Hurler Syndrome presenting in a two-year-old: A Case Report

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ABSTRACT

Background: Mucopolysaccharidosis type I (MPS I) is a rare autosomal recessive lysosomal storage disorder caused by deficiency of alpha-L-iduronidase, resulting in the accumulation of glycosaminoglycans in multiple tissues. Hurler syndrome is the severe form of MPS I, characterized by progressive multisystem involvement, developmental delay, and skeletal abnormalities. Early recognition is essential to facilitate timely intervention and improve clinical outcomes.

Case Presentation: We report the case of a 2-year-old girl who presented to the emergency department with fever, acute dysentery, chronic loose stools, postprandial regurgitation, and recurrent respiratory symptoms. Clinical evaluation revealed coarse facial features, a depressed nasal bridge, macrocephaly, mild corneal clouding, hearing impairment, delayed developmental milestones, delayed tooth eruption, musculoskeletal abnormalities, and an umbilical hernia. Her history of parental consanguinity further supported the possibility of an inherited metabolic disorder. The constellation of clinical findings raised suspicion of Hurler syndrome. The patient received intravenous fluid therapy and antibiotics for acute dysentery and dehydration. However, definitive biochemical and genetic confirmation was not documented. Management of the underlying disorder was complicated by socioeconomic constraints, limiting access to specialised treatment, including enzyme replacement therapy and hematopoietic stem cell transplantation.

Conclusion: This case highlights the importance of recognising characteristic clinical features of Hurler syndrome in children presenting with common acute illnesses. A high index of suspicion, followed by appropriate biochemical and molecular investigations, is essential for timely diagnosis and referral. Improving access to specialised diagnostic services, genetic counselling, and affordable disease-modifying therapies remains a significant challenge in resource-limited settings such as Pakistan.

Keywords: *Hurler syndrome; mucopolysaccharidosis type I; alpha-L-iduronidase deficiency; consanguinity; developmental delay; enzyme replacement therapy; Pakistan.*

Introduction

Mucopolysaccharidosis (MPS) is a group of rare, inherited metabolic disorders in which the enzymes required to break down glycosaminoglycans (GAGs), or mucopolysaccharides, are unable to do so, or the enzymes produced are non-functional [1]. These glycosaminoglycans accumulate in multiple tissues and disrupt biological mechanisms within the body. MPS is estimated at approximately 1 in 20,000 live births [2].

A subtype of MPS, MPS type I, is due to a mutation in the IDUA gene, resulting in either no or insufficient levels of the enzyme alpha-L-iduronidase. This leads to the accumulation of glycosaminoglycans, heparan sulphate, and dermatan sulphate [3].MPS-I is subdivided into two categories: attenuated (Hurler-Scheie, Scheie) and severe (Hurler syndrome). The incidence of severe MPS I is estimated at 1 in 100,000 newborns, while attenuated MPS I is 1 in 500,000 [4]. Symptoms vary by age; children with severe MPS I tend to present within the first year of life, whereas children with attenuated MPS, I develop features later in childhood. Common symptoms include large head circumference (macrocephaly), simultaneous enlargement of the liver and spleen (hepatosplenomegaly), an unusually large tongue (macroglossia), narrow airways that lead to respiratory infections, breathing repeatedly stops and starts during sleep (sleep apnea), and mobility issues due to bone deformities [4].

In Hurler syndrome, children tend to manifest symptoms right after birth, and the disease progresses rapidly within the first year of life. The risk of inheritance is equal in males and females and across different ethnicities. Children with Hurler syndrome

tend to have extreme developmental delay and progressive cognitive decline before the age of two [5].

History

The patient's name is Ayesha. She is a 2-year-old female who presented to the OPD and was transferred to the emergency department. The chief complaint included a moderate fever ranging from 100°F to 103°F, chronic loose stools, and regurgitation after eating. Her parents reported a chronic cough and intermittent loose stools since birth. In addition, she had respiratory issues that worsened at night, characterized by tongue protrusion.

