Reportes de Casos
https://doi.org/10.47990/1y1vnc79

Clinical and oral characteristics in patients affected by Mucopolysaccharidosis type IV–A: Case reports

Marcela Favaretto Paro Pereira[1], *Gabriela Leal Peres Fernandes*[2], *Isabella Silva Catananti*[3], *Eduarda Martins Fontes Cantarella de Almeida*[3], *Laura Imbriani Bento de Azevedo*[4], *Manuela Marquesini Vanim*[1], *Marcelle Danelon*[5].

Abstract: **Introduction:** Mucopolysaccharidoses (MPSs) are rare diseases related to chronic metabolic conditions caused by a genetic mutation that results in the deficiency of lysosomal enzymes responsible for the degradation of glycosaminoglycans, causing alterations in the normal functioning of the organism and oral alterations. **Aim:** To evaluate the physical, systemic and oral characteristics of two sibling patients with Mucopolysaccharidosis type IV-A treated at the clinic for patients with special needs of the University of Ribeirão Preto, Unaerp, São Paulo, Brazil. **Case Reports:** Clinical Case 1: Female patient, 34 years old; and Clinical Case 2: Male patient, 31 years old. In Clinical Case 1, the following clinical and physical characteristics were observed: respiratory difficulty, bone changes in the arms, valgus deformities of the knees, dysmorphic thorax, dysostosis with changes in the hands, decreased hearing, rheumatological problems, difficulty in locomotion, changes in motor coordination, short stature, shortened neck and trunk. Regarding oral changes: taurodontia in upper and lower molars, supernumerary tooth, low mandibular height, macroglossia, anterior open bite, vestibular exostoses, dental erosion on the occlusal and palatal/lingual surfaces in almost all teeth, limited mouth opening, atypical swallowing and deep palate. In Clinical Case 2, the same clinical and oral characteristics were observed, except: supernumerary tooth and vestibular exostoses. **Conclusion:** MPS is a rare disease that affects organs and tissues, requiring lifelong multidisciplinary treatment, as there is no cure. However, dental treatment is important to contribute to the individual's quality of life.

Key words: Mucopolysaccharidoses, Rare diseases, Heredity, Oral manifestations, Glycosaminoglycans.

Características clínicas y orales en pacientes afectados por Mucopolisacaridosis tipo IV-A: Reportes de casos

Resumen: **Introducción:** Las Mucopolisacaridosis (MPSs) son enfermedades raras relacionadas con condiciones metabólicas crónicas causadas por una mutación genética que resulta en la deficiencia de enzimas lisosomales responsables de la degradación de glicosaminoglicanos, provocando alteraciones en el funcionamiento normal del organismo y alteraciones bucales. **Objetivo:** Evaluar las características físicas, sistémicas y bucales de dos pacientes hermanos con Mucopolisacaridosis tipo IV-A atendidos en la clínica de Pacientes Especiales de la Universidad de Ribeirão Preto-Unaerp, São Paulo, Brasil. **Informe de Caso:** Caso Clínico 1: Paciente femenina, 34 años y Caso Clínico 2: Paciente masculino, 31 años. En el Caso Clínico 1 se observaron las siguientes características clínicas y físicas: dificultad respiratoria, cambios óseos en los brazos, deformidades óseas em las rodillas, tórax dismórfico. disostosis con cambios en las manos, pérdida auditiva, problemas reumatológicos, dificultad para moverse, cambios en la coordinación motora, baja estatura, cuello y tronco acortados. Respecto a las alteraciones bucales: taurodontia en molares superiores e inferiores, dientes supernumerarios, altura mandibular baja, macroglosia, mordida abierta anterior, exostosis vestibulares, erosión dental en las superficies oclusales y palatinas/linguales en casi todos los dientes, apertura bucal limitada, deglución atípica y paladar profundo. En el Caso Clínico 2 se observaron las mismas características clínicas y bucales, excepto: diente supernumerario y exostosis vestibular. **Conclusión:** La MPS es una enfermedad rara que afecta órganos y tejidos, requiriendo un tratamiento multidisciplinario de por vida, ya que no tiene cura. Sin embargo, el tratamiento dental es importante para contribuir a la calidad de vida del individuo.

Palabras clave: Mucopolisacaridosis, Enfermedades raras, Herencia, Manifestaciones Bucales, Glicosaminoglicanos.

