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Mucopolysaccharidosis Type II (Hunter's Syndrome)-A Clinical Case Report

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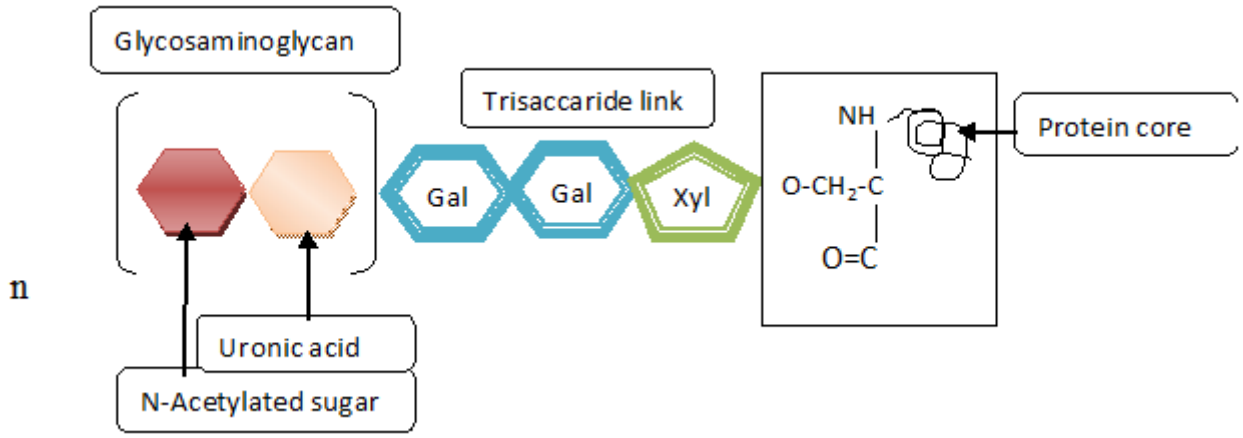
Abstract
The Mucopolysaccharidosis (MPS) are inherited lysosomal disorders caused by the absence of functional enzymes that contribute to the degradation of glycosaminoglycans (GAGs). The progressive systemic deposition of GAGs results in multiorgan system dysfunction. We report a rare case of Hunter syndrome-mucopolysacchordosis type II (MPS II) with clinical features including facial dysmorphism, hepatoslenomegaly, joint stiffness and contractures, mild mental retardation, valvular dysfunction.

Introduction

Mucoploysaccharidosis are metabolic disorders which are hereditary, progressive disease caused by deficiency of lysosomal enzymes required for degradation of GAG due to mutations of genes.

GAG is a long chain complex carbohydrate composed of uronic acids, aminosugars and neutral sugars (chondroitin 4 sulfate, chondroitin 6 sulfate, heparan sulfate, dermatan sulfate, keratan sulfate, hyaluronan).



Proteoglycans (mucoproteins) are formed of glycosaminoglycans (GAGs) covalently attached to the core proteins. Failure of degradation of proteoglycans due to mutation of lysosomal enzymes results in intralysosomal accumulation of GAG fragments and hampers cell function which leads to develop characteristic pattern of clinical, radiological and biochemical abnormalities.

We report typical case of Hunter's syndrome (MPS II) which is an X-linked recessive disease caused by deficiency of lysosomal enzyme iduronate-2-sulfatase.The purpose of presenting report is to highlight the distinctive manifestation of the Hunter syndrome.

Case Report

A 21 year old male patient, born by first pregnancy of healthy second degree consanguineous parent's. Gestation and delivery were normal, antenatal and postnatal history was uneventful. He has healthy 18year old younger sister No similar complaints in the family.

Parents gave a history of abdominal distension with bulging out of umbilicus and breathlessness since 7months.Medical past history reported about frequent respiratory infection and hepato-splenomegaly and mild mental retardation. Parents also complaints of difficulty in hearing since 5 years. No history suggestive of neurological deterioration, abnormal behavior, no history of constipation, diarrhea, vomiting, bleeding, jaundices, seizures, weight loss. His bladder habit was normal. The scholastic performance was poor.