In her past medical history, she was brought to PIMS with primary presenting complaints of respiratory issues, such as rhinitis and coughing, accompanied by severe abdominal distention.

At present, in Akbar Niazi teaching hospital, she was being treated for severe dehydration requiring IV saline solution. She was currently admitted due to acute dysentery.

The parents noted multiple delayed developmental milestones, which included:

- Gross and Fine Motor: Delayed crawling, head holding and walking.
- Dentition: delayed tooth eruption
- Sensory: notable hearing impairment
- Separation anxiety

The musculoskeletal examination revealed she had fragile bones, and the patient experienced visible pain upon standing. Her ultrasound confirmed she had umbilical hernia.

Physical examination revealed coarse facial features, including a low-set nasal bridge, mild cloudy cornea, and a large head.

Her family history revealed consanguineous parents, an elder sister with no issues, an uncle with mental abnormalities, and a father with epilepsy.



Figure 1: 2-year girl with Hurler syndrome.

Diagnosing Reasoning and Difficulty

The patient's primary complaints were fever and chronic stool. Stool analysis diagnosed dysentery, and she was managed with rehydration therapy (IV saline) and antibiotics

Furthermore, the patient's clinical features revealed prognostic characteristics of MPS I, including the following:

- **Sensory impairments:** The patient exhibited slightly cloudy eyes and hearing impairment. In Hurler syndrome, this happens due to progressive lysosomal accumulation of glycosaminoglycans (GAGs)[1.]
- **Distinctive facial features:** The patient presented with coarse facial features, including a low-set nasal bridge, a large head, and a short neck. These physical characteristics were also termed 'gargoylism' in past medical literature [7.]
- **Musculoskeletal anomalies:** Patients with MPS I experience abnormal bone and cartilage development [7.] During her musculoskeletal examination, the patient exhibited bone weakness and progressive joint stiffness, limiting mobility.
- **Respiratory complications:** The patient's medical history included frequent respiratory infections, including rhinitis, during prior hospitalizations.
- **Early clinical indicators:** One of the first clinical symptoms of Hurlers syndrome is umbilical hernia, which developed in the patient during the first few months of life [8.]

MPS I and MPS II have similar clinical characteristics and the same managing strategies. The differential

diagnosis is based on inheritance pattern and morphological factors.

MPS I is an autosomal recessive disorder, while MPS II is an X-linked recessive disorder, thus exclusively affecting males [4, 9]. In MPS II, the patient's father would have the disease, which is not the case. Additionally, this patient is female and would require two mutated alleles. In this case, her parents are carriers and had a consanguineous marriage.

The key clinical feature is cloudy corneas, which are present in MPS I but are typically absent in MPS II [9].

Treatment

The main objectives of treatment are to limit disease progression, reduce symptom severity, and improve overall quality of life, rather than cure it.

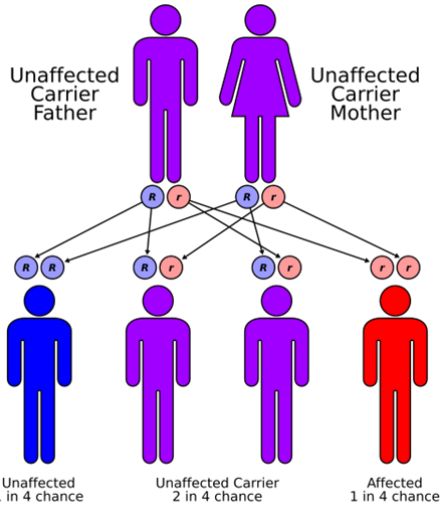


Figure 2: Pattern of Inheritance [20].

