Case Report

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Mucopolysaccharidosis type I Hurler-Scheie syndrome: a case report

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Introduction and importance: Hurler syndrome, also known as mucopolysaccharidoses type I, is a rare autosomal recessive lysosomal storage disorder with decreased activities of α-L iduronidase, resulting in the accumulation of glycosaminoglycans (GAGs) within various tissues.

Case presentation: The authors presented a case report of a 15-year-old male who presented with a lower respiratory tract infection and was admitted to the pediatrics department with a history of facial dysmorphism, skeletal abnormalities, and corneal clouding and below-normal cognitive function which is consistent with the Hurler-Scheie syndrome. Skeletal abnormalities include inverted j-shaped sella turcica, bullet-shaped phalanges, thoracolumbar kyphosis, and acetabular dysplasia.

Clinical discussion: Mucopolysaccharidosis I is classically divided into three syndromes, that is, Hurler syndrome (the severe form), Hurler-Scheie syndrome (the intermediate form), and Scheie syndrome (the attenuated form). Most of a doctor's first diagnosis is based on their observation of the signs and symptoms.

Conclusion: Early disease diagnosis, genetic counseling, and regular follow-up with recent treatment modalities can reduce mortality significantly and improve the child's health status.

Keywords: case reports, Hurler syndrome, mucopolysaccharidoses

Introduction

Mucopolysaccharidoses are an inborn heterogeneous group of rare lysosomal storage disorders caused by a defective IDUA gene that codes for α-L iduronidase and has an autosomal recessive inheritance[1]. It is a rare disease affecting 1 in 100 000 population[2]. Children affected by the disease are normal at birth, but defective catabolism of dermatan and heparan sulfates leads to progressive accumulation of dermatan sulfate and heparan sulfate in the tissues resulting in the disease affecting bones, joints, eyes, heart, respiratory system, and neurocognition[3]. Affected individuals often succumb to the condition in the first decade, from cardiac and respiratory complications[2].

We report a case of a 15-year-old male child presented to our tertiary care center with typical clinical and radiological features suggesting Hurler syndrome. This case report is in line with CARE guidelines.

HIGHLIGHTS

- A 15-year-old male with a history of facial dysmorphism, skeletal abnormalities, and corneal clouding, which are consistent with Hurler syndrome. However, his cognitive features are not impaired completely, which suggests more of attenuated form of Hurler syndrome, that is Hurler-Scheie syndrome.
- The child presented with respiratory features in our tertiary care center, which are one of the causes of mortality in cases of Hurler syndrome.
- All the radiological and gross findings are enough for the diagnosis of Hurler syndrome as testing for dermatan and heparan sulfate is not available in our part of the world.
- Clear images of facial dysmorphism, skeletal abnormalities, and corneal clouding are provided in the manuscript.

Case presentation

A 15-year-old boy, presented to our tertiary care center with complaints of shortness of breath for 12 h, headache for 3 h, and one episode of abnormal body movements with loss of consciousness 1 h back. The informant was his mother. According to the informant, he had shortness of breath for 12 h, which was gradual on onset and was associated with chest retraction. He had a generalized headache for 3 h followed by one episode of abnormal body movements for 5 min associated with uprolling of

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eyes, stiffening of the body, clenching of teeth, frothy discharge from the mouth, and loss of consciousness. For this complaint, he was taken to the nearby hospital where some intravenous medications were given following which symptoms disappeared. The patient was then referred to our center for specialized attention for respiratory problems.

There was no history of projectile vomiting, fever, neck stiffness, loose stools, burning micturition, frequency, or pain abdomen. He had a history of obstructive hydrocephalus with recurrent abnormal body movements and respiratory problems since 3 years of age. He had undergone herniotomy for a right congenital inguinal hernia at 18 months of age. He was delivered at a local hospital via normal vaginal delivery, was 2.5 kg at birth, cried immediately following birth, and had a smooth perinatal transition. He had achieved developmental milestones normally and the symptoms began to appear when the patient was of 3 years age which started with hydrocephalus and episode of seizure. The patient had attended school up to 5th grade with poor scholastic performance and left school due to diminished vision and the occurrence of abnormal body movements. The intelligence quotient test was not found documented. He had adequate nutrition and no known consanguinity in the family history.