On examination, patient features were distinctly suggestive of storage disorder, with coarse facial features with frontal bossing, large head, hypertrichosis, thick eyebrows, depressed nasal bridges with anteverted nostrils, thick lips, open mouth with protruding tongue, poor oral hygiene, macroglossia, prominent ears, short neck, short fingers with flexion contractures in fingers, elbow and knees were evident. He also had protuberant belly with umbilical herniation with moderate hepatomegaly around 16 cm below costal margin with moderate splenomegaly and inguinal hernia, lumbar lordosis. The anthropometric measurements (height for age, height for weight) were suggestive of severe growth retardation.

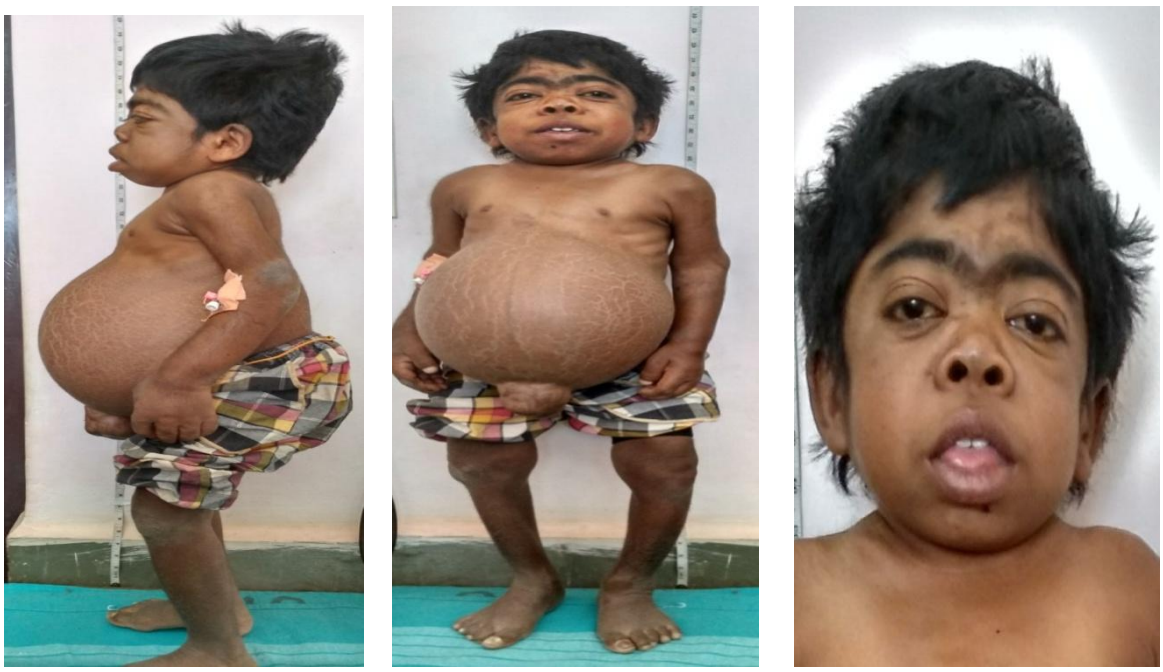


Fig 1: Characteristic short neck, depressed nasal bridge, thick lips, flexion contractures of fingers, protuberant belly with umbilical hernia.

