

Case Report

Hurler's disease presenting with quadriparesis and short stature

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Received: 10 March 2021

Revised: 12 April 2021

Accepted: 13 April 2021

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ABSTRACT

Mucopolysaccharidosis are a broad spectrum of rare lysosomal storage disorder caused by deficiency of enzymes responsible for degradation of glycosaminoglycans (GAG), thus leading to accumulation of GAG in various body tissues leading to somatic and neurological manifestations. General phenotype includes coarse facies, corneal clouding, hepatosplenomegaly, dysostosis multiplex etc. Detailed clinical and radiological evaluation and identification of type of GAG excreted in urine narrows the diagnostic possibilities. Definitive diagnosis requires assay of specific enzymes in various tissues. Till date 14 different types of MPS including subtypes are identified. We report a case of 4 years old male child presented with short stature, spastic quadriparesis, bony abnormalities and hepatosplenomegaly without intellectual impairment.

Keywords: Lysosomal, Glycosaminoglycans, Dysostosis multiplex

INTRODUCTION

A major part of connective tissue is made up of mucopolysaccharide. Due to lack of degradation in mucopolysaccharidosis, glycosaminoglycans like dermatan sulfate, heparan sulfate, chondroitin sulfate, etc. which provide a strong structural backing to the extracellular matrix and cartilaginous structures, gets accumulated in the lysosomes causing incompetence of cell structure and functions thereby resulting in excretion of partially degraded mucopolysaccharides in urine. Deposition of these glycosaminoglycans leads to various organ dysfunctions conferring to organomegaly, coarse facial features, corneal clouding, skeletal deformities etc. Incidence of this inborn error of metabolism is 1 per lakh of live births and mode of transmission is autosomal recessive except Hunter disease which is X-linked recessive.¹

The lysosomal enzyme alfa-L-Iduronidase is deficient in MPS I, which has been mapped on chromosome band 4p16.3.² Hurler Syndrome (severe), Hurler-Scheie syndrome (intermediate) and Scheie syndrome (mild) are

recognized as a disease continuum due to variation in age of onset and rate of disease progression.³ The difference in severity is due primarily to the effect of various mutations, some of which permit residual enzyme activity.⁴ Children with severe MPS I usually die within the first decade of life as a result of cardiorespiratory failure and progressive neurological disease.⁵ It is one of the very few metabolic disorders for which enzyme replacement therapy is available.^{7,9} The cloning of complementary DNA encoding α -L-iduronidase lead to the production of recombinant α -L-iduronidase.^{10,11}

CASE REPORT

A 4 years old Hindu male child, third in birth order and product of nonconsanguineous marriage presented with chief complaints of sudden nonprogressive weakness in all four limbs leading to inability to sit, stand and walk. Weakness was more on right side of body. There was no history of loss of consciousness and abnormal body movements. He was born as full term normal vaginal delivery with no history suggestive of prematurity and birth asphyxia. He achieved milestones at appropriate age.

His pedigree chart does not reveal any significant illness. Past history was also not significant.



Figure 1: Coarse facial features and flattening of rt nasolabial fold.



Figure 2: Lateral view of skull showing wide sella turcica.

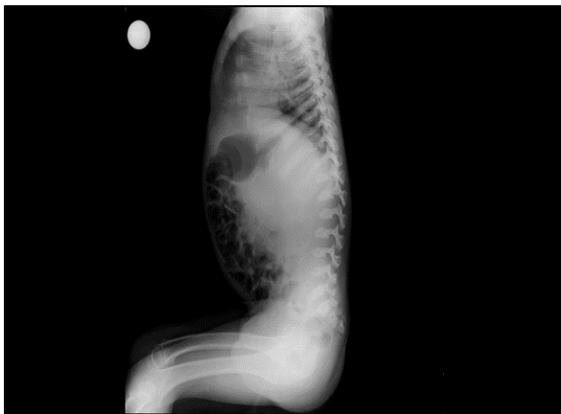


Figure 3: X-ray spine lateral view showing fish mouth vertebrae and spatula shaped ribs.

On examination his anthropometry revealed weight 8 kg (<4 SD) and height 80 cm (<4 SD) and weight for height was <3 SD. Head circumference was 49 cm which was within normal limits and mid upper arm circumference was 12 cm. Upper segment and lower segment ratio was 1.08:1 (normal 1.2:1) which was suggestive of short trunk dwarfism.

On head-to-toe examination slightly coarse facial features, large forehead, short neck, depressed nasal bridge, no corneal clouding, widely spaced primary teeth, forward protrusion of sternum, kyphosis, short and broad palms and fingers, broad wrists, double malleolus were present (Figure 1).

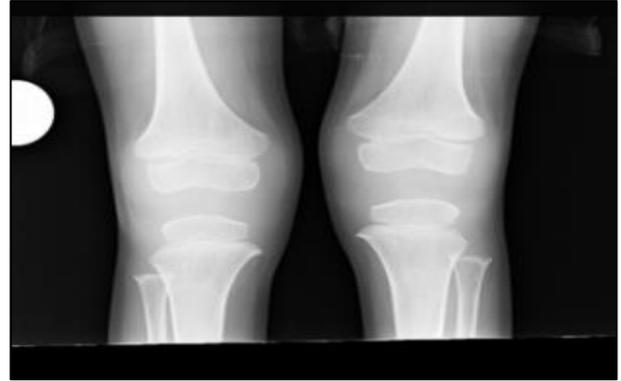


Figure 4: X-ray knee joint showing epiphyseal degeneration.



