DOI: 10.7860/JCDR/2026/85179.23769

Unwrapping the Lysosomal Dysfunction: Clinical Imaging of Hurler's Multisystem Impact

NAMRATA SANT[1], SHREYA TONPE[2], BUSHRA SHAIKH[3], NAILA SYYADA[4]

Keywords: Cardiovascular complication, Genetic testing, Genu valgum, Glycosaminoglycans, Scoliosis

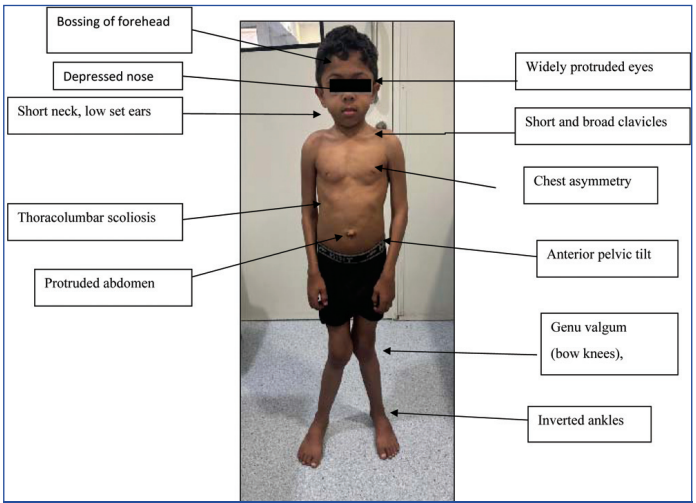
Hurler's syndrome is a rare lysosomal storage disorder caused by deficiency of lysosomal enzyme α-iduronidase. It follows an autosomal recessive pattern of inheritance, leading to progressive accumulation of Glycosaminoglycans (GAGs) within lysosomes, resulting in cellular damage and multiorgan dysfunction [1]. Individuals with mucopolysaccharidosis type I (MPS-I Hurler syndrome) cannot degrade GAGs such as dermatan and heparan sulphate, important components of extracellular matrix and cartilaginous tissues including heart valves and joints. Estimated global prevalence of Hurler syndrome is 1 in 100,000 live births usually in early childhood [2,3]. It is characterised by progressive multisystem involvement causing skeletal deformities, dental irregularities, coarse facial features, organ enlargement, and cardiovascular complications [4,5].

A seven-year-old boy born to G2P2L2A0D0 mother was delivered prematurely at 34 weeks of gestation by caesarean section due to oligohydramnios, with birth weight of 2.25 kg. There were no significant antenatal, natal, postnatal complications. Child cried immediately after birth and did not require neonatal intensive care. The parents had history of consanguineous marriage, elder sibling was healthy with normal growth and development. Immunisation completed as per Expanded Programme on Immunisation schedule, and developmental milestones were normal until four years age.