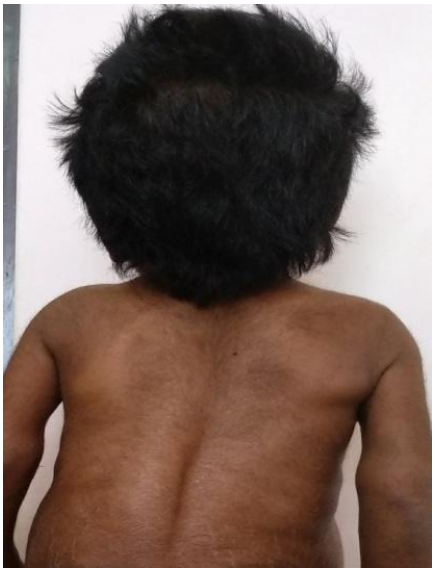


Fig 2: Hypertrichosis

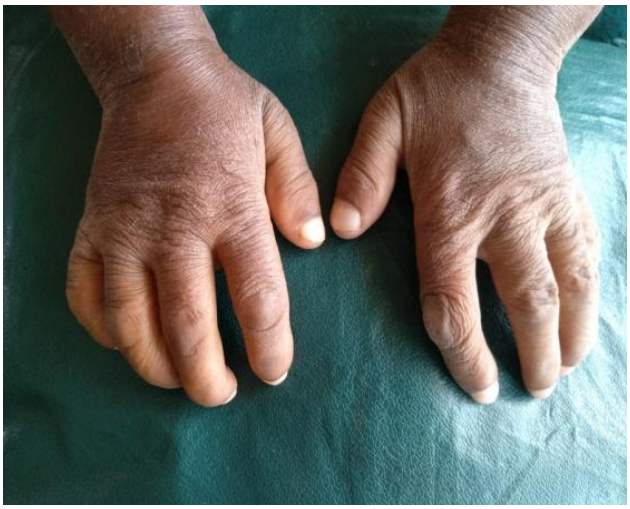


Fig 3: Short fingers

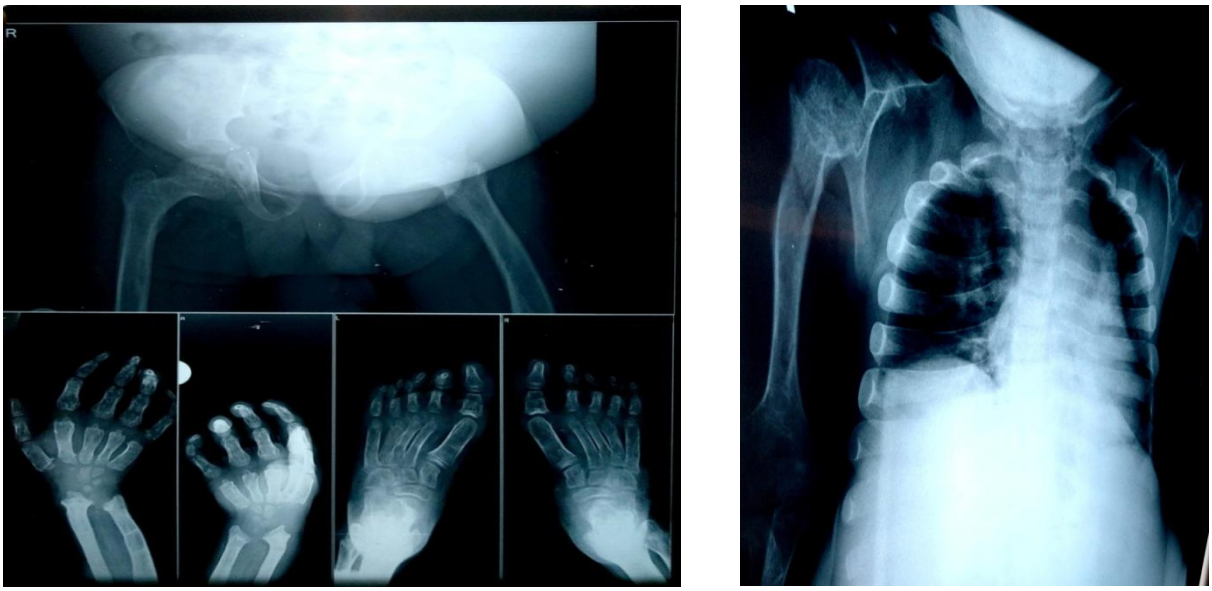


Fig 4: X-ray of wrist showed bullet shaped metacarpals with widened diaphysis of metacarpals and metatarsals with osteoporosis with epiphyseal irregularity of distal ends of radius,ulna,tibia and fibula. Pelvis x-ray depicts wide iliac blade with narrow acetabulam.

