Reporte de Casos
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Oral manifestations in children with Moebius syndrome: report of two cases

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Abstract: Moebius syndrome represents a rare congenital disorder characterized by non-progressive unilateral or bilateral paralysis of the facial and abducens nerves. The aim of this study is to report the oral, dental and general manifestations of Moebius syndrome present in two Brazilian children. The patients were referred to the Pediatric Dental Care Service of the Children's Specialties Center, Baby Clinic of the State University of Londrina. During the consultations, the cases were documented through individualized clinical examination and photographs. Clinical case 1: 9-year-old girl, diagnosed with Moebius-Poland syndrome, attended for preventive dental treatment. Clinical and radiographic examination revealed anterior open bite, unilateral crossbite, microstomia, lack of buccal elasticity, dry labial mucosa, dental fluorosis in upper and lower teeth associated with enamel hypoplasia, dental crowding, upper right canine ectopic eruption, palate ogival, micrognathism, lip sealing and adequate lingual tonus. Clinical case 2: 26-month-old girl, attended the service for preventive dental treatment. Clinical and radiographic examination revealed anterior open bite, microstomia, lack of buccal elasticity, high arched palate, hypotonic tongue, micrognathism, inadequate lip seal and dental caries. In both cases, episodes of dentoalveolar trauma were related by parents. Pediatric dentists play a fundamental role in the early diagnosis of oral and facial characteristics that may be present from birth and imply potential repercussions on the development of the stomatognathic system.

Key words: Facial Paralysis; Maxillofacial Abnormalities; Mobius syndrome.

Manifestaciones orales en niños con síndrome de Moebius: reporte de dos casos

Resumen: El síndrome de Moebius representa una enfermedad congénita rara, caracterizada por una parálisis unilateral o bilateral no progresiva de los nervios facial y abductor. El objetivo de este estudio es reportar las manifestaciones bucales, dentales y generales del síndrome de Moebius presentes en dos niñas brasileñas. Los pacientes fueron encaminados al Servicio de Atención Odontológica Pediátrica del Centro de Especialidades Infantiles de la Clínica del Bebé de la Universidad Estatal de Londrina. Durante las consultas, los casos fueron documentados a través de exámenes clínicos individualizados y fotografías. Caso clínico 1: Niña de 9 años, diagnosticada con Síndrome de Moebius-Poland, asistió para tratamiento odontológico preventivo. El examen clínico y radiográfico reveló mordida abierta anterior, mordida cruzada unilateral, microstomía, falta de elasticidad bucal, mucosa labial seca, fluorosis dental en dientes superiores e inferiores asociada a hipoplasia del esmalte, apiñamiento dental, erupción ectópica del canino superior derecho, paladar profundo, micrognatismo, sellado labial y tono adecuado de la lengua. Caso clínico 2: Niña de 26 meses, asistió al servicio para tratamiento odontológico preventivo. El examen clínico y radiográfico reveló mordida abierta anterior, microstomía, falta de elasticidad bucal, paladar alto y arqueado, lengua hipotónica, micrognatismo, sellado labial inadecuado y caries. En ambos casos, los padres informaron sobre episodios de traumatismo dentoalveolar. El odontopediatra tiene un papel fundamental en el diagnóstico precoz de las características bucales y faciales que pueden estar presentes desde el nacimiento y tener potenciales repercusiones en el desarrollo del sistema estomatognático.

Palabras clave: Anomalías Maxilofaciales; Parálisis Facial; Síndrome de Mobius.

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Manifestações orais em crianças com síndrome de Moebius: relato de dois casos