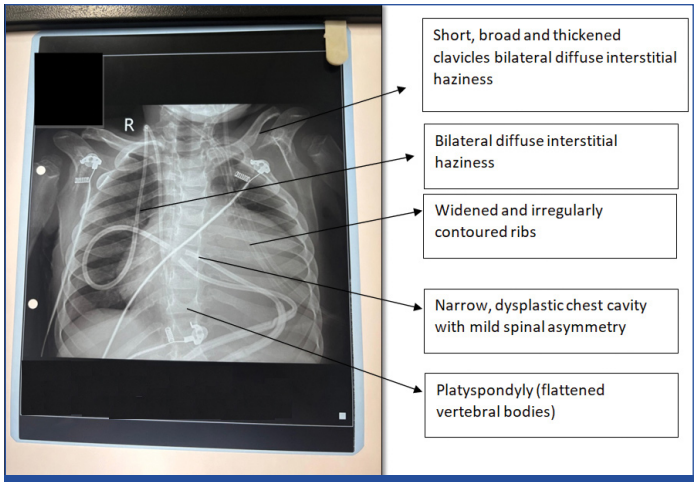
At four years, child underwent surgical repair for left inguinal hernia, and by 4.5 years progressive skeletal abnormalities appeared, including skeletal dysplasia and asymmetry of chest, spine, and knees. At six years, clinical exome sequencing revealed a homozygous pathologic variant consistent with family history of elder brother, showed homozygous c.1469T>C Pathologic variant in IDUA gene on clinical Exome. The mutation in IDUA gene (NM_000203.5), Exon 10, consistent with mucopolysaccharidosis type I, with variant nomenclature c.1469T>C p.Leu490Pro (Depth-47X) with heterozygosity and genomic location chr4:996890T>C. Enzyme assay showed markedly reduced alpha-L-iduronidase activity (0.7 µmol/hr/mg protein), with diagnosis Hurler's Syndrome. At seven years of age, child underwent matched sibling donor haematopoietic stem cell transplantation. The post-transplant course was complicated by polyserositis with pericardial and pleural effusion, correlating with mildly prominent cardiac silhouette and valvular involvement noted on 2D echocardiography which was managed medically with Inj. Furosemide (40mg i.v. per day), Tab. Enalapril (5mg once day). He also developed Graft-versus-Host Disease (GVHD), managed conservatively by Tab. Budesonide- modified release (9 mg per day, thrice weekly, for thrice weekly) and Tab. Mycophenolate Sodium (1 g per day, twice weekly for thrice weekly). Haematological evaluation revealed haemoglobin 10.3 g/dL, total leucocyte count 8,390 cells/µL, haematocrit 30.8%, CD4 percentage 14.8%, and absolute CD4 count of 180.88 cells/µL, indicating significant immunosuppression, which was managed with Inj. pneumococcal conjugate vaccine, Inj. hexavalent combination vaccine (DTP-HepB-IPV-Hib), Inj. Influenza virus vaccine, dosage 0.5 mL intramuscular vaccines to rebuild immunity and prevent life-threatening infections post GVHD and given discharge.

After discharge, at seven years, five months, child presented to paediatric physiotherapy outpatient department with classical phenotypic manifestations of mucopolysaccharidosis type I including short stature, rounded shoulders, frontal bossing, depressed nasal bridge, proptosis, corneal clouding, short neck, low-set ears, thickened palms and soles, protuberant abdomen, and short broad clavicles [Table/Fig-1]. Anthropometric assessment showed weight 15.2 kg and height 111 cm with Body Mass Index (BMI) 12.3 kg/m^2. Musculoskeletal examination revealed end range restricted extension at bilateral elbows and knees and 0-15° ankle dorsiflexion, with moderate muscle tightness in tendo-Achilles, hamstrings, and hip adductors. Postural and skeletal deformities included thoracolumbar scoliosis, anterior pelvic tilt, genu valgum, knee hyperextension, and inverted ankles. Chest radiography demonstrated prominent skeletal abnormalities of thoracic cage characterised by short, broad and thickened clavicles, widened and irregular ribs, and relatively narrow dysplastic chest cavity with mild spinal asymmetry, findings consistent with dysostosis multiplex [Table/Fig-2]. The lung fields showed mild bilateral diffuse interstitial haziness suggestive of early inflammatory or infectious changes, which may be clinically significant in this post-HSCT immunosuppressed child.

Differential diagnosis of Hurler syndrome includes other mucopolysaccharidoses such as types II, III, VI, and VII as well as GM1 gangliosidosis. Mucopolysaccharidosis type VI presents with coarse facial features, corneal clouding, hepatosplenomegaly, and skeletal deformities similar to Hurler syndrome, but intelligence is typically



[Table/Fig-1]: Phenotypic manifestations of Hurler Syndrome showcasing progressive skeletal and soft-tissue involvement.