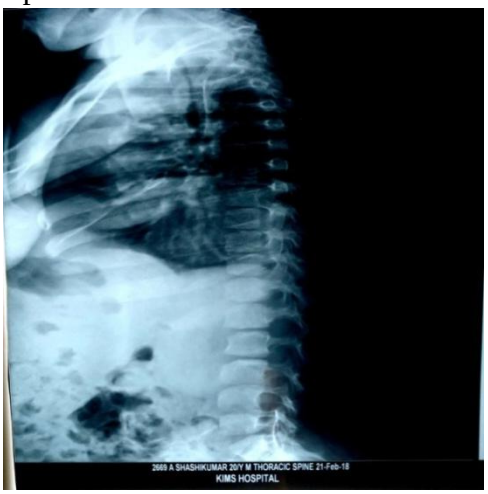


Fig 5: Spine x-ray showed anterior lipping in L2 vertebrae

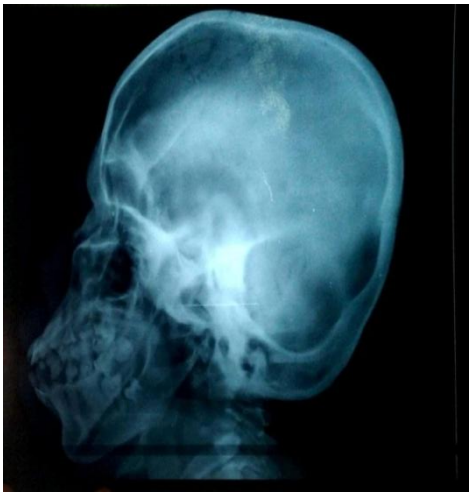


Fig 6: Lateral view of skull showed mild J shaped sella turcica

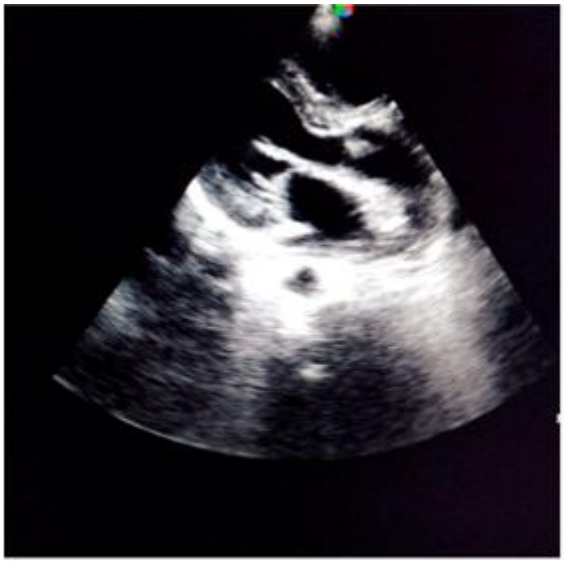


Fig 7:2 D ECHO depicts thickened aortic valve leaflet

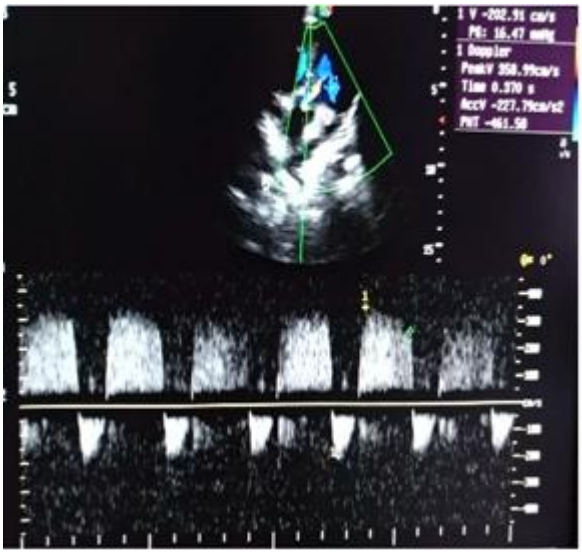


Fig 8:2 D ECHO shows mild aortic regurgitation

Disscussion

Mucopolysaccharidosis was first described by canadian physician Charles Hunter, in 1917[1] .The first case of Hunter's syndrome was reported in 14 year old male patient presentepd with complaints of bumps and coarse skin by Ogubiyi et al Ibadan in 2006[2].

MPS II is only known X-linked MPS disorder.The human gene encoding I2S has been mapped to Xq28[3] .In 1993 Whitely et al first described mutation of IDS gene, where guanine replaced by adenine in exon 9 of IDS gene and glutamine substituted guaine at postion 468 on the protein.This site is a mutational "hot spot" for IDS gene[4].

Prevalence of Hunter syndrome is one in 170,000 male live births. MPS II is classified based onCNS manifestaions and suvival length[5] .

MPS type II HB(mild)	MPS type II A(severe)
Clinical features appear in 2nd decade of life[5] Mild mental retardation. Progression of disease is very slow[5].	Clinical features appear between two and four years of age[5] Severe mental retardation Obstructive airway disease or cardiac failure are main cause of death[6]. Death occurs between the ages of 20 and 30 years[5]

Typical clinical features evident in our case

- Short staure,
- Thick coarse skin,
- Depressed nasal bridge,
- Thickening of alae nasi,ear lobules,
- Macroglossia,
- Macrocephaly,
- Facial and body hypertrichosis,
- Scalp hair coarse,straight and thatch like,
- Bilateral profound hearing,
- Lax protuberant abdomen with umbilical hernia and inguinal hernia,
- Moderate hepatosplenomegaly,
- Fixed joint abnormalities with contractures,
- Lumbar lordosis,
- Waddling gait,
- Mild mental retardation,
- X-ray features were suggestive of MPS.