[1]*Práctica odontológica en Ribeirão Preto, São Paulo, Brasil.*
[2]*São Paulo State University (UNESP), School of Dentistry, Araçatuba, Brazil.*
[3]*Department of Pediatric Clinics, School of Dentistry of Ribeirão Preto, São Paulo University, Brazil.*
[4]*Práctica odontológica en Campinas, São Paulo, Brasil.*
[5]*Policlinic of Operative Dentistry, Periodontology and Pediatric Dentistry, Medical Faculty Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany.*

Características clínicas e bucais em pacientes afetados pela Mucopolissacaridose tipo IV-A: Relato de casos

Resumo: **Introdução:** As Mucopolissacaridoses (MPSs) são doenças raras relacionadas a condições metabólicas crônicas causadas por uma mutação genética que resulta na deficiência de enzimas lisossômicas responsáveis pela degradação de glicosaminoglicanos, causando alterações no funcionamento normal do organismo e alterações bucais. **Objetivo:** Avaliar as características físicas, sistêmicas e orais de dois pacientes irmãos com Mucopolissacaridose tipo IV-A atendidos na clínica de Pacientes Especiais da Universidade de Ribeirão Preto-Unaerp, São Paulo, Brasil. **Relato de Casos:** Caso Clínico 1: Paciente do sexo feminino, 34 anos e Caso Clínico 2: Paciente do sexo masculino, 31 anos. No Caso Clínico 1, foram observadas as características clínicas e físicas: dificuldade respiratória, alterações ósseas nos braços, deformidades em valgo dos joelhos, tórax dismórfico, disostose com alterações nas mãos, diminuição da audição, problemas reumatológicos, dificuldade de locomoção, alteração da coordenação motora, baixa estatura, pescoço e tronco encurtados. Em relação às alterações orais: taurodontia em molares superiores e inferiores, dente supranumerário, baixa altura mandibular, macroglossia, mordida aberta anterior, exostoses vestibulares, erosão dentária nas superfícies oclusal e palatina/lingual em quase todos os dentes, abertura bucal limitada, deglutição atípica e palato profundo. No Caso Clínico 2 foram observadas as mesmas características clínicas e bucais, exceto: dente supranumerário e exostoses vestibulares. **Conclusão:** A MPS é uma doença rara que afeta órgãos e tecidos, necessitando de tratamento multidisciplinar ao longo da vida, pois não há cura. Entretanto, o tratamento odontológico é importante para contribuir com a qualidade de vida do indivíduo.

Palavras-chave: Mucopolissacaridose, Doenças raras, Hereditariedade, Manifestações orais, Glicosaminoglicanos.

Introduction

Mucopolysaccharidoses (MPSs) are rare diseases related to chronic metabolic conditions caused by a genetic mutation. This anomaly results from a deficiency of specific lysosomal enzymes that determine the type of MPS. These enzymes are responsible for degrading glycosaminoglycans (GAGs)[1-3]. The enzyme deficiency leads to defective catabolism of glycosaminoglycans (mucopolysaccharides), resulting in an increased accumulation of mucopolysaccharides within intracellular lysosomes in various body tissues[4-6].

The manifestations of the disease can be classified into seven types, including: Types I, II, III, IV, VI, VII, and IX[7]. The prevalence of all types of MPS is 1 case in 20,000 live births[5]. The disease is caused by a mutation in the IDUA gene (alpha-L-iduronidase), which has the necessary sequence to produce the enzyme that hydrolyzes large sugars called glycosaminoglycans (GAGs)[8]. MPS IV-A is a multisystemic and progressive disease, with the speed of symptom progression and the severity of the disease varying in each individual. Generally, at birth, these individuals exhibit a normal phenotype, and at 2-3 years of age, the manifestations of the pathology can be observed.

The most common alterations are: facial; skeletal; joint, such as genu valgum; joint hypermobility; hip subluxation and dysplasia; respiratory and cardiac diseases; visual and hearing impairments; digestive problems; umbilical and inguinal hernias; joint pain; oral alterations; inadequate growth of the spine (but the sternum grows normally, resembling the so-called "pigeon chest"), leading to respiratory difficulties; short stature (with short trunk and neck); multiple dysostosis, with changes in the skull, spine, hands, hips, and long bones. Regarding growth, it slows down after 18 months of life, stopping at the end of childhood. Cognitive is typically preserved in MPS IV-A [9-11].