On examination dolichocephaly with marked macrocephaly, short neck, corneal clouding, and stiffness of joints was present. Coarse facial characteristics were seen, including a large and depressed nasal bridge, flared nostrils, ocular hypertelorism, dental malocclusion, interdental spacing, thick eyelids, and big and thick lips as shown in (Figs 1 and 2).

The child had < – 3 SD for height for age. Blood pressure was 100/60 mmHg, heart rate of 148 beats per minute, respiratory rate of 38 breaths per minute, and temperature of 98.2°F.

Respiratory examination revealed bilateral equal entry of air with left infra-axillary and infra-scapular crepitations. The abdomen was soft, and nontender with an umbilical stump, and the liver was palpable 3 cm below the costal margin with the liver span of 10 cm.

On investigation, complete blood count was normal with normocytic normochromic red blood cells. Liver function tests and renal function tests were normal. Echocardiography screening was done, which had Moderate MS, Mild to Moderate MR, and moderate TR.

The lateral view of the skull radiograph revealed an inverted j-shaped sella turcica as shown in Figure 3. Hand and wrist radiographs showed bullet-shaped phalanges with the proximal pointing of all metacarpals given in Figure 4. The lateral view of the spine radiograph showed anterior bending of thoracolumbar vertebrae as shown in Figure 5. X-ray AP view of both hips showed acetabular dysplasia (Fig. 6).

The child was then admitted to the PICU with respiratory support with CPAP with PEEP of 8 cm of water. CPAP was removed after 43 h, and maintained saturation in room air, though he had obstructive sleep apnea occasionally and decreased SPO2 to 86–88% during sleep occasionally. Sodium Valproate was used for the treatment of seizure disorder. Neurosurgery consultation was done for the hydrocephalus and the patient party refused to proceed further with for management of hydrocephalus.

Considering the clinical history, clinical examination skeletal survey (radiograph of chest, B/L palms, hip, spine) findings were consistent with mucopolysaccharidoses type I, and considering the history of schooling and mild impairment of cognitive function the patient was diagnosed with a case of mucopolysaccharidoses type I, Hurler-Scheie phenotype. However, urine examination for increased amounts of heparan sulfate and dermatan sulfate and blood for alpha-L iduronidase enzyme activity to confirm the diagnosis of Hurler syndrome could not be done because of the unavailability of testing facilities. In the end, diagnosis of MPS I (attenuated phenotype) was considered based on the clinical features, signs and symptoms, echocardiography, and X-ray findings.

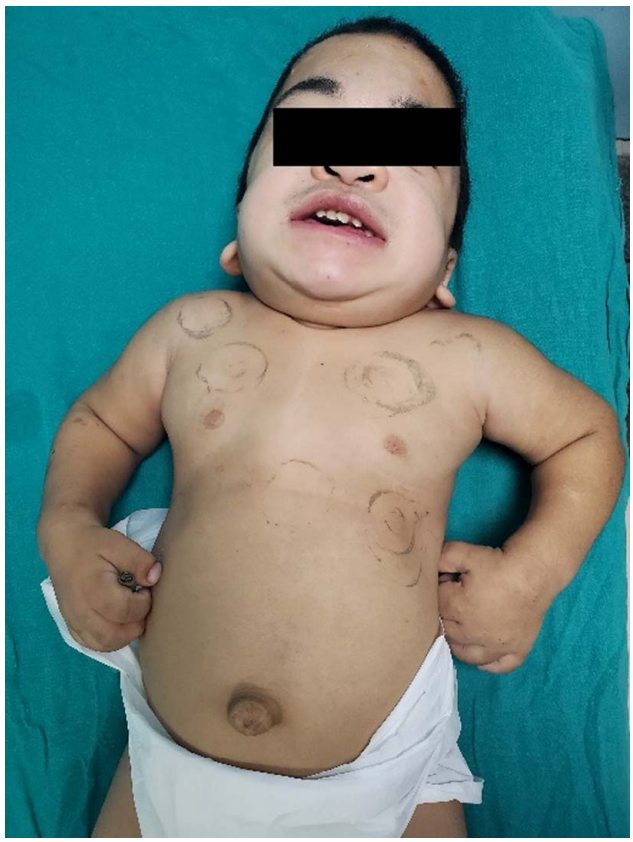

Figure 1. Coarse features with protuberant abdomen and umblical hernia.