Investigations

- Urine spot tests: Screening test for mucopolysaccharidosis[7].
- Semiquantification of urinary GAG done by spectrophotometric assays.
- Heparan, keratan, and dermatan sulfate can be distinguished by separation techniques

like electrophoresis or thin layer chromatography[8].

- Confirmatory diagnosis is by enzyme assay in leucocytes,fibroblasts or dried blood spots using substrates specific for I2S[9,10] .

Diagnosis often can be made through clinical examination and urine tests. Analysis of GAGs is a screening test for MPS type II.24 Hour urine for mucopolysaccharidosis typing (Two dimensional electrophoresis) was positive in our case.However confirmatory diagnosis is by enzyme assay in leucocytes,fibroblasts or dried blood spots using substrates specific for I2S. Absent or low I2S activity is diagnostic of Hunter's syndrome.

Enzyme replacement therapy has emerged as a new treatment for mucopolysaccharidosis disorders,including Hunter sundrome.Enzyme replacement therapy using idursulfase(Elaprase), a recombinant human I2S produced in the human cell line, has been recently approved in the human cell line, has been recently approved in the United states and the European Union for the management of MPS II. Weekly intravenous infusion is given over 3 hr at a dose of 0.5 mg/kg diluted in saline.Bone marrow transplantation and umbilical cord blood transplantation are definitive treatments for MPS

Conclusion

Mucopolysaccharidosis type II is a X linked recessive disorder which effects multiple systems because of deposition of GAGs in the heart, liver and spleen. It needs multidisciplinary approach for its management to improve quality of life,however considering size of our population many cases are undiagnosed due to difficulties in confirmation of diagnosis as enzymatic studies are not avaliable in many centres.

This case serve to highlight classical clinical manifestation of Hunter syndrome, however enzymatic studies are needed to confirm the diagnosis.

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