MPS has various clinical manifestations based on the type of enzyme defect, the affected organ, and the glycoprotein involved [12]. Diagnosis can be made through clinical exams, urine and blood tests, and radiographic examinations are also important. The most common oral alterations found are: changes in the enamel structure in both deciduous and permanent dentition; taurodontism; prominent lips; deep palate; mandible with low height and altered condyles; impacted teeth; supernumerary teeth; delayed tooth eruption; macroglossia; anterior open bite; gingival hyperplasia; mouth breathing; diastemas; microdontia; obliteration of pulp chambers; hyperplasia of dental follicles, and dentigerous cysts[10]. When there is clinical suspicion of the disease, it is recommended to confirm the diagnosis through enzyme activity and/or genetic testing[13]. Laboratory tests are also conducted through clinical examinations, urine and blood tests, and radiographic examinations are also important.

Children and adults with MPS have special healthcare needs in terms of the severity of the condition and often undergo a multidisciplinary treatment approach by specialized pediatric teams, including cardiologists, neurologists, psychiatrists, orthopedists, physiotherapists, and ophthalmologists, due to the multiple effects of the condition[12]. In light of this, the aim of this study was to evaluate the physical, systemic, and oral characteristics of two patients with mucopolysaccharidosis who were treated at the Special Patients Clinic of the University of Ribeirão Preto-Unaerp, Brazil.

Cases report

The patients' guardians provided prior consent for the treatment, documentation, and subsequent publication of the cases.

CASE 1

A 34-year-old female patient (Figure 1), 92 cm tall, weighing 19 kg, residing in Ribeirão Preto/SP/Brazil, was diagnosed with Morquio Syndrome (MPS IV-A) at the age of 2, when her mother noticed bone enlargement in the wrist area and malformation and growth issues in the thorax. However, when she took her daughter to the pediatrician, the doctor reported that these changes were normal and there was no problem with the child. Nevertheless, the mother decided to

Figure 1. *Patient female with MPS IV-A.*

consult another doctor, who diagnosed the patient with MPS type IV-A and referred her for treatment at the Clinical Hospital in Ribeirão Preto, University of São Paulo, Brazil (CHRP-USP).

In 1997, the patient attended the Special Patients Clinic at the University of Ribeirão Preto-Unaerp, São Paulo, Brazil, for routine dental care and has been under follow-up until the present year. During the anamnesis, some important data were obtained. Regarding the prenatal period, the mother did not have any illnesses during pregnancy; she took iron phosphate from the 7th month of pregnancy until 2 months after childbirth; the parents are not consanguineous and have 5 children, 3 of whom are affected by the disease. In the postnatal period, a natural delivery was performed (9 months of gestation); the patient reported breastfeeding for 3 months, she used a bottle and pacifier, had parotitis and chickenpox as a child, and stated that her parents were surprised when they received the diagnosis of the disease, although their current reaction is one of acceptance.

When asked about the sequelae related to MPS, the patient reported the following: respiratory difficulty, bone changes in the arms (Figure 2), valgus deformities in the knees (Figure 3), thoracic enlargement (Figure 4), dysostosis with changes in the hands (Figure 5), decreased hearing (she uses a hearing aid in both ears), rheumatological problems, difficulty in mobility, impaired motor coordination, short stature, low-pitched voice, and shortened neck and trunk. Therefore, she receives multidisciplinary follow-up at CHRP-USP focusing on the heart, ears, and eyes, as well as at Unaerp with

Figure 2. *Arms with bone changes.*

Figure 3. *Valgus deformity of the knees.*

Figure 4. *Enlarged chest.*

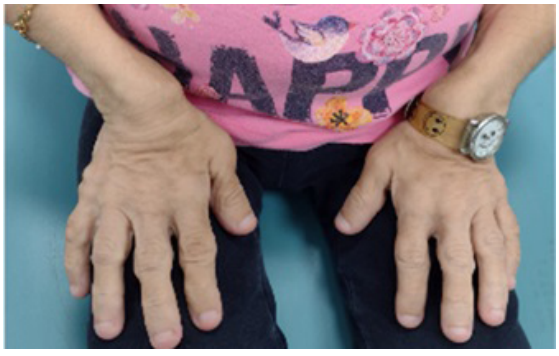

Figura 5. *Dysostosis of the hands.*

a dentist and physiotherapist. However, as of the last clinical visit, the patient reported not taking any medication due to the lack of government approval.

