal duct obstruction, nearsightedness, strabismus and ptosis are found in subjects with BOFS[4,5]. Extra-craniofacial malformations are rare in this syndrome, of which renal abnormalities are the most frequent[6]. Subjects with BOFS may occasionally present premature hair whitening and scalp cysts[5]. BOFS may be associated with moderate intellectual disability[5] and hearing loss in 70% of the subjects[7]. The absence of upper deciduous incisors has been reported as a sign present in BOFS[8].

Due to the rarity of studies related to BOFS, the description of this case report is justified, as it aims to present the existing clinical characteristics, especially the countless functional and structural alterations in the craniofacial complex.

Case report

The patient of this study attends the outpatient center of the public health care system in the *Santo Antonio* Children Hospital (which belongs to the *Santa Casa de Misericódia* Hospital Complex of Porto Alegre, RS, Brazil). In this outpatient center, the "Cleft Lip and Palate Public Outreach" of the Health Sciences Federal university of Porto Alegre (UFCSPA) carries out activities aiming at the interdisciplinary care given to the child since their birth until they turn 18 years old.

The research activities carried out were approved by the Research Ethics Committee of the health institution involved, under the number 1,900,382, and linked to the research project named "Musculoskeletal-related Clinical Procedures in Speech,Language and Hearing Sciences". The adults responsible for the patient signed the Informed Consent Form and the Permission to Use Personal Image, as did the patient herself, signing the Informed Assent Form, all of them authorizing the use of data and images present in this study. In the functional and structural speech,language and hearing evaluation, as well as in clinical orthodontic evaluation, their own protocols were used, developed by the project's research group for this population.

A white female patient with BOFS, 13 years and three months old, firstborn child of healthy non-consanguineous parents, underwent speech, language and hearing and orthodontic evaluation at the outpatient center of the "Cleft Lip and Palate Public Outreach", following countless evaluations and medical follow-ups throughout the years, including the otorhinolaryngology. The girl attends speech, language and hearing therapy sessions at

this outpatient center. Her family history is negative for both congenital defects and genetic diseases.

The clinical diagnosis of BOFS was established by the hospital's genetics clinic's team. The patient was referred for another reference hospital's medical genetics team in order to undergo complementary evaluations and exams for genetic diseases, such as the molecular tests that indicate the altered gene.

As clinical characteristics of the syndrome on the craniofacial area, the girl presented bilateral complete cleft lip and palate (corrected by lip repair surgery at two months, and palate repair at 12 months of age); iris and optic nerve coloboma; nasolacrimal duct obstruction; moderately severe bilateral conductive hearing loss; low-set ears (Figure 2); asymmetric nose with wide bridge and flat tip (Figure 1), and bilateral pits on the branchial area (retroauricular). As complementary health data, there can be mentioned multicystic right kidney, impairment in neuropsychological development, thoracolumbar scoliosis with mild curve angle, epilepsy, blepharophimosis, visual impairment, and right ear canal stenosis.

In the speech,language and hearing evaluation for orofacial motor functions, the patient presented the following orofacial characteristics: presence of anterior hard palate fistula, in which the palate was atretic; maxillary underdevelopment; alteration in cheek and lip mobility (with hypo-movement of the upper lip); tongue hypotonia and inadequate positioning (positioned at the oral floor and with tongue interposition); facial asymmetry (Figure 1); absence of lip closure at rest (Figures 1 and 2); and, alteration in soft palate mobility with nasal air escape in speech, characterizing velopharyngeal dysfunction.

The stomatognathic functions of swallowing and chewing were also evaluated. When under swallowing evaluation, the patient presented multiple swallows for solids and liquids, and hyperactivation of the mentalis muscle while performing the function. When chewing solids, the patient mouthed small amounts of food, with slow oral transit. Such findings characterize a swallowing pattern adapted to the existing anatomic conditions, including the use of orthodontic braces on the upper arch.