Resumo: A Síndrome de Moebius representa uma doença congênita rara, caracterizada por paralisia unilateral ou bilateral não progressiva dos nervos facial e abducente. O objetivo deste estudo é relatar as manifestações orais, dentárias e gerais da Síndrome de Moebius presentes em duas crianças brasileiras. Os pacientes foram encaminhados ao Serviço de Atendimento Odontológico Infantil do Centro de Especialidades Infantis, Bebê-Clínica da Universidade Estadual de Londrina. Durante as consultas, os casos foram documentados por meio de exame clínico individualizado e fotografias. Caso clínico 1: menina de 9 anos, diagnosticada com Síndrome de Moebius-Poland, compareceu para tratamento odontológico preventivo. O exame clínico e radiográfico revelou mordida aberta anterior, mordida cruzada unilateral, microstomia, falta de elasticidade bucal, mucosa labial seca, fluorose dentária em dentes superiores e inferiores associada à hipoplasia de esmalte, apinhamento dentário, erupção ectópica do canino superior direito, palato profundo, micrognatismo, selamento labial e tônus lingual adequado. Caso clínico 2: menina de 26 meses, compareceu ao serviço para tratamento odontológico preventivo. O exame clínico e radiográfico revelou mordida aberta anterior, microstomia, falta de elasticidade bucal, palato alto e arqueado, língua hipotônica, micrognatismo, selamento labial inadequado e lesões de cárie dentária. Em ambos os casos, episódios de traumatismo dentoalveolar foram relatados pelos pais. O odontopediatra tem papel fundamental no diagnóstico precoce de características orais e faciais que podem estar presentes desde o nascimento e implicar em potenciais repercussões no desenvolvimento do sistema estomatognático.

Palavras-chave: Anormalidades Maxilofaciais; Paralisia Facial; Síndrome de Möbius.

Introduction

First described in the 1880s by Moebius[1] and Von Graefe[2], Moebius syndrome (MS) is a rare congenital disorder characterized by uni or bilateral non-progressive paralysis of the facial and abducens nerves (VII and VI cranial nerves), respectively.[1,2] As well as the involvement of other cranial nerves, orofacial anomalies and limb defects may also be associated.[3,4] Cases involving pectoral muscles hypoplasia associated with a hand congenital malformation, it is called Moebius-Poland syndrome (MPS).[5]

The etiology of MS is not completely understood. It is believed to be related to genetic factors associated with abnormal development of the hindbrain.[6] On the other hand, some authors describe a relationship with environmental or mechanical factors that resulted in ischemia or hypoxia for the developing fetus; or drugs use during pregnancy, such as: thalidomide[7], cocaine[8] or misoprostol.[4,9,10]

The exact prevalence of MS remains uncertain. According to Carta *et al.* (2021)[11], it is estimated that it may occur in 0.3 per 100.000 live births, while Picciolini *et al.* (2016)[12] report a prevalence of 1 per 250.000 and Rasmussen *et al.*[13] 1 per 500.000 live births. However, the Orphanet Report Series[14], Rare Disease Collection 2019 reports the estimated prevalence per 100.000 as "unknown", with only 300 cases described in the literature, with equal incidence in both sexes.[6,11,12]

Oral and facial manifestations are varied and may include: microstomia, inelastic oral orifice, inadequate lip seal, tongue weakness and atrophy, micrognathia, malocclusion, hypodontia, high arched palate, cleft lip/palate and bifid uvula.[15-18] Additionally, poor or absent sucking due to incomplete lip closure, lack of facial mimicry (especially when crying), staring and incomplete eyelid closure may be present.[12,19] This article aimed to describe the oral and general manifestations of two children diagnosed with MS, which are relevant from a clinical point of view for dental care linked

to the prevention of dental caries, correction of malocclusion and proper functioning of the stomatognathic system. Thus, these findings are expected to assist health professionals, especially pediatric dentists, in the syndrome diagnosis, dental planning and therapeutic decision-making, based on the best scientific evidence.

Case report

All patients were treated in the Children's Dental Care Service of the Children's Specialties Center, Baby-Clinic of the State University of Londrina, after referral from the Basic Health Unit (BHU). Patients and their legal representatives were consulted and agreed to participate in the study, signing the informed consent form.

CASE 1

A 9-year-old Brazilian girl, without cognitive or motor impairment, was sent from the BHU for preventive dental treatment. Family history revealed that the patient was the third child of a non-consanguineous marriage, and siblings, without any congenital abnormalities as well as her familiars. The patient undergoes multidisciplinary follow-up with a speech therapist, osteopath, psychologist, pediatrician, endocrinologist, orthopedist, occupational therapist and started this year to enter a regular state school.