Regarding oral health, the patient brushes her teeth independently three times a day (morning, afternoon, and night), uses dental floss less frequently, and reported fracturing the upper left central incisor (tooth 21) from a fall when she was a child. After a panoramic radiograph (Figure 6), endodontic treatment was observed in teeth 21 and 36, taurodontism in both upper and lower molars, a supernumerary tooth - the 4th upper right molar (Figure 7), and a mandible with limited height. After clinical examination, a prominent lip, fissured tongue, and macroglossia (Figure 8) were noted, along with anterior open bite, vestibular exostoses, dental erosion on the occlusal and palatal/lingual surfaces of almost all teeth (Figures 9 and 10), limited mouth opening, mouth breathing, atypical swallowing, and a high palatal arch.

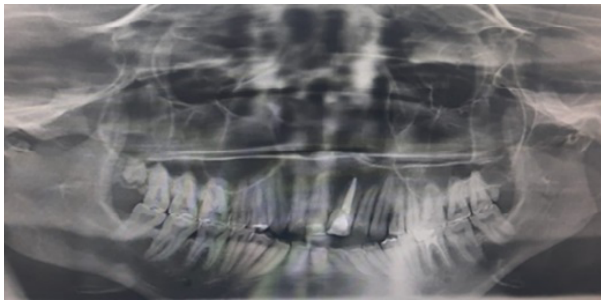

Figure 6. *Panoramic radiography*

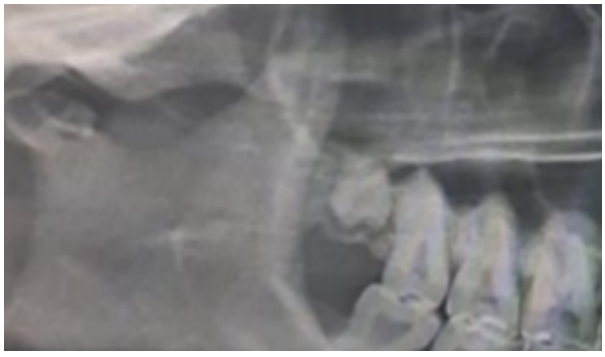

Figure 7. *1st, 2nd, 3rd and 4th upper right molars.*

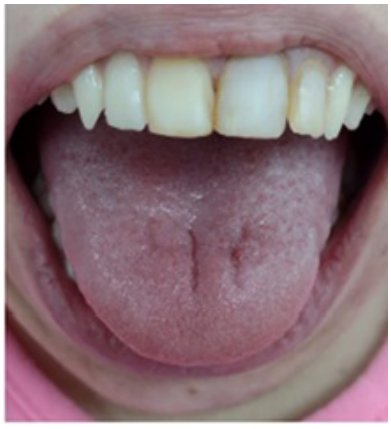

Figure 8. *Macroglossia and tongue plicata.*

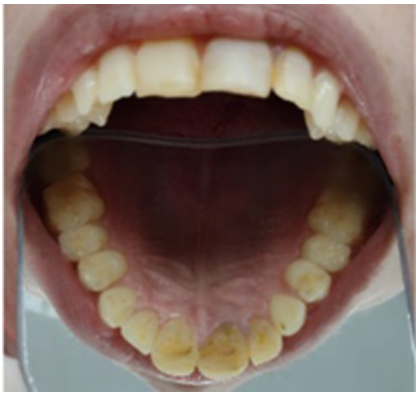

Figure 9. *Upper teeth with dental erosion.*

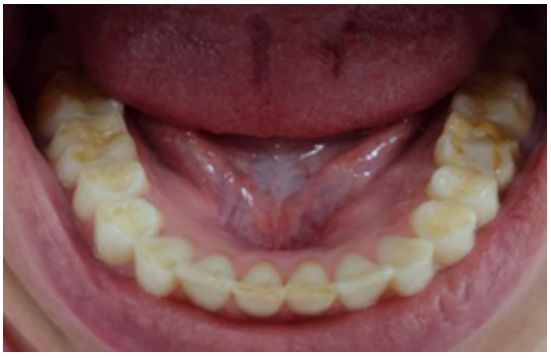

Figure 10. *Lower teeth with dental erosion.*

CASE 2

A 31-year-old male patient (Figure 11), 1.4 cm tall, weighing 25 kg, residing in Ribeirão Preto/São Paulo/Brazil, brother of patient 1, was diagnosed with Morquio Syndrome (MPS IV-A) at the age of 2, when his mother noticed some changes similar to those she had observed in his sister when she was diagnosed with MPS IV-A. As a result, he was taken to the pediatrician, who confirmed the diagnosis of MPS type IV, and he was also referred for treatment at the Clinical Hospital in Ribeirão Preto, University of São Paulo, Brazil (CHRP-USP).