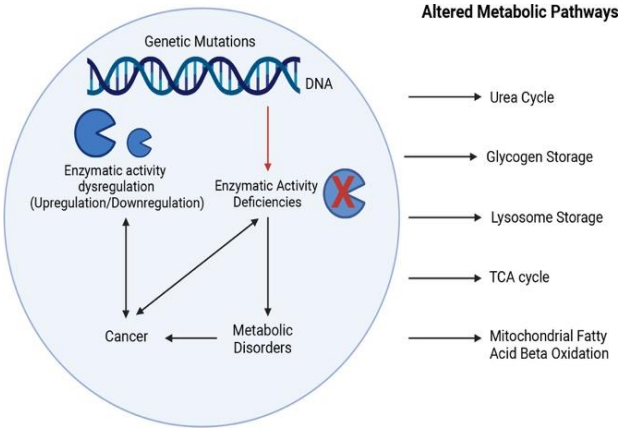


Figure 3. Genetic Mutations and Altered Metabolic Pathways

The type of MPS identified, the disease's stage, and the patient's unique characteristics—such as age and symptom severity—all play a significant role in treatment choices. Treatment regimens are highly personalised and may need to be modified if the illness worsens or new symptoms appear. Most treatments target the consequences rather than a specific underlying issue [10].

- **Enzyme replacement therapy (ERT):** ERT with laronidase enhances liver size, growth, mobility, and joint function, while also slowing the progression of respiratory disease and improving sleep apnea in individuals with mild conditions. The timing of ERT initiation is key for successful outcomes. ERT provides the missing enzyme to break down GAGs, aiding symptom control and minimising accumulation; however, it does not treat MPS or address neurological issues. Weekly infusions are required indefinitely [11].
- **Hematopoietic stem cell transplantation (HSCT):** The best treatment is HSCT, which produces blood cells that make the enzyme alpha-L-iduronidase. Although it does not treat the illness, this enzyme can be used by other cells to break down accumulated GAGs, thereby improving life expectancy and cognitive development. ERT is frequently given alongside HSCT. Therefore, only early stem cell transplantation may improve motor and cognitive issues. ERT is used in patients diagnosed after 2.5 years, when HSCT is no longer an option [12].
- **Experimental Therapy:** Research on treating severe MPS I, given its monogenic nature, has focused on gene therapy (GT) and genome editing. In vivo GT with adeno-associated viruses (AAVs) has shown success in animal models, especially with early treatment. Ex vivo GT improves upon enzyme replacement therapy by using autologous hematopoietic stem cells (HSCs) to deliver the IDUA protein [13]. An experimental strategy for MPS I, Substrate Reduction Therapy (SRT), aims to prevent the production of GAGs. It helps compensate for the body's diminished capacity to break them down by lowering GAG production, which may alleviate neurological and skeletal symptoms that are difficult to treat with existing therapies [14].

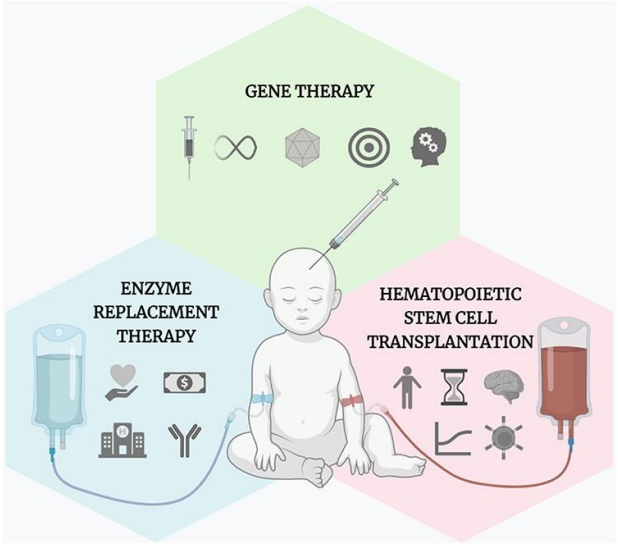


Figure 4: Types of treatments [21].

Discussion

MPS-I has three forms, which have overlapping symptoms and make it difficult to differentiate and diagnose. There are several tests that assist in its diagnosis, including physical examinations, urine testing for glycosaminoglycans, enzyme assays for alpha-L-iduronidase deficiency, and genetic testing. It is recommended that any family member diagnosed with MPS undergo genetic counselling and carrier screening, even if lacking symptoms [15]. Newborns commonly undergo screening, and MPS can be assessed by measuring IDUA and GAG levels.

