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Hurler Syndrome in a Toddler: A Rare Clinical Clue

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Abstract

Background: Hurler syndrome (Mucopolysaccharidosis type I-H) is a rare autosomal recessive lysosomal storage disorder caused by a deficiency of the enzyme α-L-iduronidase, leading to accumulation of dermatan and heparan sulfate. Early diagnosis is crucial to initiate timely enzyme replacement therapy and hematopoietic stem cell transplantation, which can significantly alter disease progression.

Case Presentation: We report a rare case of a two-year-old male who presented to the outpatient department with a complaint of right inguinal swelling. On detailed clinical evaluation, classical phenotypic features of Hurler syndrome were observed, including coarse facial features, macroglossia, frontal bossing, short neck, gibbus deformity, joint stiffness, corneal clouding, and hepatosplenomegaly. A skeletal survey revealed features of dysostosis multiplex, and audiological assessment confirmed mixed hearing loss. Whole Exome Sequencing detected a pathogenic homozygous mutation in the *IDUA* gene, confirming the diagnosis. The child was planned for enzyme replacement therapy but was unfortunately lost to follow-up.

Conclusion: This case highlights the diagnostic challenge in Hurler syndrome, particularly when initial presentation is subtle or non-specific. Awareness of the clinical spectrum and early recognition of dysmorphic features are key to prompt diagnosis, appropriate counselling, and timely intervention, which can significantly improve outcomes.

Keywords: Dysostosis, Hurler, IDUA, Lysosomal, Mucopolysaccharidosis

Introduction

Mucopolysaccharidoses (MPS) are a group of inherited lysosomal storage disorders resulting from deficiencies in specific enzymes responsible for the breakdown of glycosaminoglycans (GAGs). The defective enzymatic activity leads to the progressive accumulation of partially degraded GAGs within lysosomes, affecting cellular function and resulting in a wide range of systemic manifestations. These GAGs are also excreted in excess in urine, offering a diagnostic clue.

MPS I is caused by a deficiency of the lysosomal enzyme **α-L-iduronidase**, leading to the accumulation of **heparan sulfate** and **dermatan sulfate**. It is further subclassified into Hurler (severe), Hurler–Scheie (intermediate), and Scheie (mild) phenotypes, depending on the degree of enzyme deficiency and symptom severity [1,2].

Hurler syndrome (MPS I-H), the most severe form, presents during infancy or early childhood with coarse facial features, hepatosplenomegaly, skeletal dysplasia (dysostosis multiplex), corneal clouding, and progressive neurodegeneration. If left untreated, it often results in death within the first decade of life. Despite advancements in enzyme replacement therapy

(ERT) and hematopoietic stem cell transplantation (HSCT), delayed diagnosis remains a challenge, especially in resource-limited settings.

Herein, we present a case of Hurler syndrome incidentally diagnosed during the evaluation of a patient presenting with inguinal hernia, highlighting the importance of recognizing early signs of this multisystem disorder.

Case Report

A two-year-old male child was brought to the pediatric outpatient department with complaints of swelling in the right inguinal region, suspected to be an inguinal hernia. He was born to non-consanguineous parents after an uneventful full-term delivery and had achieved early developmental milestones with minor delays noted after 15 months of age. The family history was non-contributory for genetic or metabolic disorders.

On general examination, the child was alert and hemodynamically stable but had several distinct phenotypic abnormalities. His head appeared disproportionately large with a prominent forehead and widely spaced orbital ridges. He had protruding eyes, a flattened nasal bridge, thickened lips, wide-open eyes, and coarse facial features—classically described as **gargoylism** in historical literature. The neck was short and stiff, and his trunk was relatively shortened in comparison to limb length. The child exhibited a gibbous deformity in the lower thoracic spine, suggesting dorsal kyphosis, and showed restricted joint movements with noticeable stiffness at the elbows and fingers.

Further systemic examination revealed hepatosplenomegaly and bilateral reducible inguinal hernias. A neurological evaluation demonstrated delayed speech and cognitive regression, as well as mild hypotonia. No overt signs of increased intracranial pressure were noted at the time of presentation, but developmental stagnation raised concern for central nervous system involvement.

A **skeletal survey** showed classic features of **dysostosis multiplex**, including paddle-shaped ribs, bullet-shaped phalanges, anterior beaking of vertebral bodies, thickened calvarium, and J-shaped sella turcica. The patient's height was below the 5th percentile for age, and the growth velocity was notably reduced. Radiological findings also indicated vertebral hypoplasia and early atlantoaxial instability, posing a risk of spinal cord compression.

On ophthalmological evaluation, the patient had **bilateral corneal clouding**, reducing visual acuity. Fundoscopy did not reveal optic nerve pallor or retinal changes at that time. Audiometry suggested mixed hearing loss. There were recurrent episodes of otitis media noted in history, likely secondary to eustachian tube dysfunction from mucopolysaccharide accumulation.

