Hurler Scheie Disease

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Abstract
We present a very rare case of mucopolysaccharidosis type I (MPS I) which presented to us with respiratory distress. Our patient had short stature, coarse facial features, claw hands and clouding of both corneae. This article highlights the salient features present in a case of mucopolysaccharidosis type I.

Introduction
Mucopolysaccharidoses (MPS) is a group of rare genetic disorders characterised by mutations in the genes encoding synthesis of lysosomal hydrolases, enzymes that are involved in breakdown of glycosaminoglycans (GAG), causing accumulation of GAG in various tissues, resulting in permanent progressive cellular damage which affects the appearance, physical abilities, organ and system functioning, and in most cases mental disabilities.

There are seven different forms of mucopolysaccharidoses, each with different enzymatic mutation. Mucopolysaccharidosis-I (MPS I) is an autosomal recessive condition due to deficiency of the lysosomal enzyme α₁-iduronidase, which results in progressive accumulation of GAG’s within the lysosomes, subsequently leading to multiorgan dysfunction and damage. The purpose of presenting this case is to highlight the salient clinical and radiological features of MPS type I.

Case Report
A 17 yr old girl born out of a non-consanguineous marriage presented to us with complaints of shortness of breath. Patient had short stature, coarse facial features, hirsutism, clouding of cornea, claw hands, abdominal protrusion and umbilical hernia.

On history patient had similar episodes since childhood. Patient had delayed physical milestones without any significant birth history. On examination, macrocephaly with depressed nasal bridge, macroglossia, retrognathia, hypertrichosis, short neck and flexion deformities were present (Figure 1). Her weight was 30 kgs, height was 107 cm, both less than 3rd percentile for her age. Secondary sexual characteristics were underdeveloped for patients age. Rhonchi were present in both lung fields with normal cardiovascular system examination. Abdomen was protuberant with hepatosplenomegaly and umbilical hernia (Figure 2). Higher mental functions were normal for the literacy level of the patient. Spine examination revealed thoraco-lumbar scoliosis. Her blood examination showed Hb-12.6 g/dl, TLC-8800 cells/mm³, random blood glucose- 101.08mg/dl, SGOT/SGPT- 48/45 U/L, total protein- 6.3g/dl, serum albumin-4.54 g/dl, serum calcium- 8.76 mg/dl and phosphorous-3.61 mg/dl, blood urea-28 mg/dl, serum creatinine-0.6 mg/dl and fT3-4.51 pg/ml, fT4-1.84 ng/ml, TSH-1.83 microU/ml. Electrocardiography and echocardiography were normal. Chest radiograph showed cardiomegaly, ribs were ‘Oar’ shaped with narrowing of the vertebral ends and broadening of sternal ends (Figure 3). Radiography of the hands and foot showed short metacarpals, metatarsals with osteopenia and bullet shaped 2nd to 5th metacarpals (Figure 3). Skull and pelvis radiographs showed thickening of calvarium and hip dysplasia respectively. Obstructive pattern was noted on pulmonary function test. Polysomnography was significant with apnea-hypopnea index of 36.8/hr (severe >30/hr) with mixed central and obstructive pattern of apnea. Patient was given a trial of CPAP but she had repeated episodes of apnea with multiple sessions of CPAP. Enzymatic analysis showed deficient activity of α1-iduronidase 1.07 nmol /hr/ mg(normal >11 nmol/hr/mg). Further work-up of the patient for genetic mutation was not possible in view of patients unwillingness.

Four siblings of the patient expired within a few hours of birth due to respiratory distress, and had similar phenotypic features with corneal clouding. One of her cousins has similar features (Figure 4).

Discussion
Mucopolysaccharidosis type I (MPS I) is a panethnic, chronic and progressive, autosomal recessive lysosomal storage disease in which catabolism of GAG- heparin and dermatan sulphate is deficient. This is due to deficient activity of the enzyme α₁-iduronidase, a product of gene IDUA mapped to chromosome 4p16.3, causing accumulation of these GAG’s within the lysosomes of virtually all tissues. First described by Hurler in 1919, a milder phenotype was later identified by Scheie in 1962.

MPS I has an estimated incidence rate of 1 in 100,000 live births.¹ ² An International panel comprising of 12 experts on MPS I revised and updated the international guidelines in 2008, based on their recommendations, MPS I has been classified into two broader groups, severe MPS I H (Hurler Syndrome) and attenuated MPS I (Hurler-Scheie:H/S and Scheie:S syndromes).³ The attenuated type which includes intermediate and mild forms of the disease constitutes about 20% of MPS I.¹ The deficient enzyme in MPS I is α₁-iduronidase responsible for removing terminal iduronic acid residues. The disease is characterized by organ enlargement and excretion of abnormal quantities of GAGs in urine.

Patients with MPS I H (Hurler) syndrome may present with learning difficulties, hepatosplenomegaly, cardiac disease (cardiomyopathy and valvular disease), respiratory problems with upper airway obstruction and

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obstructive sleep apnea. Skeletal problems include dysostosis multiplex, odontoid dysplasia, spondyloolisthesis, thoracolumbar gibbus. Other problems include caries and dental abscesses, middle ear disease, sensorineural deafness and umbilical hernias. MPS I H patients often die in the first decade of life without treatment.

Patients with MPS I H/S (Hurler/Scheie) have an intermediate phenotype. They usually have normal intelligence and only mild facial changes, and die in their twenties or later of associated cardiorespiratory disease. Diffuse corneal opacification and retinopathy occur.

Patients with MPS I S (Scheie) syndrome often have a normal lifespan and intelligence. They develop restrictive respiratory disease and obstructive sleep apnea, hepatosplenomegaly, umbilical and inguinal hernia, and aortic valve stenosis. Mild corneal opacification affects MPS I S patients.

Traditionally treatments for MPS I have aimed at relieving symptoms. More radical treatments have been explored including bone marrow transplantation which has become the treatment of choice for carefully selected Hurler patients. After successful haematopoetic stem cell transplantation, patients have been found to have normal levels of enzyme α1-iduronidase. After transplantation cardiac pathology is resolved, vision and hearing improve, odontoid hypoplasia is prevented and there is reversal of psychomotor retardation. Enzyme replacement therapy (α-iduronidase) is now available to treat MPS I H/S and MPS I S phenotypes.

**Conclusion**

Mucopolysaccharidosis Type I has typical clinical and radiological features. The severity of symptoms and signs depend on the relative deficiency of enzymes. Enzyme replacement is now available in selected patients with this disease.

**References**