On follow up, child is currently on intermittent oxygen support for respiratory difficulties. Other features of MPS I were not improving and the child is currently on valproate for seizure disorder and is seizure-free at the time of follow-up.

Discussion

In this study, we present a case of a 15-year-old male with MPS I presenting with complaints of headache, abnormal body movements, loss of consciousness, and shortness of breath.

Figure 2. Corneal clouding.

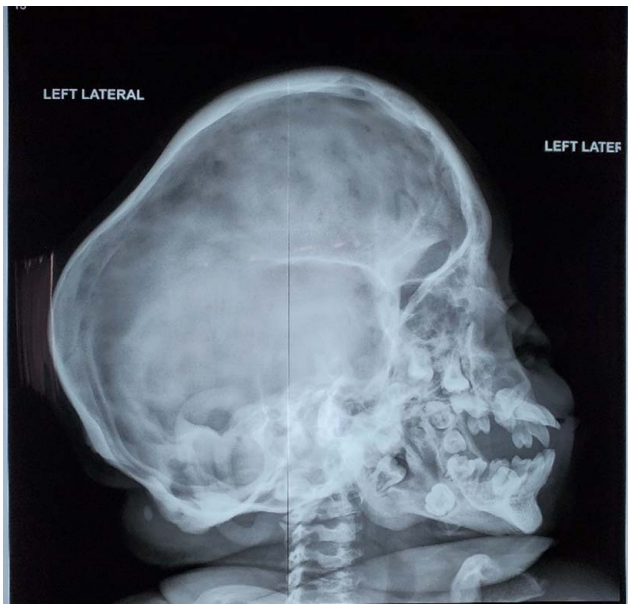

Figure 3. Lateral view of skull showing inverted j-shaped sella turcica.

Mucopolysaccharidoses are rare autosomal recessive disorder (1:100 000 population) that is caused by lack or relative deficiency of the enzyme α- L- iduronidase (IUDA). This impairs the lysosomal degradation of glycosaminoglycans (GAGs) (heparan sulfate and dermatan sulfate). These glycosaminoglycans are major components of the extracellular matrix where they help for the cell to cell-to-cell and cell-to-extracellular matrix adhesion. The deficiency of enzyme α- L- iduronidase(IUDA) leads to the accumulation of dermatan and heparan sulfates in lysosomes and extracellular matrix[4].

Mucopolysaccharidosis is classically divided into three syndromes, that is Hurler syndrome (the severe form), Hurler-Scheie syndrome (the intermediate form), and Scheie syndrome (the attenuated form), the latter of which has little to no cognitive impairment[5,6].

Significant variation in the presentation and course of MPS I is found. This might be a result of the severity of the underlying mutations and the subsequent degree of remaining enzyme activity varying between patients[6]. The attenuated form of MPS I (Scheie syndrome) will have normal cognition but will be of short stature with multiple musculoskeletal problems. They have the same progressive features of the head and neck and other systems that will become significant in the teenage years or later.

The clinical manifestation of Hurler syndrome is diverse including coarse facial features (large and depressed nasal bridge, flared nostrils, thick eyelids, and big and thick lips), musculoskeletal manifestations (dysostosis multiplex, joint stiffness, valgus/varus deformities, and carpal tunnel syndrome), pulmonary manifestation (obstructive sleep apnea), cardiac manifestation (moderate MS, mild to moderate MR, and moderate TR) and neurological manifestation including hydrocephalus along with ocular manifestation (corneal clouding, glaucoma, blindness, and ocular hypertelorism), otorhinolaryngological manifestations (chronic recurrent rhinitis, chronic recurrent otitis media, chronic sinus infections, and hearing loss of variable degree) and dental manifestation (dental malocclusion and interdental spacing). The patient with Hurler syndrome also has a short neck along with stunted growth, macrocephaly, umbilical hernia, and hepatosplenomegaly. Our case had most of the above-mentioned features highly consistent with Hurler syndrome[4, 7–9].