Father (33 years old), mother (29 years old), with an abortion history 3 years before the child's birth, reported placental and cervix detachment in the first trimester of pregnancy. During pregnancy, mother used Thalidomide, Amoxicillin with Potassium Clavulanate for urinary infection and Cytotec® (Misoprostol) to control abdominal cramps and low blood pressure, the latter two having teratogenic potential. In addition, the mother reports that she underwent endodontic dental treatment under local anesthesia and was exposed to radiation for periapical radiography. Cesarean delivery at 39 weeks, Apgar 8 and 9, weighing and measuring, respectively, 2.145 kg and 44 cm.

After birth, the patient went to the room without the need for intensive care unit monitoring. The diagnosis of MS was made at 1 month of age through clinical criteria that involved bilateral facial paralysis and paralysis of lateral eye movements due to paralysis of the sixth cranial palsy.

The patient was received at the dental clinic at age of 9 measuring 117 cm in height 117 cm, weight 21 kg, syndromic face, normal ear positioning, vertical strabismus and normal hair appearance (Figure 1). Ectrodactyly in the left hand (Figure 2), without changes in the feet and fingers of the other limbs and left pectoral musculature agenesis. The child has bronchiolitis and asthma, and lacks the heart, hearing, and behavioral problems characteristic of autism spectrum disorder (ASD).

The patient has a good communicative profile, mild speech impairment, excellent socialization and interaction. Balanced diet with foods of different consistencies without dietary restrictions, mild impairment of chewing on the left side and no difficulty in swallowing. Furthermore, the patient does not have facial expressions on the left side due to

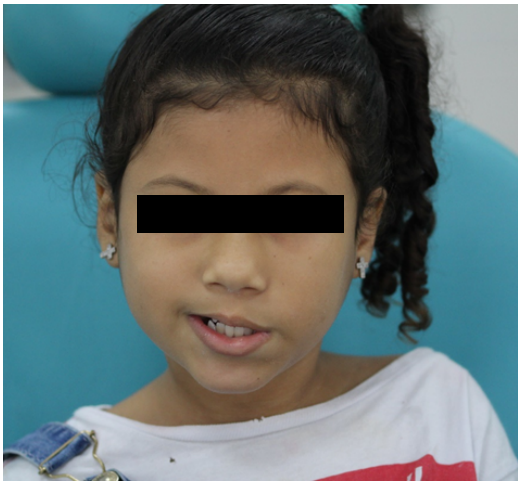


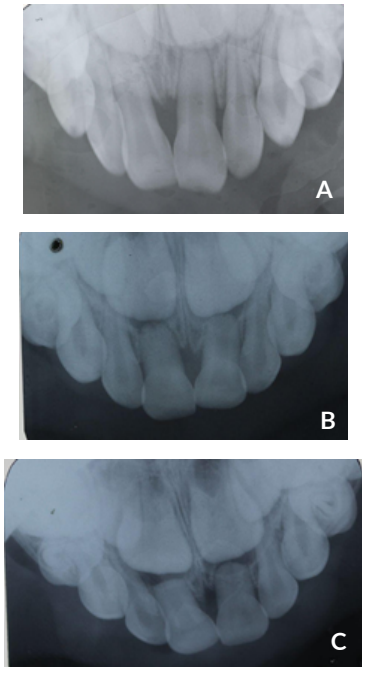
Figure 1. *Facial photograph showing vertical strabismus and normal capillary appearance.*

Figure 2. *Ectrodactyly affecting the left hand.*

congenital facial nerve palsy inherent to MS.

Patient without natal or neonatal tooth history. Deciduous dentition eruption started at 8 months of age and established at 2 years and 7 months, with no history of dental caries. At 4 years and 3 months, the child suffered a dentoalveolar trauma (DT), due to a fall on the playground, where she hit her mouth against a metal bar. Clinical examination and anamnesis, carried out in delayed treatment, showed concussion of tooth #51 and subluxation of teeth #61 and #62. In a 24-month longitudinal clinical and radiographic follow-up, there was a color change in teeth #61 and #62 with no periapical lesion, periodontal ligament thickening, in addition to physiological tooth resorption that led to tooth mobility (Figures 3A, 3B and 3C).