Figure 5: X-ray wrist joint showing bullet shaped phalanges and epiphyseal degeneration.

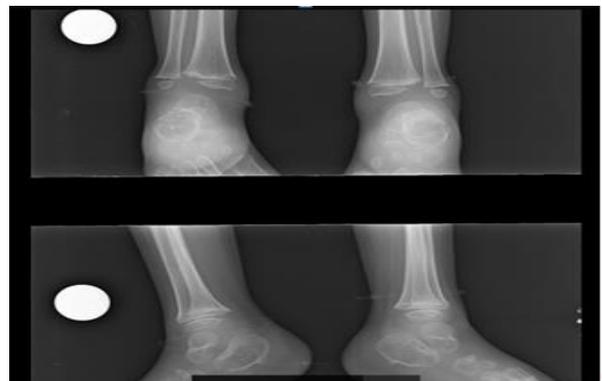


Figure 6: Coarsely trabeculated diaphysis with irregular metaphysis and diaphysis.

On systemic examination conscious, oriented, there was decreased tone and decreased power on all four limbs, more affected was right side of body. Deep tendon reflexes

were exaggerated in all limbs, more on right side. Planter reflex was extensor. Sensory system and autonomic nervous system were found to be not affected. Cranial nerves examination revealed flattening of nasolabial fold on right side, although eye closure on right side was present suggestive of UMN type of facial nerve involvement. Examination of other systems revealed significant hepatosplenomegaly.



Figure 7: MRI brain lateral view showing narrowing of spinal canal at level of foramen magnum.



Figure 8: MRI brain lateral view revealing widened and J shape sella.

Investigations done revealed normal cell counts. Serum calcium (9.6 mg%), serum phosphorus (6.9 mg%) and Vit D3 levels (27 ng/ml) were also found within normal limits. CPK levels were also in normal limits.

Skiagrams of all body parts revealed various abnormalities. X Ray skull lateral view revealed widened Sella-turcica (Figure 2), spine X ray spine lateral view revealed ovoid vertebral bodies with fish mouth opening anteriorly, anterior end of the ribs was widened appearing as spatula shaped ribs (Figure 3). X ray of both hands revealed bullet shaped phalanges along with metaphyseal dysplasia of long bones (Figure 5, 6).

His MRI brain finding revealed hypoplastic dens, with J shape widened sella. There was narrowing of vertebral canal at the level of foramen magnum noticed. There were also features of platyspondyly with end plate irregularities of all vertebral bodies with abnormal shapes. Acute

sacrococcygeal angulation was also noticed dorsally suggestive of skeletal dysplasia or metabolic disorder (Figure 6, 7).

Thus, a physical diagnosis of Disproportionate short stature with hepatosplenomegaly with acute onset quadriparesis with upper motor neuron palsy was made.

Specific investigation done in urine revealed urinary Glycosaminoglycans (GAG) levels very high 95.6 mg/mm creatinine as compared to normal range of (7.6-14.4) estimated by method of dimethyl methylene blue dye binding, confirming the possibility of mucopolysaccharidosis. Though lack of corneal clouding and mental retardation were against the diagnosis. Dry blood spot (DBS) test was sent to higher laboratory for evaluating specific enzyme deficiency revealed deficiency of alfa-L iduronidase thus confirming the diagnosis of MPS 1H type.

DISCUSSION

Presence of disproportionate short stature (short trunk type), coarse facial features, visceromegaly and skeletal deformities arouse the suspicion of HURLER type of MPS in this case. Though absence of corneal clouding and normal intellect was not in favor of above diagnosis. Presence of UMN type of quadriparesis and right facial palsy were again atypical feature led to thinking about another subtype of MPS.

Differential diagnosis included Hurler disease, Scheie disease, Morquio disease, Hunter disease etc. Points in favour of MPS 1H (Hurler disease were onset between 3-8 years of age, dysostosis multiplex, progressive visceral involvement, absence of intellectual dysfunctions and presence of signs of cord compression.⁸

Presence of short trunk dwarfism, significant bony abnormalities, normal IQ, instability of odontoid process directed towards diagnosis of Morquio disease (MPS 4), though presence of visceromegaly and absence of teeth and enamel defects were against the diagnosis. Hunter disease (MPS 2) was suspected due to absence of corneal clouding and slow progressiveness of disease and age of onset between 2-4 years. Though neurological features were strongly against the diagnosis. Scheie's disease (MPS 1S) was a remote possibility due to earlier onset of disease and presence of short stature and other bony deformities.⁶

UMN type of quadriparesis with facial involvement were explained by the fact that hypoplastic dens (odontoid process of axis vertebrae) and narrowing of vertebral canal at level of foramen magnum as detected in MRI brain led to compression on spinal nerves leading to above features. Enzyme estimation confirmed our physical and radiological diagnosis.

Enzyme replacement therapy could not be started due to nonavailability and cost factors.

CONCLUSION

MPS should be suspected in children presenting with short stature, coarse facial features, skeletal abnormalities, organomegaly with or without intellectual impairment. These patients should undergo enzymatic assay to obtain a definite diagnosis. Early enzyme replacement therapy can be treatment modality of choice.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Sanadhya A, Poswal L, Gupta N, Sharma S, Yadav P. Hurler's disease presenting with quadripareisis and short stature. *Int J Contemp Pediatr* 2021;8:927-30.