Children with Hurler syndrome are normal at birth except umbilical hernia may be present. Then progressive accumulation of mucopolysaccharides in multiple organs leads to complications

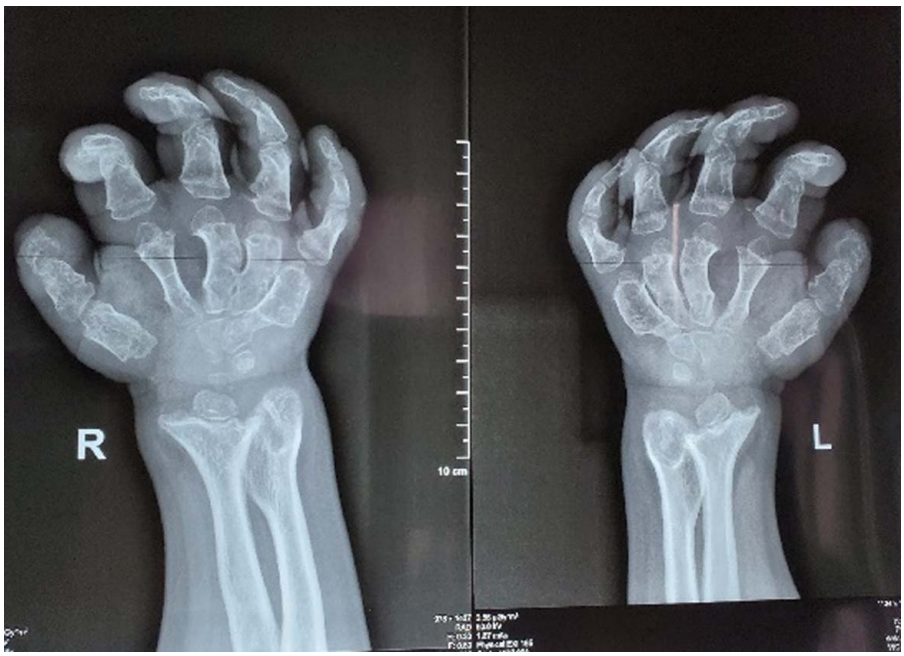

Figure 4. Bullet shaped phalanges with proximal pointing of all metacarpals.

