Hurler’s Syndrome - A Case Report
(Mucopolysaccharidosis Type-IH)

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Abstract
A girl named Tania, aged 5yrs was brought to Shaheed Ziaur Rahman Medical College Hospital, Bogra with the complaints of swelling of both legs for 5days & low grade intermittent fever for 1month & she also had severe mental retardation, facial dysmorphism, hepatosplenomegaly, umbilical hernia, corneal clouding, large calvaria & features of dysostosis multiplex. Her clinical as well as radiological features arouse strong suspicion suffering from a rare genetic disease (autosomal recessive) hurler’s syndrome though it wasn’t confirmed by deficiency of specific enzyme or urinary excretion of GAG (glycosaminoglycan).

Introduction
Hurler syndrome is an autosomal recessive disorder of mucopolysaccharide metabolism caused by a deficiency of the enzyme α-L-iduronidase.[¹] The inability to degrade these macromolecules, which are ubiquitous, results in their storage in a variety of tissues including the liver, spleen, heart, connective tissue and others, resulting in premature death, usually by 10 years of age. These disorders display extensive genetic heterogeneity. In addition to somatic features, there may be severe mental retardation. Hurler syndrome represents the classical prototype of a mucopolysaccharide disorder, with a very low prevalence: 1:150,000 births.[²] The diagnosis is usually made between the age of 6 and 24 months with evidence of coarse facial features, prominent forehead with large tongue, hepato-splenomegaly, corneal cloudiness, skeletal deformities, joint stiffness, short stature, acquired cardiomyopathy and progressive lenticular enlargement with increased intracranial pressure caused by communicating hydrocephalus.[³]

Case report
Tania aged 5yrs was brought to Shaheed Ziaur Rahman Medical College Hospital with the complaints of swelling of both legs for 5days & low grade intermittent fever for 1month with history of severe mental retardation and recurrent attacks of respiratory tract infection. She is only child of her parents giving history of 1st degree of consanguineous marriage & all family members including parents are apparently well. Her antenatal, natal, neonatal periods were unremarkable. Her feeding was normal & immunization was completed as per EPI schedule. According to informant (mother) the girl’s development was delayed from 6months of age with progressively
increasing head size & repeated attacks of RTI occurred since then. She started sitting at age of 2yrs, can’t crawl, can stand with support only.

She appeared ill, irritable with no sign of socialization & self control. Gross facial dysmorphism was noted in the form of frontal bossing, depressed nasal bridge, opened mouth with large protruded tongue, thick eyebrows. Her calvarium was large disproportionately (OFC:52cm), dentature was misaligned, neck was short, chest was small, abdomen was distended with presence of umbilical hernia, shortening of limbs with small fingers & toes. Her skin was pale, thick, coarse & she had copious nasal discharge. Her height was 80cm, weight 9kg that reveals weight: height, height: age & weight: age are below normal range. Her systemic examinations during period of hospitalization revealed following features:

Though higher psychic & cerebellar functions could not be evaluated, cranial nerves appeared intact. Bulk of all limb muscles are reduced with increased tone but reflexes were normal. During per abdominal examination hepatosplenomegaly was found with normal external genitalia & there was no shifting dullness or fluid thrill. Bilateral corneal opacity and apparently normal throat, ear & cardiovascular system was found. Hematological investigations showed iron deficiency anaemia on PBF & biochemical profile was within normal limits. Normal urine r/e & negative for urinary albumin was detected. Radiological examinations included X-ray skull (L/V) showing widening of calvaria with wide, J-shaped sella. On chest x-ray flattened, oar shaped ribs (narrowed at vertebral ends & wide at sternal ends) with normal cardiothoracic ratio was found including cavitary lesion in mid & lower zone of right lung. X-ray of spine showed hypoplasia of several lumbar vertebral bodies with prominent inferior beaking. In X-ray of forearm & hands there was angulation of lower ends of radius & ulna with slopping of lower surfaces towards each other, characteristic proximal tapering of metacarpal bones.
For confirmation of hurler’s syndrome urinary GAG excretion test & enzyme assay from neutrophil or cultured fibroblasts were recommended. Differential diagnosis be: 1) congenital hypothyroidism, 2) Hunter’s syndrome.

Discussion

Mucopolysaccharidosis type I (MPS I) is an autosomal recessive lysosomal storage disorder resulting from deficiency of the enzyme α-L-iduronidase. Deficiency of this enzyme results in the accumulation of dermatan sulfate and heparan sulfate, which are complex sugars known as glycosaminoglycans (GAGs). The resulting accumulation of GAGs in the lysosomes leads to progressive, multi-system organ damage. There are no known ethnic predilection however some mutations are more common in certain populations. The incidence of the severe form is estimated to be approximately 1 in 100,000, and the attenuated form is even more rare. The clinical variability among the mucopolysaccharidoses is broad. Individuals with the severe form of MPS I are classified as having Hurler syndrome and those with attenuated or milder form as having Hurler-Scheie or Scheie syndrome. A genotype-phenotype correlation may identify those at risk for the more severe clinical manifestations. Parents of children with MPS I are obligate carriers of the condition and have a 25% chance of having other children with MPS I. Carriers do not have any known symptoms of MPS I.

The onset of symptoms and course of disease varies in MPS I, depending on the severity of the condition. If untreated, the prognosis of individuals with the severe form of MPS I (Hurler syndrome) is very poor, with onset very early in life and rapidly progressive manifestations, often resulting in death by ten years of age. Onset of symptoms in the attenuated forms of MPS I is usually in childhood or adolescence and survival to adulthood is common. Individuals with the attenuated forms, however, will still require stringent clinical management, particularly related to their cardiac and skeletal manifestations at diagnosis, which is usually is made between 6-24 months of life. Clinical features usually noted are growth delay, profound neurological involvement (in the severe form only), hepato-splenomegaly, progressive skeletal dysplasia (dysostosis multiplex), coarse facial features, corneal clouding, large tongue, frequent upper airway infections with otitis media, joint stiffness and short stature. Other constant features are inguinal and umbilical hernias, large and scaphoid head, small widely spaced teeth and limited joint mobility. Later signs include cardiac murmurs, deafness, blindness and short stature. The constellation of skeletal abnormalities is known as dysostosis multiplex. Odontoid dysplasia and radiographic subluxation of C1 on C2 is common. This may cause anterior dislocation of the atlas and spinal cord compression. When the MPS disorder is suspected based on clinical features, radiographic results or urinary screening tests, definitive diagnosis is established by enzyme assay.

Management of the multiple organ system involvement in MPS I requires a multi-specialty and multi-disciplinary approach. Two relatively new treatment interventions are available to decrease the impact of the metabolic abnormalities patients with MPS I:

1) Successful hematopoietic stem cell transplantation (HSCT) increases survival, reduces facial coarseness and hepatosplenomegaly, improves hearing, and preserves normal heart function, however cardiac valvular disease, skeletal manifestations and corneal clouding may continue to progress. If HSCT is accomplished before evidence of significant developmental delay (usually under 2 years), the degree and rate of cognitive decline will likely be reduced.
2) Enzyme replacement therapy can significantly reduce liver size, increase height and weight, decrease joint restriction, lessen sleep apnea, and improve breathing in individuals with intermediate MPS I. The benefit of ERT in those with severe disease has not been assessed, however one patient with severe MPS been treated for 3 years with ERT, continued to experience decline in respiratory status, musculoskeletal and spinal involvement, and developmental skills. [Thomas: 2006] Because the recombinant enzyme is not thought to cross the blood-brain barrier, the best option to reduce the risk of cognitive impairment remains early HSCT.[9]

References

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