

Mucopolysaccharidosis Type 111: A Case Report

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Introduction

Mucopolysaccharidoses (MPSs) are rare group of inherited lysosomal storage disorders. These are autosomal recessive disorders, with the exception of Hunter disease, which is X-linked recessive. The mucopolysaccharidoses are caused by the deficiency or absence of specific lysosomal enzymes.

Case Report

A 10-year-old boy was brought to the pediatric unit with a history of two episodes of generalized tonic clonic convulsions over two weeks duration. At the age of 6 months he had been investigated for delayed development. He has impaired hearing and was on hearing aids for last 5 years. His speech is also delayed. There is global developmental delay with regression of milestones. He is severely limited in his activities and totally dependent. He is always irritable. He is a product of 2nd degree consanguineous parents. His elder brother and younger sister are healthy. He had never been to school [1-5].

On examination;

Weight 17 kg (-4SD), Height 107 cm (-4SD) Upper segment/Lower segment ratio=1.1 Motor developmental age is 03 years and mental developmental age is one year.

He has mild coarse facial features with frontal bossing and large head. There are no corneal opacities. He has generalized hirsutism and his hair is coarse. He has wide short fingers and short neck (Figure 1).



Figure 1: On examination.

He is physically handicapped with partially flexed hands, bilateral flexion contractures of elbows and knees. Muscle bulk is reduced in both legs.

He has a pigeon chest and lumbar lordosis. He has mild hepatomegaly without splenomegaly.

His special investigation reports are as follows.

Skeletal survey – Dysostosis multiplex with retarded bone age.

Ovoid vertebral bodies (11) with central anterior beaking (1),

Mild gibbus at thoraco lumbar transition (low dorsal kyphosis). Bone age is approximately 2 years (111) (Figures 2 and 3).

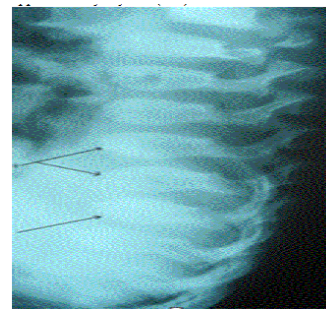


Figure 2: 1) Skeletal survey – Dysostosis multiplex with retarded bone age. Ovoid vertebral bodies (11) with central anterior beaking 2) Mild gibbus at thoraco lumbar transition (low dorsal kyphosis).



Figure 3: Bone age is approximately 2 years.

EEG did not show seizure activity.

TSH: 2.2 IU/mL (0.28-4.3), free T4: 0.9 ng/dL (0.9-1.7).

Analysis of spot urine sample revealed the following:

Berry spot test for mucopolysaccharidoses is positive

Spectrophotometric study for urinary GAG's=10.6 (3.1 ± 1.2 mgGAG/mmol/creatinine).

One diamentional Electroporesis for Glycosaminoglycans revealed Chondroitin Sulphate: ++ Dermatan Sulphate: Negative.

Heparan Sulphate: +++, Urine pH: 6.0.

Urinary Creatinine: 101 mg/dl, GAG/Creatinine Ratio: 10.6.

Enzymes study in leucocytes,

Heparan Sulphamidase: undetectable (1.3-6.8 nmol/17 hrs/mg protein).

Plasma N-Acetyl- α -D-glucosaminidase: 405.0, (300-600 nmol/hr/ml plasma).

β -galactosidase: 131.3 (79.6-480.0 nmol/hr/mg protein).

Diagnosis of MPS type 111 A was confirmed by specific enzymatic assay.

Discussion

Sanfilippo syndrome results from the deficiency or absence of 4 different enzymes that are necessary to degrade the GAG heparan sulfate.

Heparan-N-sulfamidase (SGSH) is deficient in MPSIIIA, a-N-acetylglucosaminidase (NAGLU) is deficient in MPSIIIB,

AcetylCoA:alpha-glucosaminide N-acetyltransferase is deficient in MPSIIIC, and N-acetylglucosamine 6-sulfatase is deficient in MPSIIID.

Patients with Sanfilippo syndrome are born without symptoms and typically have normal development for the first 2 years of life.

In all types of Sanfilippo syndrome, CNS disease predominates, with less skeletal and soft tissue involvement compared with the other mucopolysaccharidoses (MPSs).

By the age of 10 years, patients are severely limited in their activities and movements. Most children with type IIIA have severe neurological impairment by the age of 6 years.

Heparan sulfate accumulates in the lysosomes of tissues and organs leading to the diverse morphological abnormalities. Large amounts of heparan sulfate are excreted in the urine.

Screening by Berry spot test helps in detecting patients with MPS. This is the only available test in Sri Lanka at present for the detection of MPS.

One dimensional electrophoresis of urine helps in differentiating types of MPS. However the confirmatory test is to detect the deficient enzyme for all samples were sent to Genetic Centre India.

Prenatal diagnosis and Carrier testing can be done with enzymes study.

No treatment for the underlying cause is available. Enzyme replacement, bone marrow replacement and gene therapy are still under research level.

Hence, the aim of management is to minimize the handicapping effects of diffuse systemic disease and improve the quality of life. Regular assessment of hearing, neurological, organomegaly and joint function is required.

This progressive disorder has a devastating prognosis. Severe CNS degeneration occurs, with progression to a vegetative state.

Most patients do not live beyond age 20 years, with death primarily due to respiratory complications.

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