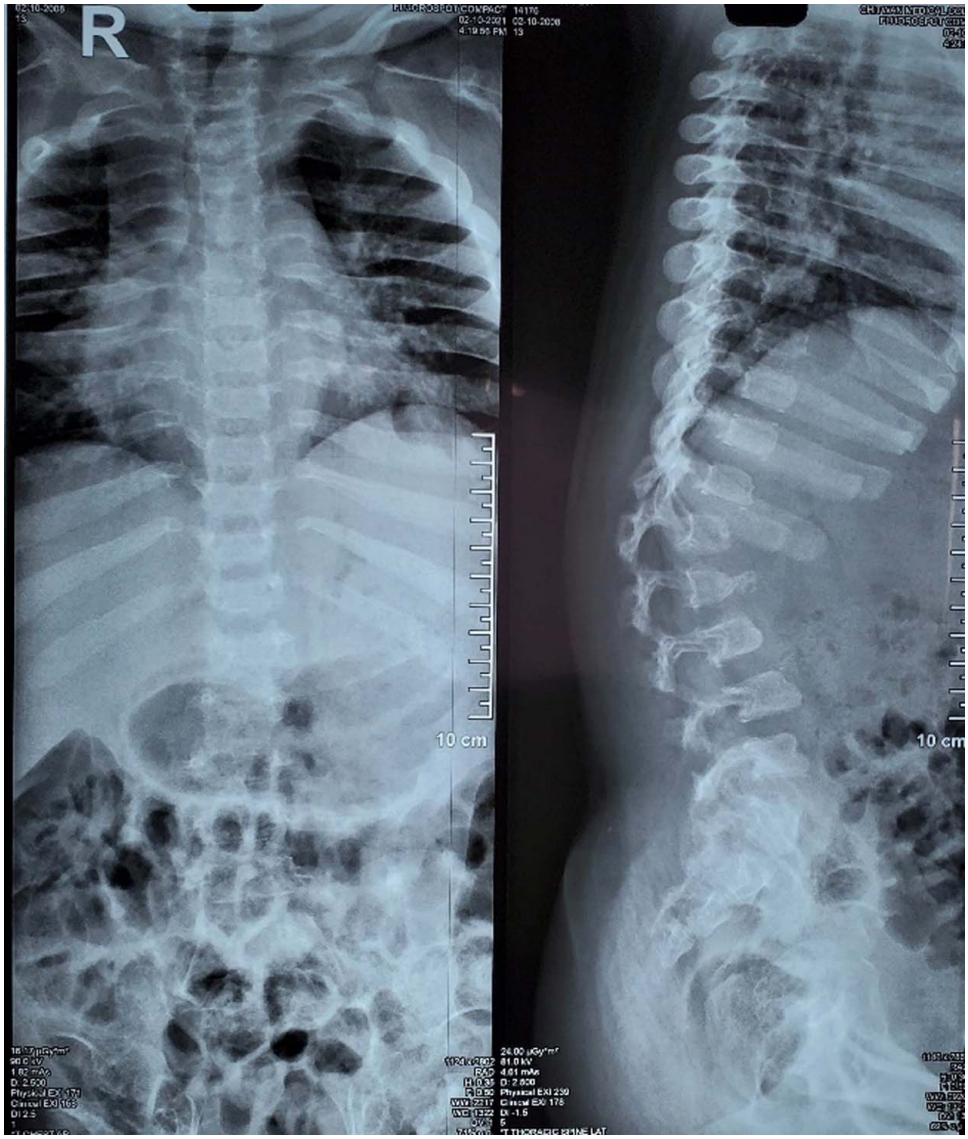

Figure 5. X ray spine lateral view showing thoracolumbar kyphosis.

like cardiac failure and bronchopneumonia resulting in the unfortunate demise of the patient by the first decade[7]. In our case, first symptom of disease occurred at the age of 3 years, which was hydrocephalous with coarse appearance of child and recurrent respiratory tract infection.

The diagnosis of MPS I in all of its manifestations is extremely difficult. Most of a doctor's first diagnosis is based on their observation of the signs and symptoms. The primary diagnostic laboratory finding is the absence of lysosomal enzyme α-L iduronidase activity in peripheral blood leukocytes, cultured fibroblasts, and plasma, and excessive urine GAG excretion, although neither adequately predicts illness severity or form[2,10]. Our patient had most of the typical characteristic clinical and radiological features of MPS I suggesting the diagnosis. The diagnosis could have been confirmed by the above-mentioned tests but could not be done due to the unavailability of the tests.

The management protocol of Hurler syndrome is shown in Figure 7.

The currently available treatment modalities include Hematopoietic stem cell transplantation (HSCT) or enzyme replacement therapy along with additional management of symptoms such as respiratory support by continuous positive pressure ventilation with oxygen supplementation, and medications for pain and gastrointestinal disturbances. Ventriculoperitoneal shunt, spinal decompression, median nerve decompression, and carpal tunnel release surgical intervention can be done for symptomatic management. Patients could also get benefits from speech, occupational, and physical therapy[10].

When performed before the age of 2 years and before cognitive impairment, allogeneic HSCT is thought of as the gold standard for treating Hurler syndrome and can reduce the number of symptoms and lengthen the patient's life[12]. By engrafting donor-derived hematopoietic stem cells, it may offer a long-term supply of the deficient enzyme. Additionally, HSCT permits the local production of the lacking enzyme in the brain by the engraftment of donor-derived microglial cells[13]. For individuals identified and treated for the severe form of MPS I who have a