In 2002, the patient attended the Special Patients Clinic at the University of Ribeirão Preto-Unaerp, São Paulo, Brazil, for routine dental care and has been under follow-up until the present year, 2022. During the anamnesis, some important data were obtained. Regarding the prenatal period, the mother did not have any illnesses during pregnancy; the parents are not consanguineous and have 5 children, 3 of whom are affected by the disease. In the postnatal period, a natural delivery was performed (9 months of gestation); the patient reported breastfeeding for 3 months; he used a bottle; used Aerolin®; had parotitis and chickenpox as a child, and stated that his parents were surprised when they received the diagnosis of the disease, but their current reaction is one of acceptance.

Figure 11. *Male patient with MPS IV-A.*

When asked about the sequelae related to MPS, the patient reported the following: dysostosis in the hands (Figure 12), valgus deformities in the knees (Figure 13), respiratory difficulty, thoracic enlargement, decreased hearing, rheumatological problems, difficulty in mobility, impaired motor coordination, short stature, and shortened neck and trunk. Therefore, he receives multidisciplinary follow-up at CHRP-USP focusing on the heart, ears, and eyes and at Unaerp, São Paulo, Brazil, with a dentist and physiotherapist. Unlike

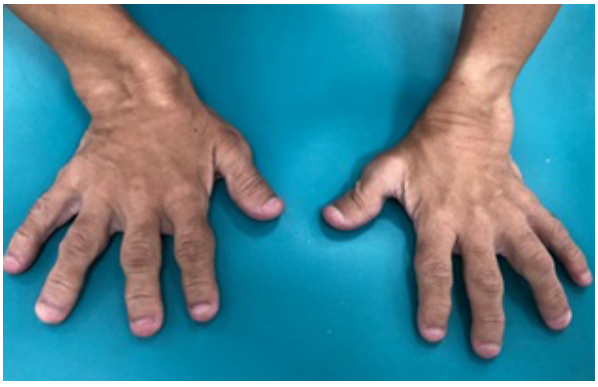

Figure 12. *Dysostosis of the hands.*

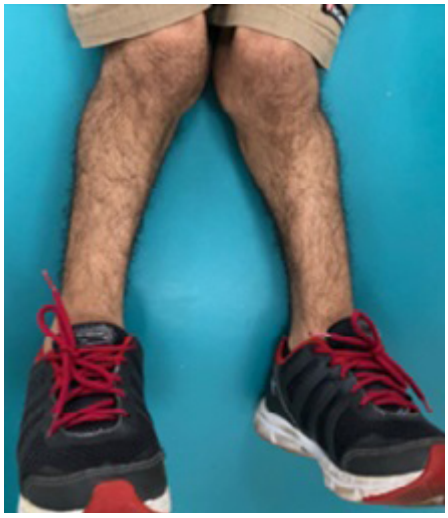

Figure 13. *Valgus deformity of the knees.*

his sister, he has been using medication (Vimizim®) since 2016, administered intravenously once a week. Due to the pandemic, the medication is now given at his home, as it was previously administered at CHRP-USP. With Vimizim®, he has noticed improvements in his breathing.

Regarding oral health, the patient brushes his teeth independently three times daily (morning, afternoon, and night) and uses dental floss less frequently. Additionally, he has the habit of biting his nails. After a panoramic radiograph (Figure 14) showed taurodontism in both the upper and lower molars.

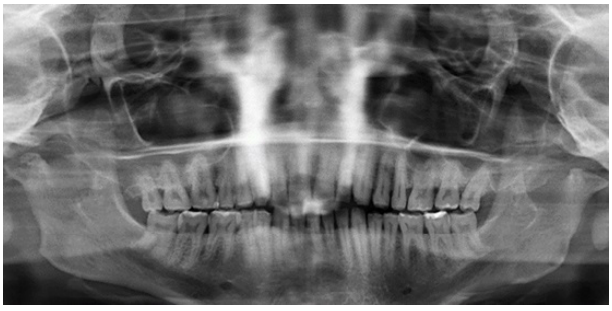

Figure 14. *Panoramic radiography.*

After clinical examination, a diastema between the upper incisors was noted (Figure 15), a fissured tongue and macroglossia (Figure 16), dental erosion on the occlusal and palatal/lingual surfaces of almost all teeth (Figures 17 and 18), an anterior open bite (Figure 19),