Micrognathism, anterior open bite, unilateral crossbite, tooth crowding, upper right canine ectopic eruption, dental fluorosis in upper and lower teeth associated with enamel hypoplasia, high arched palate (Figure 4), microstomia, lack of buccal elasticity, dry labial mucosa, adequate lip sealing and lingual tone were observed. On radiographic examination, taurodontism was identified in permanent molars and a slight rotation



Figures 3A, 3B and 3C. *24-month radiographic follow-up after dentoalveolar trauma.*

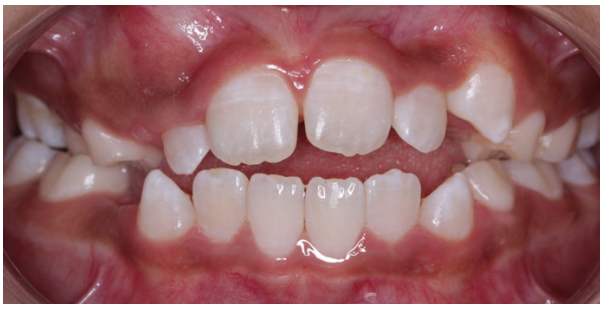


Figure 4. *Anterior open bite, unilateral crossbite, dental fluorosis on upper and lower anterior teeth associated with enamel hypoplasia, tooth crowding and upper right canine ectopic eruption. Teeth #53 and #83 exfoliated.*

of the permanent upper right lateral incisor, without number or size changes (Figure 5).

This treatment plan consists of dietary counseling, dental biofilm evidence, oral hygiene instruction, dental prophylaxis, fluoride varnish application, dental fissure sealants on permanent molars and orthodontic treatment for correction of anterior open bite, alignment of ectopic canine and treatment of micrognathia.

CASE 2

A 26-month-old Brazilian girl, without cognitive or motor impairment, was sent from the BHU for preventive dental treatment. Family history revealed that the patient was the third child of a non-consanguineous marriage, and her sisters were 22 and 12 years old, without any congenital abnormalities, as well as her family members. The patient undergoes multidisciplinary follow-up with a speech therapist, ophthalmologist, osteopath, pediatrician, neurologist and occupational therapist.

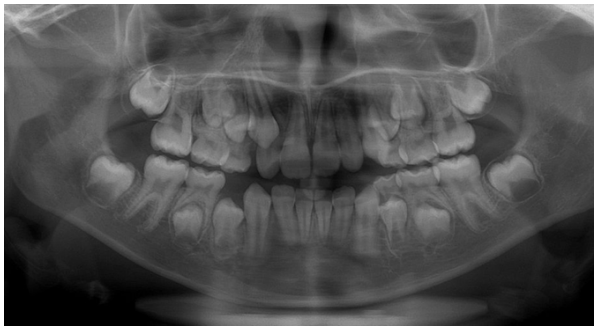


Figure 5. *Taurodontism in the first permanent molars, lack of space, difficult upper right canine eruption and right lateral incisor slight rotation.*

Father (42 years old) and mother (39 years old), with no abortion history, reported placental abruption in the first trimester of pregnancy. During pregnancy, the mother used Methyldopa® due to high blood pressure and there was no use of medication for abdominal cramps or abortifacients (Misoprostol). Furthermore, she has not been exposed to radiation, alcohol or drugs. Normal and induced delivery at 34 weeks of age, Apgar 7 and 8, weighing and measuring 2.600 kg and 42 cm, respectively.

After birth, the patient spent 10 days in the Intensive Care Unit for monitoring due to prematurity. During this period, there was a hypothesis of the presence of some syndrome. However, the diagnosis of MS was made at 9 months of age through clinical criteria that involved bilateral facial paralysis and paralysis of lateral eye movements due to paralysis of the sixth cranial palsy.