Skin examination revealed coarse and abundant hair with **bluish-gray Mongolian spots** on the lower back. There were no signs of ichthyosis or other dermatologic lesions.

A urine spot test for glycosaminoglycans was positive. Enzymatic assay showed markedly reduced levels of **α-L-iduronidase**, confirming the clinical suspicion of **Hurler syndrome (MPS I-H)**. Genetic testing through **Whole Exome Sequencing (WES)** identified a pathogenic homozygous mutation in the *IDUA* gene, further substantiating the diagnosis.

The family was counseled in detail about the nature of the disorder, its multisystemic involvement, progression, and the available treatment modalities such as enzyme replacement therapy (ERT) and hematopoietic stem cell transplantation (HSCT). Despite recommendations for further workup and referral to a metabolic center, the patient was lost to follow-up.

This case underscores the importance of early recognition of phenotypic and systemic signs of lysosomal storage disorders. Timely diagnosis can facilitate early intervention, which is crucial in altering the otherwise progressive and debilitating course of Hurler syndrome.

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Figure 1.

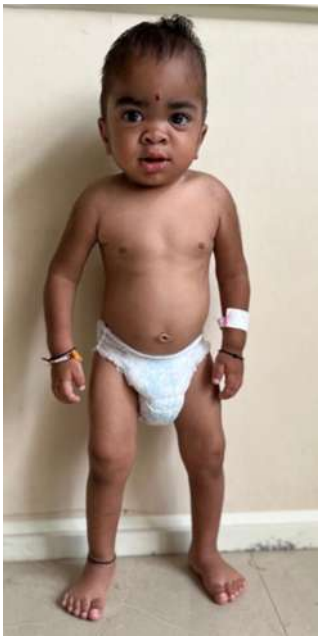

Figure 2.

Figure 3

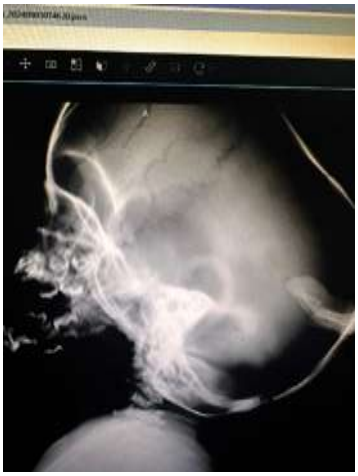

Figure 4.

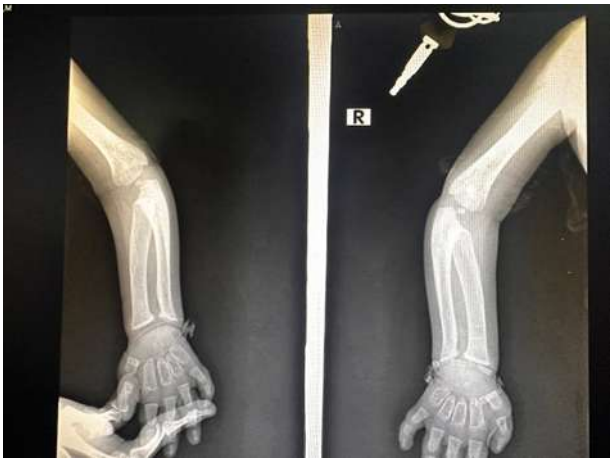

Figure 5

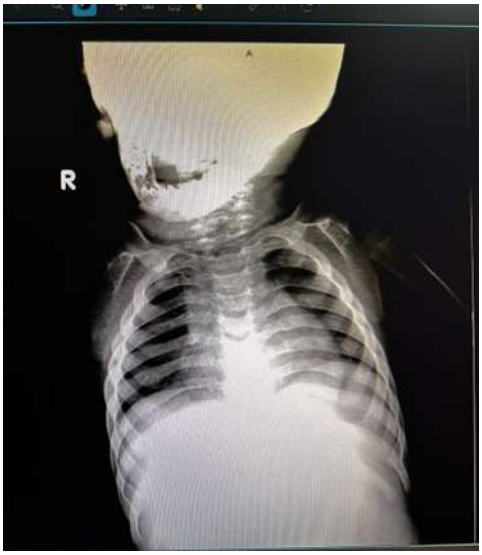

TABLE 1. CLINICAL FEATURES	
Figure 1.	1. The nasal bridge appears flat or depressed 2. The child has relatively short limbs, especially when compared to the torso, suggesting dysostosis multiplex. 3. Thickened lips and nostrils 4. Broad nose with flared nostrils