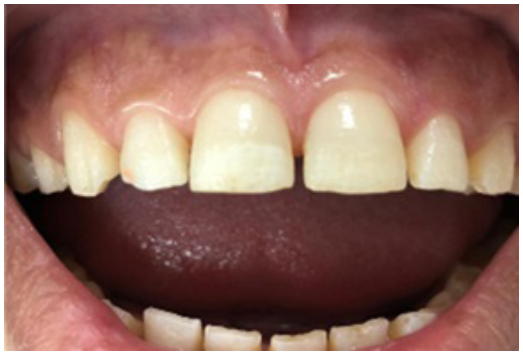

Figure 15. *Diastema between central incisors.*

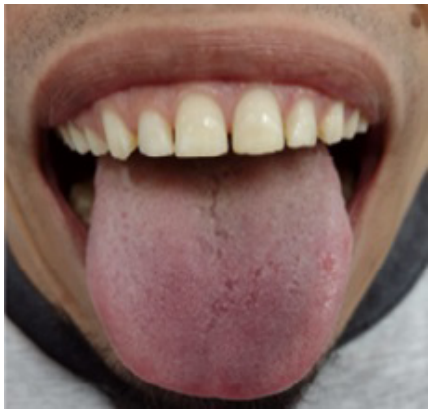

Figure 16. *Macroglossia and tongue plicata.*

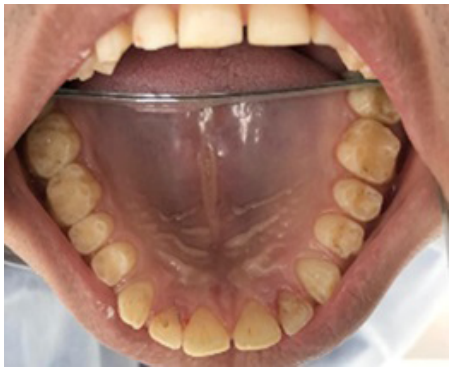

Figure 17. *Upper teeth with dental erosion.*

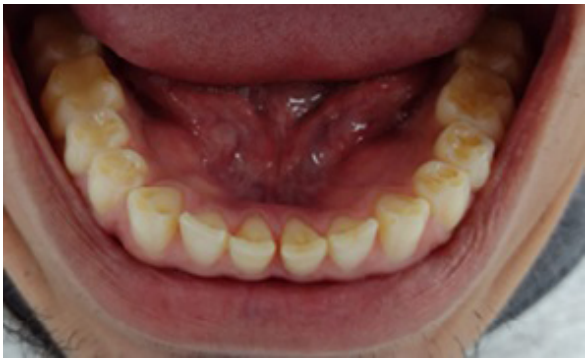

Figure 18. *Lower teeth with dental erosion*

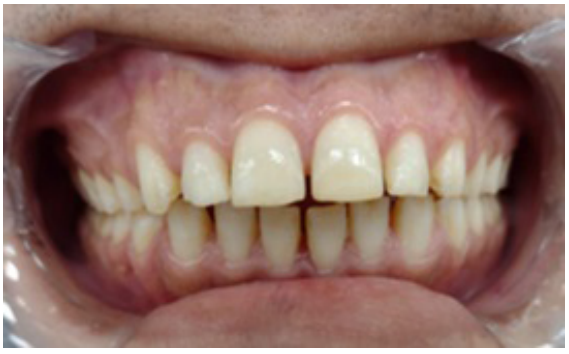

Figure 19. *Anterior open bite.*

a prominent lip, mouth breathing, atypical swallowing, a high palatal arch, and a mandible with limited height.

Discussion

The dental treatment plan should be based on all the changes presented by patients with MPS. Examples include cardiorespiratory issues, difficulty in mobility, and auditory and visual perception, with the goal of providing safe and comfortable care to the patient. Therefore, upon noticing signs and symptoms of clinical decompensation, the treatment should be interrupted, and the appointment should be rescheduled. Additionally, it is important to be alert to bacterial endocarditis in more invasive procedures, prescribing, when necessary, the use of prophylactic antibiotics[10].

Moreover, most patients with MPS complain of respiratory difficulty, and many are mouth breathers. It is recommended to position them in the dental chair as close to a 90° angle as possible, to avoid the supine position. The use of relative isolation should also be preferred, as absolute isolation may cause a dyspnea[10]. Regarding hearing loss or diminished hearing, the professional may choose to communicate with the patient using diagrams or explanatory drawings. Hearing aids should be removed when using noisy equipment, as excessive noise may be uncomfortable for the patient. As for visual changes, the main symptoms are photophobia and vision loss.

