International Journal of Contemporary Pediatrics
*Magar SG et al. Int J Contemp Pediatr. 2022 May;9(5):491-493*
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20221022

**Case Report**

# Experience of enzyme replacement therapy for attenuated mucopolysaccharidosis I in Marathawada, India-a case report

**Suvarna G. Magar*, Anjali V. Kale, Vinod lngale, Ana Kalia**

Department of Pediatrics, MGM Medical College, Aurangabad, Maharashtra, India

**Received:** 23 March 2022
**Revised:** 07 April 2022
**Accepted:** 08 April 2022

***Correspondence:**
Dr. Suvarna G. Magar,
E-mail: drsuvarnamagar@gmail.com



## ABSTRACT

Mucopolysaccharidosis (MPS) type I is an autosomal recessive lysosomal storage disease caused by deficiency on the enzyme α-L-iduronidase. The spectrum of severity ranges from most severe Hurler syndrome, Hurler-Scheie syndrome to mildest form as Scheie syndrome. Enzyme replacement therapy (ERT) with recombinant α-L-iduronidase (laronidase) has shown to significantly improve the quality of life in children. Here we want to describe clinical characteristics, enzyme activity and genetic finding in the first patient with MPS type I who received aldurazyme replacement therapy in Marathwada, India.

**Keywords**: MPS type I, Hurler Scheie disease, ERT, Lysosomal storage disease, Attenuated MPS

## INTRODUCTION

Mucopolysaccharidosis **(**MPS**)** type I (OMIM # 607014) is an autosomal recessive lysosomal storage disease caused by deficiency on the enzyme α-L-iduronidase. The spectrum of severity ranges from most severe Hurler syndrome, Hurler-Scheie syndrome to mildest form as Scheie syndrome. Affected individuals are best described as having either a phenotype consistent with either severe (Hurler syndrome) or attenuated MPS I, a distinction that influences therapeutic options. The prevalence is 1 in 1,00,000. Infants with type 1 MPS appear normal at birth but gradually develop multi organ involvement in the form of umbilical hernia, dysostosis multiplex skeletal deformities, hepatosplenomegaly, corneal clouding, neuro-regression and death occurs due to respiratory failure in first to second decade.[1] Attenuated MPS is gradually developing disease with mild brain involvement. Here we describe clinical characteristics, enzyme activity and genetic finding and clinical response in a patient with MPS type I who received aldurazyme replacement therapy for first time in Marathwada, India.

## CASE REPORT

This was a retrospective, review of a case of MPS 1 conducted at MGM medical college, Aurangabad. This patient with MPS I diagnosed by biochemical enzyme assay and molecular analysis was treated with laronidase according to prescribing information (weekly intravenous infusions of 100 U/kg of body weight).

We noted down the signs and symptoms of MPS I prior to and following ERT (timeline T1 and T2 respectively). Data from patient record, medical history and neurological, cardiovascular, pulmonary, gastroenterology, musculoskeletal, ophthalmologic, audiologic, and psychomotor developmental examinations were noted.

He was born of non-consanguineous marriage with full term normal delivery and 2.6 kg birth weight. He presented with gradually increasing joint stiffness of all finger joints and knee joint over a period of 2 years. On examination he had dolichocephaly, oval face, broad forehead, upturned nasal tip, long philtrum, bilateral

interphalangeal joints stiffness of all fingers and bilateral knee, elbow and shoulder joint stiffness. His anthropometric parameters were head circumference of 51 cm (-1 to -2 SD), Length of 100 cm (-2 to -3 SD) and weight of 13.4 kg (-SD). He also had 3 cm hepatomegaly, 1 cm splenomegaly and unremarkable neurological examination (Figure 1). On further evaluation, child had bilateral corneal haziness, normal hearing response on brain stem evoked potential response test. His thyroid profile, 2D echo was normal and IQ (Intelligence quotient) was 84, which was normal. Skeletal survey was suggestive of dysostosis multiplex changes (Figure 2).