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Figure 2.	1. Prominent forward curvature of the upper spine (mid-thoracic kyphosis or gibbus), 2. The child has a short trunk compared to the limbs 3. Frontal bossing
Figure 3.	1. The sella appears widened and has a characteristic "J" shape due to anterior and inferior remodeling of the sellar floor. 2. The cranial bones are thickened, especially the frontal and occipital bones
Figure 4.	1. The proximal phalanges appear thickened and have a bullet-shaped or tapering configuration, which is a hallmark of dysostosis multiplex 2. The proximal ends of the metacarpal bones are narrowed and pointed 3. Joint space widening
Figure 5.	1. The ribs appear widened anteriorly and narrow posteriorly, giving a paddle or oar-like appearance 2. Bullet-shaped Clavicles: The clavicles appear short and thick, a feature suggestive of dysostosis multiplex. 3.The ribs appear thickened, especially at the costochondral junctions.

Discussion

In the current case, the clinical findings closely mirrored the classical descriptions of Hurler syndrome reported in the literature, though with certain variations in timing and presentation. Hurler syndrome, an autosomal recessive lysosomal storage disorder caused by a deficiency of α-L-iduronidase, results in the pathological accumulation of dermatan sulfate and heparan sulfate. This accumulation leads to progressive multisystem involvement, affecting skeletal, neurological, ocular, auditory, and cardiopulmonary systems [1,3].

Typically, children with Hurler syndrome appear normal at birth, with symptoms emerging between 6 to 12 months of age. These include developmental delay, hepatosplenomegaly, coarse facies, and joint stiffness [5,6]. In contrast, our patient was diagnosed at the age of two years, suggesting a delayed recognition of the condition. Such delays are not uncommon, especially in low-resource settings, and are often attributed to the nonspecific early symptoms and overlapping features with other neurodevelopmental conditions [6].

Interestingly, in our case, the initial complaint was a reducible inguinal hernia, which is a recognized but often overlooked manifestation of MPS I. Upon detailed examination, the patient exhibited classical dysmorphic features including frontal bossing, depressed nasal bridge, macroglossia, thick lips, short neck, and gibbous deformity. These findings led to further evaluation and a diagnosis of Hurler syndrome. While the literature reports hernias as one of many concurrent signs [5], in our patient, it served as the primary reason for consultation, emphasizing the importance of thorough clinical evaluation even in seemingly routine presentations.

Neurologically, the child exhibited developmental regression and hypotonia, both consistent with literature descriptions. However, he had not yet developed hydrocephalus or seizures, which are commonly seen as the disease progresses due to GAG accumulation in the meninges and cerebrospinal fluid pathways [4]. Radiological findings in our case revealed vertebral anomalies including anterior beaking and atlantoaxial instability, consistent with dysostosis multiplex and risk for spinal cord compression, as previously reported in literature [2,4].

Ocular examination showed bilateral corneal clouding, aligning with the known feature of progressive corneal opacification due to GAG

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deposition in the corneal stroma [4]. Audiometric testing confirmed mixed hearing loss, which is also well-documented in MPS due to chronic middle ear effusions and sensorineural involvement [6].

The diagnosis was confirmed through urine glycosaminoglycan screening, followed by enzymatic assay demonstrating low α-L-iduronidase levels and whole exome sequencing identifying a pathogenic homozygous mutation in the *IDUA* gene. These methods are consistent with the diagnostic gold standards described in the literature [7].

Treatment options for Hurler syndrome, including enzyme replacement therapy (ERT) and hematopoietic stem cell transplantation (HSCT), are known to significantly improve survival and preserve neurocognitive function if initiated early [8]. Unfortunately, in our case, the patient was lost to follow-up before these therapies could be initiated. This highlights a recurrent challenge in managing rare metabolic disorders—limited access to specialized care, poor awareness, and lack of long-term follow-up infrastructure—especially in resource-constrained settings [6,8].

In summary, while the clinical manifestations in our patient were consistent with classical Hurler syndrome, the delayed presentation, the route of initial detection through an unrelated complaint, and the loss to follow-up reflect real-world barriers to early diagnosis and comprehensive management. This case underscores the need for heightened clinical suspicion and better awareness of early phenotypic cues among frontline healthcare providers to facilitate timely referral, diagnosis, and initiation of disease-modifying therapy.

Conclusion

Hurler syndrome is a progressive, life-limiting lysosomal storage disorder that often goes undiagnosed in its early stages due to its subtle onset and variable presentation. This case highlights the importance of a thorough clinical examination and a high index of suspicion, especially when classic dysmorphic features and multisystem involvement are present, even in cases presenting with unrelated complaints such as hernia. Early diagnosis, followed by appropriate genetic counseling and timely intervention with enzyme replacement or stem cell transplantation, can significantly improve the prognosis and quality of life. This case also emphasizes the need for improved awareness, robust referral systems, and follow-up care in managing rare metabolic disorders in pediatric populations

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