During treatment, instruments can be presented to the patient through touch to avoid sudden movements or shock while the dentist is working. Additionally, attention should be paid to the light from the reflector to ensure it does not shine directly into the patient's eyes[10]. Another aspect to be considered is oral hygiene, as joint changes may limit movement, and patients may report difficulty brushing and flossing. One option for this is the use of electric or adapted toothbrushes and floss with a handle[10].

Oral changes are diverse, so it is important to recognize them in order to determine the best approach for treatment and prevention. Enamel hypoplasia may be treated with sealants; delayed tooth eruption highlights the importance of longitudinal monitoring with the dentist, so they can observe whether the teeth are erupting in the correct order and age; mouth breathing can also be observed by

the dentist, who should refer the patient to a physician; dentigerous cysts are diagnosed through routine radiographic exams; dentomaxillary anomalies[10].

Anomalies are defects and/or variations in the structure, size, shape, and position of dental elements and can have congenital, hereditary, acquired, or idiopathic causes. Therefore, knowledge of these variations is crucial, as they may indicate the presence of genetic alterations and influence dental treatments[14].

The first anomaly identified in both patients studied was taurodontism. A tooth with taurodontism can only be diagnosed through radiographic exams, as its external characteristics are the same as those of a normal tooth. When performing the radiograph, it is possible to observe the elongation in the corono-apical direction of the pulp chamber, and with this enlargement of the chamber and the structure of the canal, endodontic treatment becomes more complex because it complicates the location of the root openings, as well as the instrumentation and obturation of the canals. Therefore, the use of magnification is essential to increase the chances of success in the treatment [14].

The second dentomaxillary anomaly is the supernumerary tooth, which exceeds the normal series. Its occurrence can cause alterations such as eruption difficulties, tooth displacement, crowding, cysts, and odontogenic tumors. Diagnosis is usually made through routine radiographs, as most supernumerary teeth are impacted and asymptomatic. A supernumerary fourth upper right molar was found in the female patient studied, but its extraction was not indicated [15].

Another common feature of MPS IV-A found in both patients studied was dental erosion. This refers to the dissolution of the tooth surface, with demineralization of the enamel due to acids of extrinsic origin (acidic foods, medications, etc.) or intrinsic origin (as seen in patients suffering from reflux), with no bacterial involvement. The female patient (Case 1) did not report any factor in her medical history that would indicate the cause of the erosion, but according to[10], it is common in MPS IV-A patients to present changes in the enamel structure in both the primary and permanent dentitions. Thus, there may be a correlation between the erosion and this common alteration associated with the disease.

On the other hand, the male patient (Case 2) reported using the medication Aerolin® when he was a child. This medication is used to control and prevent bronchial spasms (contractions) during asthma attacks, chronic bronchitis, and emphysema. Fardin *et al.* (2011)[15] analyzed the cariogenic and erosive potential of various medications, including Aerolin®, which was one of the syrups studied with the highest acidity and low pH, and consequently, the greatest erosive potential. Therefore, the erosion in this patient can be correlated with the use of Aerolin®. As a preventive measure, the patient can rinse with water after using the medication, use toothpastes with low abrasivity, and brushes with soft bristles.

Regarding treatment with enzyme replacement therapy (ERT), it was reported that only the male patient (Case 2) is currently using it, as his sister is waiting for government authorization to begin treatment. The main benefits of this therapy include improvement in the 6-minute

walk test and a reduction in urinary GAG excretion. Adverse effects do not always occur, and those that have been reported include: pneumonia, hypersensitivity, pain at the infusion site, lower respiratory infections, otitis media, urticaria, viral respiratory tract infections, vomiting, and anaphylactic reactions. The patient in this study reported only an improvement in breathing[11]. It can be concluded that MPS is a rare disease that affects various organs and tissues, requiring lifelong treatment from a multidisciplinary healthcare team, as there is still no cure. Dental treatment is very important in contributing to the individual's quality of life, as its connection with certain systemic diseases has already been established. There are several oral alterations that these patients may present, which highlights the importance of follow-up from childhood to old age, so that preventive treatments can be carried out with safety and comfort for the patient.

Conclusion

MPS is a rare disease that affects various organs and tissues, requiring lifelong treatment by a multidisciplinary healthcare team, as there is no cure yet. It is important to raise awareness about the existence of this disease so that treatments can be started as early as possible.

Dental treatment is highly relevant in contributing to the individual's quality of life, as its connection with certain systemic diseases has already been proven. There are several oral alterations that these patients may experience, which is why it is important to monitor them from childhood to old age, ensuring that preventive treatments are carried out safely and comfortably for the patient.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding information

This paper was not supported by any funding institution.