Detecting the disease early is important for a progressive disease like MPS; its progression can be slowed with certain treatments, with hematopoietic stem cell transplantation being most effective when initiated at an early stage of the disease [16].

The patient came in for acute dysentery, while further evaluation revealed signs of Hurler syndrome.

The probability of MPS occurring increases with genetic similarity among individuals, as the likelihood of a rare, mutated gene arising in parents who are closely related or who are part of a distinct ethnic or geographically clustered community increases. Even parents who are asymptomatic but carry a gene associated with the disorder or have a family history of carrying the genetic disorder are at higher risk of passing MPS to their children.

A combination of HSCT and ERT may provide the best outcome. However, even when performed under ideal settings, such as at a young age and with a matching non-carrier donor for the HSCT, the therapeutic benefit in some systems appears to fade over several years. Certain organs are altogether resistant to treatment. The bones, eyes, and heart valves are the most resistant organs and tissues [17].

In Pakistan, Hurlers syndrome treatment is very costly. Depending on the facility, the type of transplant, and whether donor cells are needed, the average cost of a bone marrow transplant in Pakistan is between PKR 3.5 and 7 million [18]. This option is not feasible for the patient due to socioeconomic constraints. The patient lives in a house with nine other people, only two of whom work and earn money to provide for them all.

Ongoing research is aimed at developing viable treatments for other LSDs, with clinical trials exploring solutions for different kinds of MPS. Treatment has evolved over the last 25 years, but the cost of ERT remains a concern, particularly in low/middle-income countries such as Pakistan. The annual cost of ERT for MPS-I can be USD 67,600 for a 10 kg patient, with costs rising dramatically as weight increases [19].

The need for lifelong ERT, combined with multidisciplinary care involving numerous specialists, creates a significant cost burden. Home healthcare, which is often available in higher-income nations, is generally unavailable in Pakistan, making treatment adherence difficult and requiring numerous hospital visits [19].

Conclusion

This case highlights the critical role of recognizing characteristic symptoms for the timely diagnosis of Hurler syndrome. Early detection, followed by individualized management strategies, is fundamental for improving patient outcomes and quality of life. Furthermore, the report discusses available treatment options and examines the challenges posed by socioeconomic constraints, thereby emphasizing the need for accessible and cost-effective care in developing countries like Pakistan. Collectively, these findings highlight the importance of early intervention and tailored therapeutic approaches.

Declarations

Ethics Approval: Ethical approval for this case report was obtained from the Institutional Review and Ethics Board (IREB), Islamabad Medical and Dental College (IMDC), under approval number **308/IMDC/IREB-2026**.

Patient Perspective, Consent, and Confidentiality: Informed consent was obtained from the patient for publication of the case report and any accompanying

clinical information or images, as applicable. Patient confidentiality and privacy were maintained throughout the preparation of this report.

Conflict of Interest: The authors declare no conflict of interest.