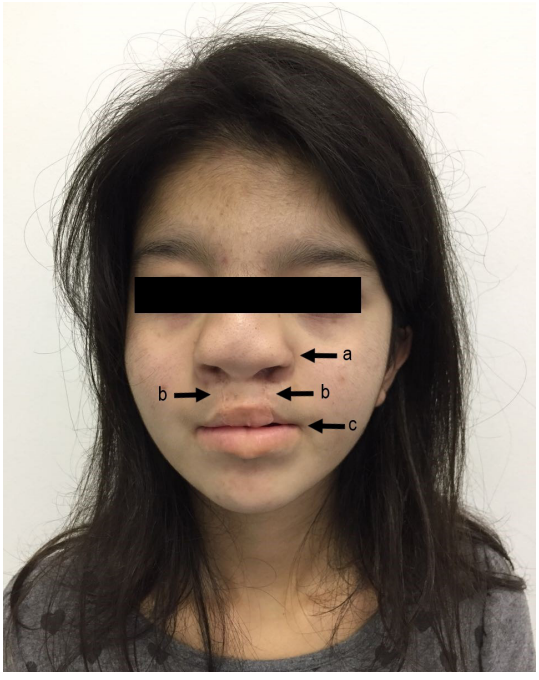

Figure 1. Frontal face image. Special attention to asymmetric face, asymmetric nose with wide bridge and flat tip (a), scar in the area of the bilateral lip repair surgery (b), and absence of lip closure at rest (c).

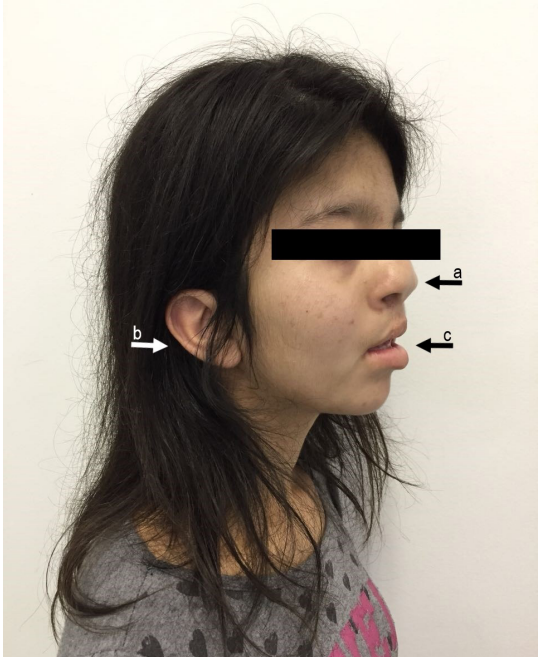

Figure 2. Right side view face image. Special attention to flat nose tip (a), low-set ear (b), and absence of lip closure at rest (c).

In the speech evaluation, phonological and phonetic alterations were found. She presented nasal air escape in the fricative sounds, with tongue interposition when producing the coronal consonants; devoicing of stops and fricatives; substitution of palatal phonemes by dentilingual ones; substitution of the liquid alveolar in coda by the velar trill phoneme; production of middorsum palatal stop; imprecision when producing the liquid alveolar in initial onset; and, alteration of the articulatory spot of the sound /l/, raising the tip of the tongue to the vestibular side of the upper incisors while producing it.

Concerning the clinic orthodontic characteristics presented by the patient, after the interceptive orthodontic treatment was begun, the following were noticed: Angle Class I (Figures 4 and 5); anterior open bite (Figure 3), and lateral open bite on both right and left sides (Figures 4 and 5); severe upper midline deviation to the left (Figure 3); permanent upper lateral incisor semi-erupted by vestibular of the upper left deciduous canine (Figure 5); prolonged retention of the second inferior right deciduous molar (Figure 4); and, lower dental crowding (Figures 3, 4 and 5). Furthermore, she presents orthodontic diagnosis of dentinogenesis imperfecta and signs of gingivitis (Figure 3).

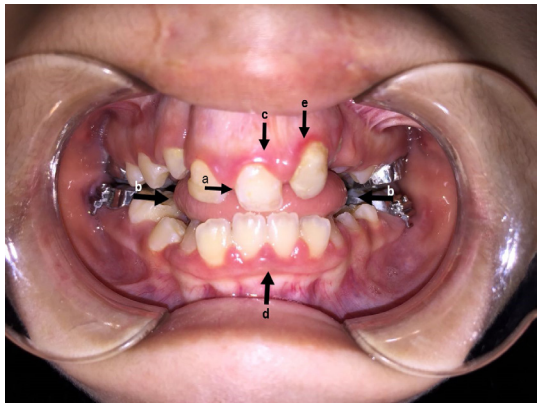

Figure 3. Intraoral image with front occlusion. Special attention to dentinogenesis imperfecta visible on upper incisors (a), anterior and bilateral open bite, and anterior and bilateral tongue interposition (b), severe upper midline deviation to the left (c), lower dental crowding (d), and signs of gingivitis (e).

