Comprehensive Preventive and Therapeutic Oral Health Care: A Case Report of Mucopolysaccharidosis Type IV A in a Pediatric Patient

Dr. Chanchala HP*; Dr. Gunica Harjai†; Dr. Vidya G. Doddawad‡; Dr. Manjula S¶

Mucopolysaccharidosis (MPS) is a metabolic disorder resulting from a deficiency of lysosomal enzymes. It is an autosomal recessive disorder with similar incidences in men and women. Mucopolysaccharidosis type IV A is caused by a deficiency of N-acetylgalactosamine-6-sulfatase, which deficiency is, in turn, caused by alterations in the GALNS gene. It is marked by a short stature, a pigeon chest, frontal bossing, kyphosis, and a flat nasal bridge. Intraorally, macroglossia, hypodontia, dentinogenesis imperfecta, a broad mouth, and an anterior open bite are some of the common features. The present paper reports on a case of MPS in a 5-year-old male patient, along with providing a review of the literature and insight into the oral manifestations related to MPS IV A, also called Morquio A syndrome, and its dental treatment. It aims to highlight the clinical recommendations for oral health care in such cases during different phases of MPS IV A treatment. [*P R Health Sci J 2023;42(4):332-334*]

Key words: Mucopolysaccharidosis type IV, Syndrome, Graft-vs-host disease, Dental caries, Dental enamel, Morquio syndrome, Glycosaminoglycans

Mucopolysaccharidosis (MPS) is a group of inherited conditions in which the body is unable to effectively break down mucopolysaccharides (1). It is a lysosomal storage disorder that causes the failure of the breakdown of various nutrients, such as carbohydrates and lipids, resulting in the abnormal accumulation of complex carbohydrates (mucopolysaccharides and glycosaminoglycans) in the liver, bone marrow, central nervous system, arteries, skeleton, eyes, joints, ears, skin, and/or teeth. There are several types and subtypes of MPS, which are explained by gene mutations and enzyme deficiencies (described in Table 1) (2).

The prevalence of MPS varies from 0.14 to 0.22 per 100,000 live births: 1 per 76,000 in India, 1 per 450,000 in Europe, 1 per 200,000 in the USA and Canada, and 0.07 per 100,000 in Sweden (3,4).

The severity, age of onset, and associated symptoms vary significantly from person to person and range from a severe and rapidly progressive, early-onset form to a slowly progressive, later-onset form. The severe form is diagnosed between ages 1 to 3, while the milder form may not be evident until late childhood or adolescence (5). No specific sex predilection has been noted. If left untreated, MPS IV A patients do not survive beyond the third decade of life; however, with appropriate management, the progression of the disease can be slowed down (6).

The oral manifestations of MPS IV A include dentinogenesis imperfecta, hypodontia, osteogenesis imperfecta, a broad mouth and short nose, an anterior open bite, macroglossia, and a flattened condyle, with the tooth enamel of the afflicted individual being abnormally thin and porous (7). The permanent teeth are misaligned and spaced and there is a delay in eruption (8). To the best of our knowledge, this is the 15th case report in the literature of a pediatric patient with MPS IV A. The purpose of the current case report was to highlight said patient's oral manifestations, with suggested treatment, and to highlight, as well, the paucity of research on the subject.

Case Report

A 5-year-old boy reported to the Department of Pediatric and Preventive Dentistry complaining of bilateral pain in the lower teeth for 1 month. The patient was the first child of a consanguineous marriage and presented with a pigeon chest, a broad forehead, bent legs, and a short neck; his speech was normal. He had short, claw-shaped hands, kyphosis, and delayed developmental milestones with normal intelligence. The observed craniofacial features were brachycephaly, full lips, a wide mouth, and a closed nasolabial angle (Figure 1). The lower third of his face was more prominent than the rest of his face was.

*Assistant professor, Department of Paediatric and preventive dentistry; †Post-graduate, Department of Paediatric and preventive dentistry ‡Associate professor, Department of oral pathology and microbiology; ¶Associate professor, Department of oral and Maxillo facial surgery, JSS Dental College and Hospital, A constituent college of the JSS Academy of Higher Education & Research, Karnataka, India

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Address correspondence to: Dr. Vidya G. Doddawad, Associate professor, Department of Oral pathology and Microbiology, JSS Dental College and Hospital, A constituent college of the JSS Academy of Higher Education & Research, Mysore-570015, Karnataka, India. Email: drvidyagd@gmail.com

Table 1. Different types and subtypes of mucopolysaccharidosis (2).