The patient was received at the dental clinic at age of 2 measuring 78 cm in height, weight 13 kg, syndromic face, normal ears implantation, convergent strabismus and normal hair appearance (Figure 6). Absence of alteration in the upper and lower limbs and pectoral musculature. In addition, the

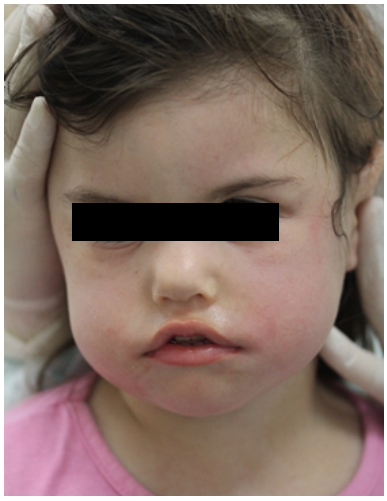


Figure 6. Facial photograph showing convergent strabismus and normal capillary appearance.

patient does not have respiratory, cardiac and/or hearing problems. The patient exhibited uncooperative behavior during consultations.

The patient has significant speech impairment and little interaction with the dental team. Inadequate food diet rich in sucrose, without dysphagia, preference for liquid and pasty foods and chewing impairment for hard foods. Also, the patient has no facial expressions on either side.

Patient without natal or neonatal tooth history. Deciduous dentition eruption started at 6 months of age and established by 2 years. Intraoral examination revealed complete deciduous dentition, anterior open bite due to pacifier use, microstomia, lack of buccal elasticity, (Figure 7), high arched palate (Figure 8), hypotonic tongue, micrognathism, inadequate lip seal. Additionally, presence of dental caries in teeth #74 (ICDAS 6) and #75 (ICDAS 5) was observed (Figures 9A and 9B).

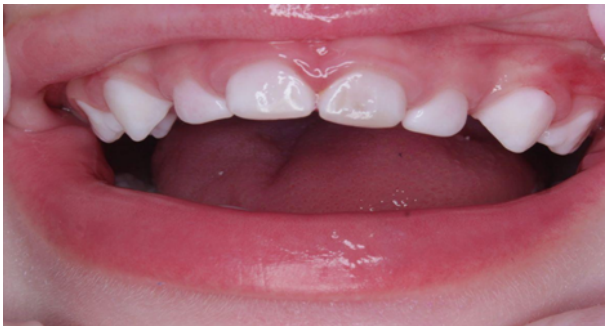


Figure 7. Anterior open bite, microstomia, lack of buccal elasticity, darkening on tooth #61.

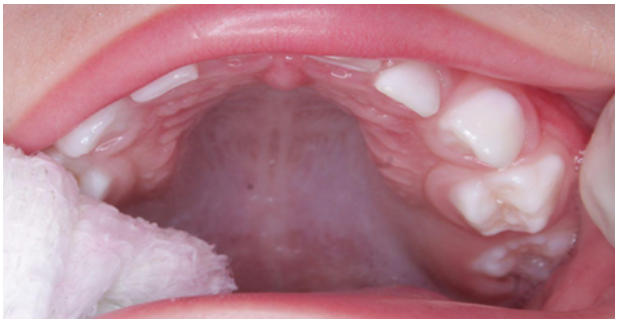
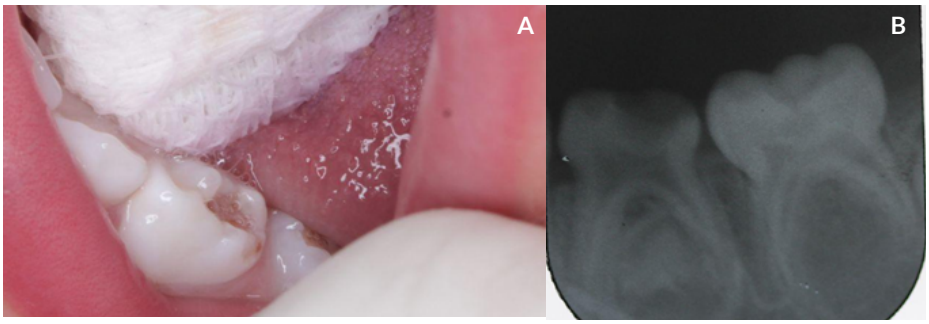


Figure 8. High arched palate.

Parents reported a DT history at 1 year and 9 months, due to a fall from standing height. On clinical and radiographic follow-up, tooth darkening was observed on tooth #61 (Figure 7) and periodontal ligament thickening and pulp calcification on teeth #51 and #61 (Figure 10).