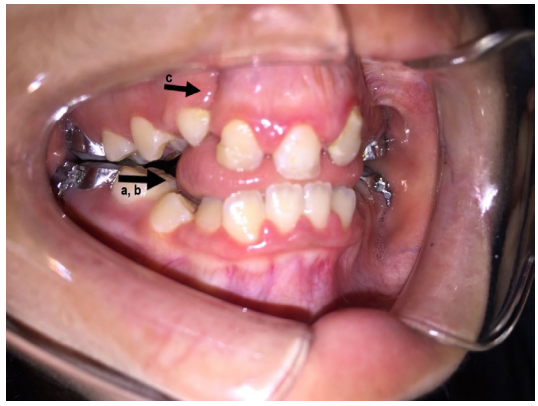

Figure 4. Image with right side occlusion. Special attention to lateral open bite (a), tongue interposition (b), and presence of cleft alveolus on the right side (c).

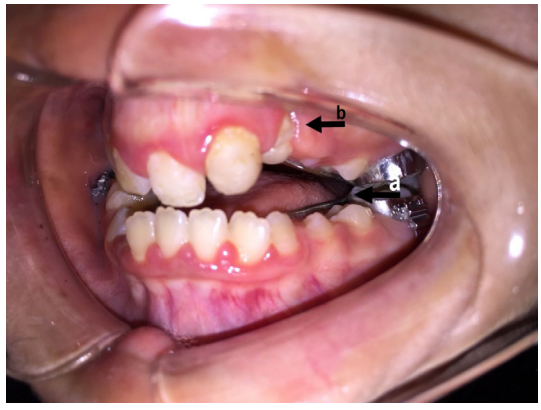

Figure 5. Image with left side occlusion. Special attention to left side open bite (a), and permanent upper left incisor semi-erupted by vestibular of the upper left deciduous canine where the cleft alveolus is located (b).

The patient undergoes interceptive orthodontic treatment outside the public outreach, with the use of maxillary and lingual arch expander. The speech, language and hearing therapy developed until the present moment aims at adjusting issues related to speech, velopharyngeal dysfunction and reported orofacial alterations. The patient will continue to receive medical care until the respective orthodontic and speech, language and hearing therapeutic plans are concluded.

Discussion

There's a shortage of publications related to BOFS in literature, given its rarity. In a literature

review carried out in 2010, only 81 articles related to the theme were found[2]. Reports describing the orthodontic and speech, language and hearing characteristics of patients with BOFS are even rarer[8].

The patient in this report presented clinical aspects related to BOFS already described in literature, such as auditory, craniofacial and ocular alterations[4,5]. Hearing Loss, which occurs in 70% of the cases[7], may have repercussions on speech, as the phonologic process of devoicing stops and fricatives observed on the patient's spontaneous and guided speech. Rare extra-craniofacial malformations may occur in BOFS, such as renal abnormalities[6]; the patient in this study presented multicystic right kidney and intellectual disability[5], with neuropsychological development being impaired.

Flores' study (2015)[8], reports alteration in speech in patient with BOFS, though it doesn't present details regarding the kinds of speech substitutions or adaptive processes practiced by the subject[8]. People with BOFS with cleft lip and palate may present alterations in speech related to dental occlusion alterations and the velopharyngeal dysfunction due to functional-anatomic abnormalities on the palate[9]. Subjects with CLP may present a wide range of alterations concerning the spot and the manner of producing sounds[9], as it has been verified with the patient in this study. The articulation presented by the patient when producing lateral liquid phonemes, using the vestibular side of the upper incisors in contact with the tip of the tongue, maybe justified by the presence of important structural imperfections that culminate on articulations unlikely to be produced[9], as the negative overjet, anterior and bilateral open bite, and transverse maxillary atresia. Although the speech, language and hearing and orthodontic evaluations were performed along with orthodontic treatment, the presence of the maxillary expander indicates that there was transverse maxillary atresia; and the lingual arch expander was there to preserve the room necessary for teeth exchange, thus not interfering with the alterations found. The positioning of the tongue both at rest and during the stomatognathic functions may have been influenced by the presence of the orthodontic devices. However, the orofacial motor function alterations found are normally associated with the existing structural alterations.

The anteroposterior maxillary deficiency may appear in patients submitted to surgeries such as lip and palate repair[10]. The patient reported in this study did undergo these surgeries, which may have generated the negative overjet. The maxillary deficient growth may alter the development of the midface, posteriorly affecting dental occlusion, speech, and nose shape[10], as it's the case in this study.

Conclusion

Some functional and structural alterations of the craniofacial complex present in this patient with BOFS are in agreement with literature. Other ones, though, hadn't yet been reported. Even though there's phenotype heterogeneity, further research studies with significant samples are made necessary to characterize the alterations found as characteristic of the syndrome. Attention is called to the need of interdisciplinary intervention in BOFS as early as possible, with emphasis to otorhinolaryngology, speech, language and hearing, and orthodontics, due to the alterations found.

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