Type	Name	Gene	Deficient enzyme	Accumulated product
I	Hurler syndrome	*IDUA*	α-Iduronidase	Dermatan sulfate Heparan sulfate
II	Hunter syndrome	*IDS*	Iduronate sulfatase	Dermatan sulfate Heparan sulfate
III A	Sanfilippo syndrome A	*SGSH*	Heparan sulfamidase	Heparan sulfate
III B	Sanfilippo syndrome B	*NAGLU*	N-Acetyl glucosaminase	Heparan sulfate
III C	Sanfilippo syndrome C	*HGSNAT*	Acetyl coenzyme A: α-gluco S-aminide acetyltransferase	Heparan sulfate
III D	Sanfilippo syndrome D	*GNS*	N-Acetylglucosamine-6-sulfatase	Heparan sulfate
IV A	Morquio syndrome A	*GALNS*	Galactose 6-sulfatase	Keratan sulfate Chondroitin sulfate
IV B	Morquio syndrome B	*GLB1*	β-Galactosidase	Keratan sulfate
VI	Maroteaux–Lamy syndrome	*ARSB*	Arylsulfatase B	Dermatan sulfate Chondroitin sulfate
VII	Sly syndrome	*GUSB*	β-Glucuronidase	Dermatan sulfate Heparan sulfate Chondroitin sulfate
IX	Natowicz syndrome	*HYAL1*	Hyaluronidase	Hyaluronan

The patient had reports of lab investigation and treatment for MPS IV A. A deficiency of the enzyme galactose 6-sulfatase, a high level of keratan sulfate in the urine, and the *GALNS* gene mutation were noted. A bone marrow transplant (BMT) was planned, with the mother as the donor, and the patient was put on multivitamins, steroids, and antibiotics. However, the patient had symptoms (loose stools and fever) that suggested graft-vs-host disease–like engraftment syndrome and cytokine release syndrome; he was treated with immunosuppressants. A second transplant was planned with the father as the donor; this one met with success. Post-transplant, the patient was put on immunosuppressants and multivitamins.

The patient's intraoral findings included macroglossia, pitted enamel, and yellow teeth. The teeth had concave buccal and occlusal surfaces. The soft tissues and temporomandibular joints were normal. There were deep dental caries in the primary upper and lower molars, bilaterally, and moderate dental caries on the proximal surfaces of the upper incisors and the lower left canine.

An intraoral periapical radiograph revealed radiolucency in the upper left and lower right first primary molars in the coronal region involving enamel, dentin, and pulp with no periapical and furcal changes suggestive of reversible pulpitis and radiolucency in the coronal region involving enamel, dentin, and approaching the pulp suggestive of deep dentinal caries in upper right first primary molar.

The medications prescribed by the medical professional had no drug interactions with the medications and procedures planned for the child's dental rehabilitation. An adequate restorative/endodontic treatment plan was designed, and consent was obtained from the parents. The patient was recalled and reviewed and has been followed-up for 6 months.

Discussion

The present article describes both an oral manifestation of and a treatment plan for MPS IV A (Morquio syndrome, described by both Luis Morquio and James Frederick Brailsford in 1929). It is caused by a mutation in the *GALNS* gene (9). There are 2 types of MPS IV, type A and type B; they can be distinguished by molecular genetic or biochemical testing. In type A (which was diagnosed in the case under discussion) there is a deficiency of the enzyme galactose 6-sulfatase, which lack leads to the accumulation of keratan/chondroitin sulfate. Type B is caused by a deficiency of the enzyme β-galactosidase, which lack leads to the accumulation of keratan sulfate in the body.

In most cases, the affected infants appear normal at birth, and symptoms become apparent around the age of 1 or 2 years. Symptoms include growth retardation, a prominent lower face, a short neck, genu valgum, flat feet, kyphoscoliosis, the abnormal development of the epiphyseal ends of long bones, a pigeon chest, and a prominent forehead. In some cases, hearing loss, weakness of the legs, and/or additional abnormalities may occur (10). In the above case, the patient had a short stature, including a short trunk, short, clawed hands, and a pigeon chest.

The cases reported in the literature mention yellow teeth with thin and pitted enamel, spade-shaped incisors, concave buccal and occlusal surfaces, and anterior open bites (11). The present report was consistent with what has been reported in the literature, which helped in confirming the patient's condition.