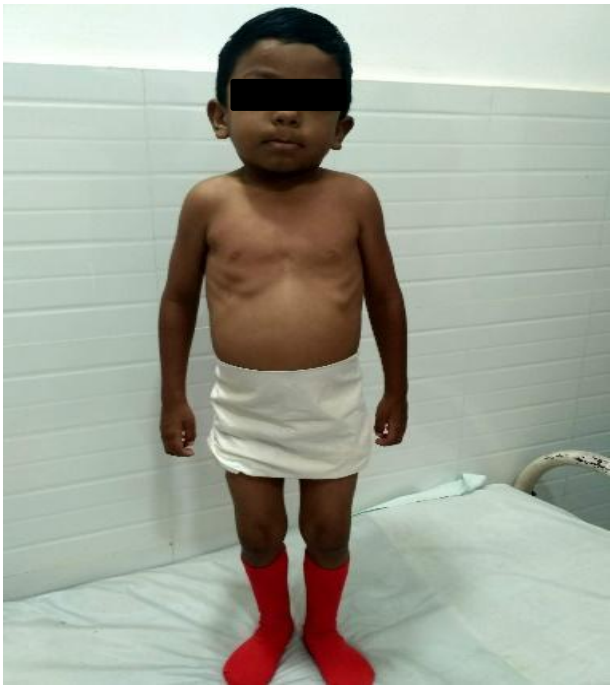

**Figure 1: 5-year-old boy with attenuated MPS with clinical features.**

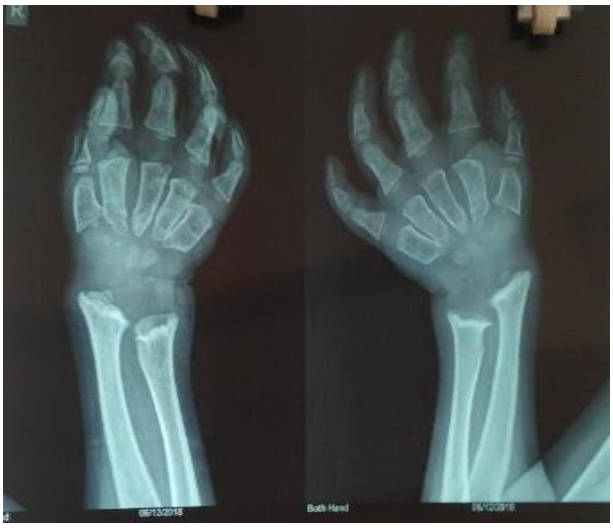

**Figure 2: Dysostosis multiplex changes in hand and wrist X-ray (bullet shaped phalanges, with metaphyseal dysplasia.**

The frequency of signs and symptoms at T1 was determined from a maximum value of 14 symptoms that included coarse facial features, corneal clouding, hearing loss, sleep apnea, recurrent respiratory symptoms, cardiac abnormalities, hepatomegaly, splenomegaly, hernia, dysostosis multiplex, joint contractures, motor developmental delay, language/cognitive delay, and restrictions in ADL.

His enzyme α-Iduronidase levels were 0.14 nmoL/hr/ml (normal: 2.4-12 nmol/hr/ml). On next generation sequencing based DNA testing, homozygous pathogenic known variant c.1874A<G (pTyr625Cys) was detected in IDUA gene confirming the diagnosis of MPS type 1. With Sanofi genzyme company's India Charitable access program, patient received 10 months of recombinant enzyme aldurazyme. The patient has been treated with aldurazyme infusion every week with the dose of 0.58 mg/kg/week or 100 IU/Kg of body weight.

Age at diagnosis was 5 years and age at initiation of ERT was at 5 years and 10 months. Amongst 14 symptoms, child had 7 symptoms and signs. After 10 months of weekly ERT: Child's liver size became normal. Corneal haziness disappeared. Child became more active, joint mobility in all joints improved. Amongst the 14 symptoms, child had only 3 symptoms dysostosis multiplex, joint contractures but with improved mobility and improvement in activities of daily living.

## DISCUSSION

As per the Cochrane review in laronidase treatment for MPS1, statistically significant improvements were noted in forced vital capacity, reduction in urinary GAG levels, hepatomegaly, splenomegaly, sleep apnoea etc. in patients treated with laronidase.[2]

Another multinational case series on sibships with MPS 1 showed that younger siblings with milder manifestations started on ERT had much better quality of life as compared to older siblings with late diagnosis.[3] Success stories and challenges of treatment with ERT in India for various LSDs like Gaucher disease, MPS I, MPS II and Fabry disease etc have been mentioned in experience published by Muranjan et al.[4] Indian patients access ERT through charitable initiatives of manufacturers and clinical trials. Few affected children of central and state government organization employees, are now getting ERT as their expenses are being borne by these organizations. Sanofi-Genzyme provided ERT to patient through India charitable access program (INCAP) and results were rewarding to patient, especially attenuated MPS with normal motor and intellectual development.

## CONCLUSIONS

Enzyme therapy improves clinical manifestation leading to improvements in life expectancy and quality of life in MPS I patients. Therapy started as early as possible will

reduce the irreversible complications of joint contractures in attenuated MPS.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: Not required*

## REFERENCES

1. Clarke LA. Mucopolysaccharidosis Type I. In: Adam MP, Ardinger HH, Pagon RA editors. GeneReviews®. Seattle (WA): University of Washington, Seattle, 1993-2021.
2. Jameson E, Jones S, Remmington T. Enzyme replacement therapy with laronidase (Aldurazyme®) for treating mucopolysaccharidosis type I. Cochrane Database Syst Rev. 2019;6(6):CD009354.
3. Al-Sannaa NA, Bay L, Barbouth DS. Early treatment with laronidase improves clinical outcomes in patients with attenuated MPS I: a retrospective case series analysis of nine sibships. Orphanet J Rare Dis. 2015;10:13.
4. Muranjan M, Karande S. Enzyme replacement therapy in India: Lessons and insights. J Postgrad Med. 2018;64:195-9.

**Cite this article as:** Magar SG, Kale AV, lngale V, Kalia A. Experience of enzyme replacement therapy for attenuated mucopolysaccharidosis I in Marathawada, India-a case report. Int J Contemp Pediatr 2022;9:491-3.