This treatment plan consists of dietary counseling, instructions for removing the cup and bottle, dental biofilm evidence, oral hygiene instructions, dental prophylaxis, application of cariostatic in the deciduous molars, dental restoration in composite resin on teeth #74 and #75, and clinical and radiographic follow up of the DT.



Figures 9A and 9B. *Dental caries in teeth #74 and #75 without pulp exposure.*

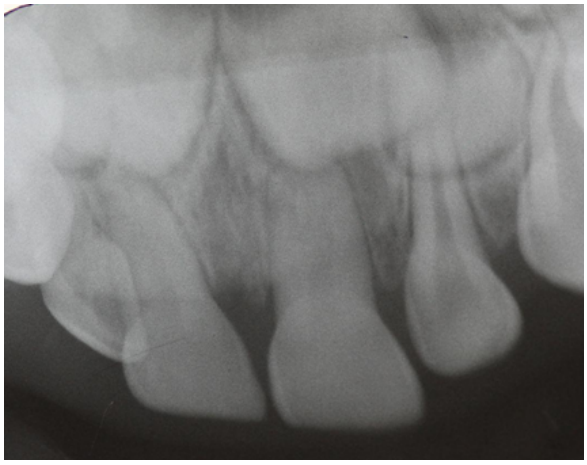


Figure 10. *Periodontal ligament thickening and pulp calcification on teeth #51 and #61.*

Discussion

Moebius syndrome (MS) is an extremely rare congenital disorder with prevalence about 0.002% among live births[20], which is characterized by uni and/or bilateral paralysis of the facial and abducens nerve.[4,12] These nerves are responsible for sucking, swallowing, chewing, facial movements and eye movement. In addition to these cranial nerves, it can be associated with other cranial nerve palsies such as: trigeminal, oculomotor, auditory, spinal accessory, or hypoglossal.[4,10,21] Orthopedic anomalies and intellectual disabilities may also be present in MS.[20] The condition is non-progressive, patients usually have a full life expectancy.[10]

The MS diagnosis is based exclusively on clinical criteria, although recent studies are beginning to document causative genetic patterns.[4,22] The etiology is not fully understood; however studies suggest etiological factors include dysplastic or degenerative developmental disorders such as hypoxic–ischemic injuries, especially around 5–6 weeks of gestation, peripheral neuropathies, vasculopathies, gestational trauma, drug exposure, and a genetic component.[21] In the present article, in both reported cases, there was placental abruption in the first trimester of pregnancy, an event that may result in impaired fetal blood oxygenation and, consequently, with the syndrome development. Furthermore, in clinical case 1, the mother reported the use of Misoprostol and Thalidomide, drugs that may be associated with MS and malformations.

Regarding clinical case 1, the patient presents association of Poland syndrome (PS) with Moebius, described in the literature as Moebius-Poland syndrome.[10,22] PS is a rare and congenital anomaly that causes musculoskeletal changes in the ribcage and upper limbs. It is believed that the simultaneous occurrence of these syndromes is related to the presence of a genetic alteration that causes a common failure during embryonic development[23,24],

which would make the MS and PS part of the same spectrum of disorders of rhombencephalic development.[22,23] Ectrodactyly of the left hand and unilateral absence of the left pectoralis major and minor muscles, which causes a slight thoracic and mammary asymmetry, were observed in case 1.

In addition to PS, ASD is strongly associated with Moebius syndrome.[15,25,26] Studies show that the prevalence of ASD associated with the syndrome is greater than the prevalence of ASD in the general population: 30% to 40% of individuals affected by the syndrome have behaviors characteristic of ASD.[27] However, it is worth noting that children with MS may have difficulties in interaction, social or emotional adaptation due to the paralysis of the facial muscles responsible for facial expression and speech.[3,12] These characteristics may be exacerbated or be confused with aspects of the ASD and may represent a challenge in the care of pediatric dental patients diagnosed with MS. Therefore, it is necessary that emotional and social aspects are not confused with the diagnosis of ASD, confirming the importance of multidisciplinary monitoring. Non-collaborative behavior and attitudes not compatible with age were observed during dental consultations in clinical case 2. Thus, it is necessary for the professional to be attentive to define the best technique for behavioral management during dental care.