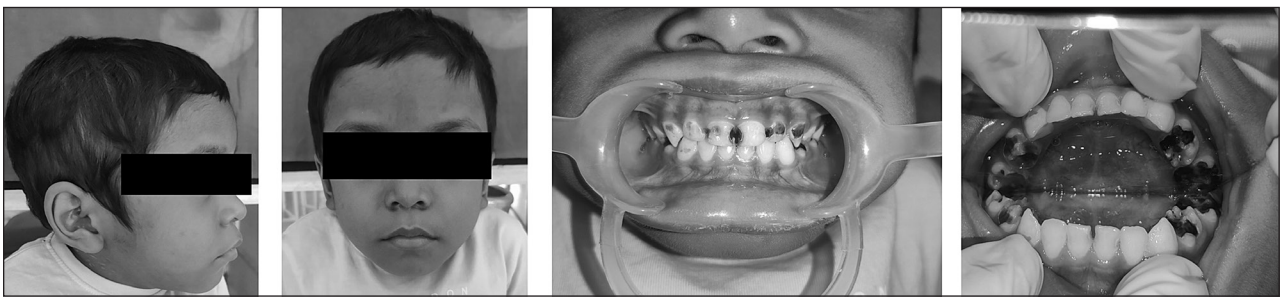

Figure 1. Pre-operative Image of the Extraoral and Intraoral Features of Mucopolysaccharidosis Type IV A.

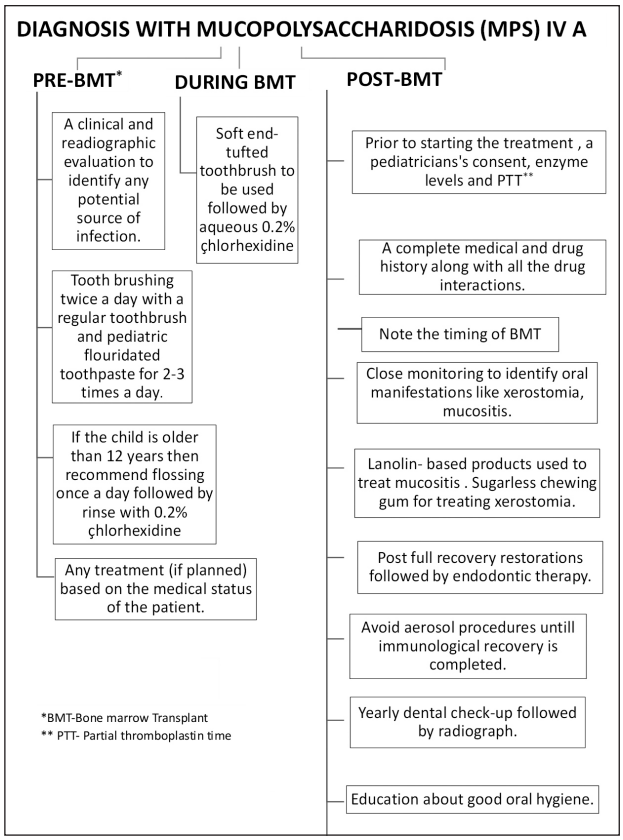

Figure 2. Diagnosis of and Treatment Plan for Mucopolysaccharidosis Type IV A.

The treatment options include enzyme replacement therapy (Vimizim, 2 mg/kg, intravenously, once a week) and BMT. The most frequently documented source of sepsis in an immunosuppressed patient is the mouth; therefore, early and thorough dental intervention, including aggressive oral hygiene measures, reduces the risk of oral and associated systemic complications (11).

The Figure 2 recommendations aim to educate health care personnel about oral care for individuals with MPS IV. Emphasis on medical history is vital for a diagnosis and treatment planning to reduce medical risks. Pediatric dentists should be familiar with the relevant characteristics and manage cases effectively to improve overall health and quality of life.

Resumen

La mucopolisacaridosis (MPS) es un trastorno metabólico que resulta de una deficiencia de enzimas lisosomales. Es un trastorno autosómico recesivo con una incidencia similar en hombres y mujeres. El tipo IV A es causado por deficiencia de N-acetilgalactosamina-6-sulfatasa (GalNac6S), debido a alteraciones en el gen *GALNS*. Se caracteriza por baja estatura, pecho de paloma, protuberancia frontal, cifosis y puente nasal plano. Intraoralmente, macroglosia, hipodoncia, dentinogénesis imperfecta, boca ancha y mordida abierta anterior son algunas de las características comunes. El presente trabajo reporta un caso de MPS en un paciente masculino de 5 años de edad junto con una revisión de la literatura y profundización en las manifestaciones orales relacionadas con MPS Tipo IV A, también llamado síndrome de Morquio A, y su tratamiento odontológico. Su objetivo es resaltar las recomendaciones clínicas para el cuidado de la salud oral en estos casos durante las diferentes fases del tratamiento MPS Tipo IV A.

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