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References

1. National Institute of Neurological Disorders and Stroke. Mucopolysaccharidoses [Internet]. National Institute of Neurological Disorders and Stroke. 2023. Available from: https://www.ninds.nih.gov/health-information/disorders/mucopolysaccharidoses
2. Ago Y, Rintz E, Musini KS, Ma Z, Tomatsu S. Molecular mechanisms in pathophysiology of mucopolysaccharidosis and prospects for innovative therapy. International Journal of Molecular Sciences. 2024 Jan 17;25(2):1113.
3. Khalid N, Abdullah M, Awais A bin, Hassan M, Muhammad A. Hurler Syndrome (Mucopolysaccharidosis Type 1): A Case Report. Cureus. 2023 Apr 18
4. Mucopolysaccharidosis type I: MedlinePlus Genetics [Internet]. Medlineplus.gov. 2024. Available from: https://medlineplus.gov/genetics/condition/mucopolysaccharidosis-type-i/#frequency
5. Raghachaitanya Sakuru, Bollu PC. Hurler Syndrome [Internet]. Nih.gov. StatPearls Publishing; 2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532261/
6. Gellis SS, Feingold M. Atlas of Mental Retardation Syndromes, Visual Diagnosis of Facies and Physical Findings [with Lists of References. 1968.
7. Sakuru R, Bollu PC. Hurler Syndrome. 2023 Jul 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan–. PMID: 30335294.
8. Clarke LA. Mucopolysaccharidosis Type I. 2002 Oct 31 [updated 2025 Dec 4]. In: Adam MP, Bick S, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2026. PMID: 20301341.
9. Hampe CS, Yund BD, Orchard PJ, Lund TC, Wesley J, McIvor RS. Differences in MPS I and MPS II disease manifestations. International journal of molecular sciences. 2021 Jul 23;22(15):7888.
10. Mucopolysaccharidosis – Treatment – Overview of Information and Clinical Research [Internet]. European Clinical Trials Information Network. 2026 [cited 2026 Jun 8]. Available from: https://clinicaltrials.eu/disease/mucopolysaccharidosis/mucopolysaccharidosis-treatment/
11. Europe PMC. Europe PMC [Internet]. Europepmc.org. 2019. Available from: https://europepmc.org/article/nbk/nbk1162
12. Hurler Disease (MPS I) in Childhood: Treat or Cure? Available from: https://biomedgrid.com/pdf/AJBSR.MS.ID.003966.pdf
13. Ponti GD, Donsante S, Frigeni M, Pievani A, Corsi A, Bernardo ME, et al. MPSI Manifestations and Treatment Outcome: Skeletal Focus. International Journal of Molecular Sciences [Internet]. 2022 Sep 22 [cited 2025 Jul 5];23(19):11168–8. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC9569890
14. Derrick-Roberts A, Jackson M, Pyragius C, Byers S. Substrate Deprivation Therapy to Reduce Glycosaminoglycan Synthesis Improves Aspects of Neurological and Skeletal Pathology in MPS I Mice. Diseases. 2017 Feb 23;5(1):5.
15. Mucopolysaccharidosis – Diagnostics – Overview of Information and Clinical Research [Internet]. European Clinical Trials Information Network. 2026 [cited 2026 Jun 1]. Available from: https://clinicaltrials.eu/disease/mucopolysaccharidosis/mucopolysaccharidosis-diagnostics/
16. Machnikowska-Sokołowska M, Myszczuk A, Wieszała E, Wieja-Błach D, Jamroz E, Paprocka J. Mucopolysaccharidosis type 1 among children—neuroradiological perspective based on single centre experience and literature review. Metabolites. 2023 Jan 31;13(2):209.
17. Hampe CS, Wesley J, Lund TC, Orchard PJ, Polgreen LE, Eisengart JB, et al. Mucopolysaccharidosis Type I: Current Treatments, Limitations, and Prospects for Improvement. Biomolecules [Internet]. 2021 Jan 29;11(2):189. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7911293/
18. Nibd. Bone Marrow Transplant in Pakistan: Complete Patient Guide [Internet]. NIBD. 2025 [cited 2026 Jun 9]. Available from: https://nibd.edu.pk/bone-marrow-transplant-in-pakistan-patient-guide/
19. Afroze B -. ETHICAL ISSUES IN MANAGING LYSOSOMAL STORAGE DISORDERS IN CHILDREN IN LOW AND MIDDLE INCOME COUNTRIES. Pakistan Journal of Medical Sciences. 2017 Aug 4;33(4).
20. Burnett CML. Autosomal recessive gene. Inkscape. 18AD.
21. Poswar F de O, Henriques Nehm J, Kubaski F, Poletto E, Giugliani R. Diagnosis and Emerging Treatment Strategies for Mucopolysaccharidosis VII (Sly Syndrome). Therapeutics and Clinical Risk Management. 2022 Dec;Volume 18:1143–55.