Classic oral and dental characteristics found in this patient corroborate those described by several authors: microstomia, inelastic oral orifice, dry labial mucosa, inadequate lip seal, tongue atrophy, micrognathia, malocclusion, and high arched palate.[15-18] Table 1 presents and compares the main manifestations of MS.

Table 1. *Moebius syndrome oral manifestations in the literature compared to the clinical cases in this article.*

ORAL MANIFESTATIONS REPORTED IN THE LITERATURE	ORAL MANIFESTATIONS PRESENT IN CLINICAL CASE 1	ORAL MANIFESTATIONS PRESENT IN CLINICAL CASE 2
Microstomia	Present	Present
Inelastic oral orifice	Present	Present
Dry labial mucosa	Present	Present
Inadequate lip seal	Not present	Present
High arched palate	Present	Present
Cleft palate	Not present	Not present
Bifid uvula	Not present	Not present
Tongue bifid	Not present	Not present
Tongue atrophy	Not present	Present
Microglossia	Not present	Not present
Micrognathia	Present	Present
Malocclusion	Present	Present
Anterior open bite	Present	Present
Dental caries (cavity)	Not present	Present
Hypodontia	Not present	Not present
Enamel Hypoplasia	Present	Not present
Tooth Eruption Ectopic	Present	Not present

In clinical case 1, the presence of taurodontism was detected in the bilateral lower first permanent molars. The present report is the first clinical case reported in the literature of this variation from normality associated with MS. Taurodontism is characterized by apical displacement of the pulp floor and shortening of the roots. It is believed to be caused in early fetal life due to the failure of the diaphragm of the epithelial sheath of Hertwig to invaginate at the proper horizontal level.[28,29]

In addition to the characteristics reported above, the patient in clinical case 2 had dental caries, a complex disease that can be explained owing to changes in salivary flow and chemical properties of saliva in children diagnosed with MS.[30,31] Nonetheless, parents reported a diet with a high frequency of sugar intake and difficulty in controlling dental biofilm effectively. Additionally, chewing difficulties present in MS may favor a more liquid and pasty diet and increase the risks of developing dental caries lesions.

Present in both reported cases, DT concerns common adverse events during child development. Although there are no consistent studies between MS and the occurrence of DT, developmental delays and poor motor coordination of the syndrome represent factors that may be related to the increased risks of DT.[12,26] In addition, factors such as anterior open bite and inadequate lip seal favor DT episodes.[32,33]

Ultimately, it is worth highlighting that in both cases, the legal guardians reported being monitored by different professionals. However, interestingly, the pediatric dentist's care was performed after other professionals, which may indicate difficulty in access, limitations in the articulation between the primary and secondary care services, as well as a lack of knowledge of the relevance of this professional to the child patient. In this sense, we believe that the multidisciplinary approach is essential and should be carried out concomitantly, as it favors the adequate functioning of the stomatognathic system, with implications for sucking, speech, swallowing and, consequently, impacts on quality of life, self-esteem, well-being and socialization. Synergistic action between professionals is favorable for the patient and can directly influence the oral condition and stomatognathic system, since the harmony and balance of these structures require joint and individualized professional action.

Conclusion

Based on the reported clinical cases, it can be concluded that Moebius syndrome represents a rare autosomal recessive disorder with varied and inherent oral, facial and general manifestations that require an interdisciplinary and multidisciplinary approach. In this sense, pediatric dentists play a fundamental role in the early diagnosis of oral and facial characteristics that may be present from birth and imply potential repercussions on stomatognathic system development.

Considering the characteristics found in the two clinical cases, the challenge of dental care in terms of effectiveness of care demands individualized treatment strategies based on prevention and promotion of oral health from an early age. treatment based strategies on prevention and promotion of oral health from an early age. In the long term, the maintenance

of favorable oral conditions associated with occlusal rehabilitation and aesthetic interventions should be considered, since they represent factors that require action between specialties and professionals and that aim to improve the quality of life, well-being and self-esteem of the child and the family nucleus.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Ethics Statement

The authors declare that the parents gave consent for images and clinical information of the case to be reported in scientific publications. Parents understand that the child's name and initials will not be published and efforts will be made to conceal the child's identity. This article complies with the protocols of the Research Ethics Committee of the State of University of Londrina

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