[Table/Fig-2]: Chest X-ray showing radiographic features of dysostosis multiplex.

preserved compared to progressive intellectual disability seen in Hurler syndrome. Mucopolysaccharidosis type III primarily affects central nervous system with behavioural problems, hyperactivity, sleep disturbances, and neurodegeneration, and can be distinguished by absence of corneal clouding. Mucopolysaccharidosis type VII may present with skeletal deformities, organomegaly, and intellectual impairment but is associated with hydrops fetalis at birth. GM1 gangliosidosis can also present with skeletal dysplasia, organomegaly, and coarse facial features, but is characterised by rapid neurodegeneration and frequently cherry-red spot on retinal examination, so ruled out.

The overall clinical picture, imaging findings, biochemical enzyme assay, and genetic testing confirmed diagnosis of Hurler syndrome, caused by deficiency of α-L-iduronidase activity in leucocytes or fibroblasts, elevated urinary GAG particularly dermatan sulphate and heparan sulphate, and identification of pathogenic variants in IDUA gene. The patient is receiving regular physiotherapy sessions three times per week and is currently on multivitamin supplementation along with Calcimax tablets.

These morphological changes are progressive and frequently associated with medical conditions such as hepatosplenomegaly, left inguinal hernia, and mitral regurgitation. Recognition of these features through physical examination and imaging is essential for early diagnosis, as timely intervention with enzyme replacement therapy or haematopoietic stem cell transplantation can significantly modify disease progression and improve patient outcomes. Thus, findings are consistent with mucopolysaccharidosis type I resulting from α-L-iduronidase deficiency.

REFERENCES

[1] Tulebayeva A, Mukhambetova G, Sharipova M, Tylki-Szymanska A. The birth prevalence of mucopolysaccharidosis types I, II, III, IVA, VI, and VII in the Republic of Kazakhstan Between 1984 and 2023. Diagnostics (Basel, Switzerland). 2025;15(6):679. https://doi.org/10.3390/diagnostics15060679.
[2] Muenzer J, Wraith JE, Clarke LA; International Consensus Panel on Management and Treatment of Mucopolysaccharidosis I. Mucopolysaccharidosis I: Management and treatment guidelines. Pediatrics. 2009;123(1):19-29. Doi: 10.1542/peds.2008-0416.
[3] Meikle PJ, Hopewood JJ, Clague AE, Carey WF. Prevalence of lysosomal disorders. JAMA. 1999;281(3):249-54.
[4] Khalid N, Abdullah M, Awais AB, Hassan M, Muhammad A. Hurler syndrome (Mucopolysaccharidosis Type 1): A case report. Cureus. 2023;15(4):e37785. Doi: 10.7759/cureus.37785. PMID: 37213966; PMCID: PMC10195038.
[5] Sakuru R, Bollu PC. Hurler syndrome. InStatPearls [Internet] 2023 Jul 10. StatPearls Publishing. 2026 Jan, Available from: https://www.ncbi.nlm.nih.gov/sites/books/NBK532261/.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Neurophysiotherapy, MGM School of Physiotherapy, Chh. Sambhajinagar, A Constituent Unit of MGMIHS (Navi Mumbai), Maharashtra, India.
2. Intern, Department of Physiotherapy, MGM School of Physiotherapy, Chh. Sambhajinagar, A Constituent Unit of MGMIHS (Navi Mumbai), Maharashtra, India.
3. Intern, Department of Physiotherapy, MGM School of Physiotherapy, Chh. Sambhajinagar, A Constituent Unit of MGMIHS (Navi Mumbai), Maharashtra, India.
4. Extern, Department of Physiotherapy, MGM School of Physiotherapy, Chh. Sambhajinagar, A Constituent Unit of MGMIHS (Navi Mumbai), Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Namrata Sant,
A1, 403, Millenium Park, E 26/27, Chikalthana, MIDC, Chh. Sambhajinagar, Maharashtra, India.
E-mail: namratassant@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Dec 08, 2025
- Manual Googling: Apr 11, 2026
- iThenticate Software: Apr 14, 2026 (1%)

ETYMOLOGY: Author Origin

EMENDATIONS: 8

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Oct 31, 2025**
Date of Peer Review: **Jan 07, 2026**
Date of Acceptance: **Apr 16, 2026**
Date of Publishing: **Jul 01, 2026**