References

1. Mesquita ACC, Leite EVNC, Neto CM, Oliveira AR, Guedelha LPS, Nunes PLS. Perfil sociodemográfico e clínico de pacientes com mucopolissacaridose em um hospital de São Luís – MA / Sociodemographic and clinical profile in patients with mucopolissacaridose in a hospital in São Luís – MA. Braz. J. Hea. Rev. 2021; 4(3):10996-100.
2. Teodoro JVT, Ribeiro LAB, Ferreira Neto JM, Ferreira VM, Grangueiro, CHP, Oliveira, ANM. Mucopolissacaridoses IV e VI: Aspectos ao Ecocardiograma Bidimensional com Strain pelo Speckle Tracking em uma Série de Casos. Abc., Imagem Cardiovasc. 2021; 34(2):1- 4.
3. Alencar PHR, Lima KVM, Tourinho EF, Barbosa MSN, Leite CL, Queiroz P dos SS, Nascimento NG da C, Lins GOL, Lopes SMT, Lima Junior FA. Nursing care for patients with mucopolysaccharidosis VI: an integrative literature review. RSD. 2022;1(1):e2211123435.
4. Kubaski F, de Oliveira Poswar F, Michelin-Tirelli K, Burin MG, Rojas-Málaga D, Brusius-Facchin AC, Leistner-Segal S, Giugliani R. Diagnosis of Mucopolysaccharidoses. Diagnostics (Basel). 2020;10(3):172.

5. Hampe CS, Wesley J, Lund TC, Orchard PJ, Polgreen LE, Eisengart JB, McLoon LK, Cureoglu S, Schachern P, McIvor RS. Mucopolysaccharidosis Type I: Current Treatments, Limitations, and Prospects for Improvement. Biomolecules. 2021;11(2):189.
6. Nourbakhsh N, Esfahani EA. "Mucopolysaccharidosis syndrome in a 9-Year-old boy: oral-dental management and diagnostic considerations": a case report. BMC Oral Health. 2024; 27;24(1):1140.
7. Khan SA, Peracha H, Ballhausen D, Wiesbauer A, Rohrbach M, Gautschi M, Mason RW, Giugliani R, Suzuki Y, Orii KE, Orii T, Tomatsu S. Epidemiology of mucopolysaccharidoses. Mol Genet Metab. 2017;121(3):227-240.
8. Poletto E, Pasqualim G, Giugliani R, Matte U, Baldo G. Worldwide distribution of common IDUA pathogenic variants. Clin Genet. 2018;94(1):95-102.
9. Hendriksz CJ, Berger KI, Giugliani R, Harmatz P, Kampmann C, Mackenzie WG, Raiman J, Villarreal MS, Savarirayan R. International guidelines for the management and treatment of Morquio A syndrome. Am J Med Genet A. 2015;167A(1):11-25.
10. Cancino H, Marcela C, Isabel NVS, De Souza MF, Oliveira M. Mucopolysaccharidosis: characteristics and oral changes. RFO UPF. 2016;21(3):395-400.
11. Brasil. Ministério da Saúde. Secretaria de atenção especializada à saúde. Secretaria de ciência, tecnologia e insumos estratégicos. Protocolo Clínico e Diretrizes Terapêuticas da Mucopolissacaridose tipo IV A, 2019.
12. Fecarotta S, Tarallo A, Damiano C, Minopoli N, Parenti G. Pathogenesis of Mucopolysaccharidoses, an Update. Int J Mol Sci. 2020;21(7):2515.
13. Saville JT, Herbst ZM, Gelb MH, Fuller M. Endogenous, non-reducing end glycosaminoglycan biomarkers for the mucopolysaccharidoses: Accurate diagnosis and elimination of false positive newborn screening results. Mol Genet Metab. 2023;140(3):107685.
14. Afonso JCN. Taurodontia: os desafios no tratamento endodôntico não-cirúrgico. 63 f. Tese (Doutorado) - Curso de Ciências da Saúde, Universidade Fernando Pessoa, Porto, 2014.
15. Fardin AC, Gaetti-Jardim EC, Aranega AM, Júnior EGJ, Júnior IRG. Quarto molar retido: a importância do diagnóstico precoce. Revista da Faculdade de Odontologia-Upf, Passo Fundo. 2011;16 (1):90-94.

Recibido 06/02/2025
Aceptado 12/03/2025
Correspondencia: Marcelle Danelon, correo: marcelledanelon@hotmail.com