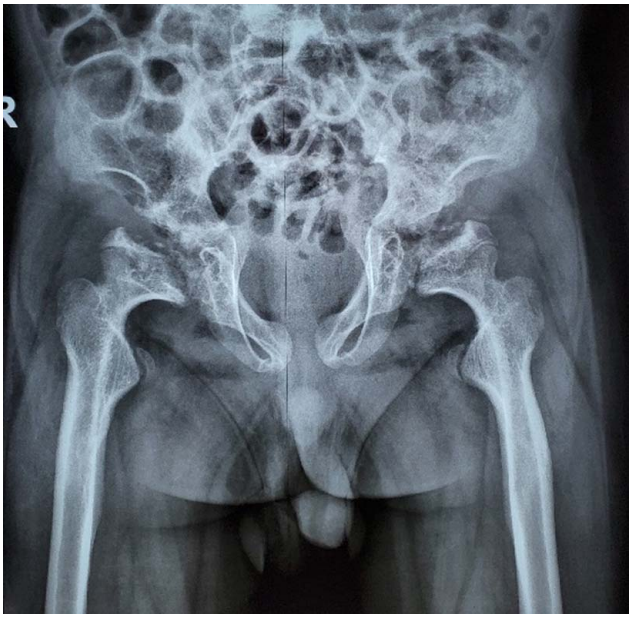

Figure 6. X ray both hip AP view showing acetabular dysplasia.

developmental quotient (DQ) greater than 70 at the time of HSCT, it has emerged as the best procedure, which is successful in halting the progression of cognitive delay and also slows the progression of damage to other organs due to GAGs deposition. It is well established that as earlier HSCT is performed, the better the chances are of a positive outcome[14].

Another method of treatment is Enzyme Replacement Therapy with human recombinant laronidase (a polymorphic form of human α-L iduronidase). A randomized, double-blinded, placebo-controlled, international trial by Wraith *et al*. showed the efficacy and safety of lronidase treatment for MPS I patients. Laronidase's considerable decrease of GAG substrate resulted in clinically significant enhancements in physical capacity (6 min walk test and shoulder flexion) and respiratory function (FVC and Apnea hypopnea index) in just 26 weeks[15]. There is no evidence that recombinant enzyme supplied intravenously at the recommended levels passes the blood–brain barrier, and clinical evidence does not indicate a neurocognitive advantage for individuals with severe MPS I[16].

However, in low middle-income countries like ours where the diagnosis is based on clinical and radiological findings, the treatment is more symptomatic rather than gold standard treatment like HSCT and ERT. Thus, couples with a family history of Hurler syndrome need to do genetic counseling and genetic testing before having children.

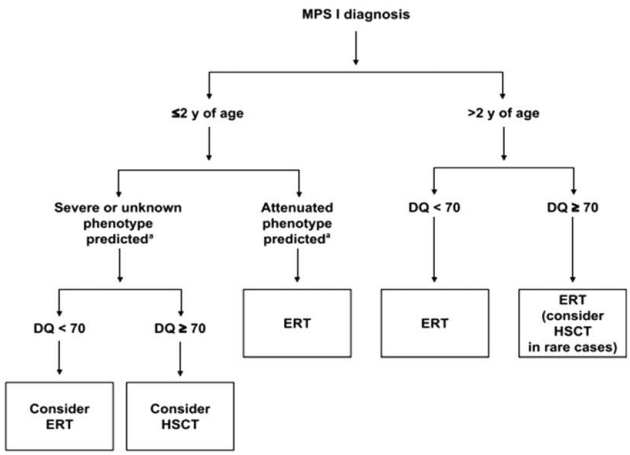

Figure 7. Treatment algorithm for patients with a diagnosis of mucopolysaccharidosis I by Muenzur *et al.*[11].

Conclusion

Mucopolysaccharidosis is a rare metabolic disorder with multiple organ system involvement and poor outcome. Early diagnosis and treatment can improve the health status and prevent worsening of the patient. Couples with a family history of Hurler syndrome need to do genetic counseling and genetic testing before having children.

Ethical approval

Not required.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review on request.

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None.

Author contribution

S.L., A.S., and N.A.: were involved in the evidence collection and conceptualization of the study; S.L., A.S., P.A., and S.A.: drafted the initial version of the manuscript; S.S.: guided the whole process of conceptualization and finalization of the manuscript. All the authors approve of the final version of the manuscript.

Conflicts of interest disclosure

The authors declare that there are no conflicts of interest.

Research registration unique identifying number (UIN)

Not required.

Guarantor

Sanjiv Sapkota, Samit Lamichhane, and Aashish sapkota.

Data availability statement

All the clinical case files can be reviewed upon reasonable request.

Provenance and peer review

Not invited paper.

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