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CASE REPORTS

Clinical presentation of Mucopolysaccharidosis type II (Hunter syndrome): A Case Report

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Abstract:

Mucopolysaccharidosis (MPS) is a rare disease, caused by deficiency of lysosomal enzyme. MPS cases have been reported throughout the world. MPS patient typically appear normal at birth, but clinical features appear between two to four years of age. We report a case of 12-years-old boy presented with progressive deformity of multiple joints for eight years duration and gradual decline the cognitive function for the same period. On examination, his head was large, short stature, a coarse facial feature with depressed nasal bridge and stubby finger with flexion of distal interphalangeal joint. There was severe mental retardation. We diagnose the patients as Hunter Syndrome, on the basis of clinical findings, radiological features and positive for MPS screening test in urine. Although the golden standard for diagnosing the type of MPS is enzyme analysis. We could not do enzyme analysis as it is not available in Bangladesh.

Introduction:

Mucopolysaccharidosis (MPS) is a group of autosomal recessive metabolic disorders caused by the absence or malfunctioning of the lysosomal enzymes needed to break down molecules called glycosaminoglycans (GAGs). GAGs are oligosaccharide components of proteoglycans which provide structural integrity to connective tissues. Accumulation of partially degraded GAGs causes thickening of tissue and compromise of cell and organ function. This results in permanent, progressive cellular damage which affects the appearance, physical abilities, organ and system functioning and, in most cases, mental development. Common clinical presentation includes facial dysmorphism, hepatosplenomegaly, joint stiffness and contractures, pulmonary dysfunction, myocardial enlargement and valvular dysfunction and neurological involvement. We report this case of MPS type II because of its rarity and the atypical features of severe mental retardation, macrocephalic head, no corneal clouding and all other features suggestive of MPS type II. The purpose of presenting this case is to highlight the distinctive manifestation of Hunter syndrome.

Case presentation:

A twelve-year-old boy was admitted in neurology department with progressive deformity of multiple

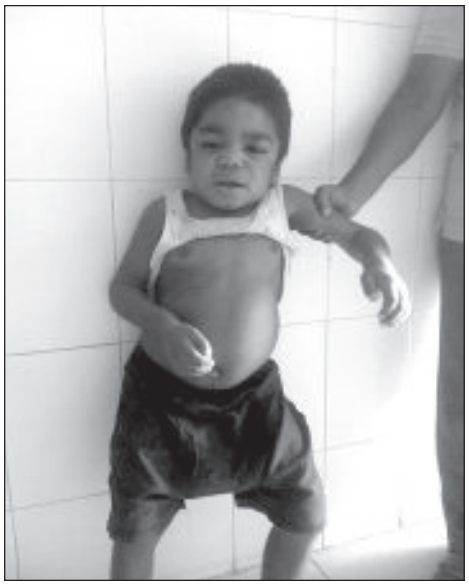

Fig.-1: *Male boy with mucopolysaccharidosis showing an macrocephalic head, coarse facial appearance with depressed nasal bridge and a protuberant abdomen.*

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joints for eight years duration and gradual decline of cognitive function for the same period. Deformity initially started in right interphalangeal joint since he was four, without any history of trauma and joint pain. It was gradual and progressive, later involved in wrist, elbow, and knee joint bilaterally. Last two months, his deformity so severe that he was bed-ridden. At same period, his cognitive function showed gradual declining. He was second issue of a consangious parents. His birth history was uneventful and milestone of development was normal upto age four. He had no history of prolonged fever, unconsciousness, seizure, any focal neurological deficit.

On examination his head was macrocephalic in shape, with a head circumference of 53.5 cm. He had a depressed nasal bridge, a short neck, coarse facial appearence,and small stubby fingers with flexion of the distal interphalangeal joint, (Figure 1). Anthropometric examination showed him to be severely stunted growth (height 41.5 inch). His abdomen was soft and slightly distended with a protruding umbilicus. Fundoscopy revealed bilateral papilloedema .

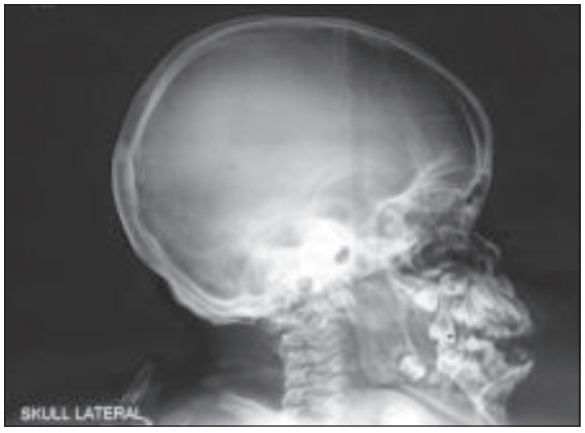

Fig.-2: *Lateral x-ray of the skull showing an enlarged skull.*

Suspecting MPS, we performed a skeletal survey. Anteroposterior and lateral X-rays of the skull showed an enlarged and normal sella turcica (Figure2). The bones of the skull and sutures appeared normal for his age.

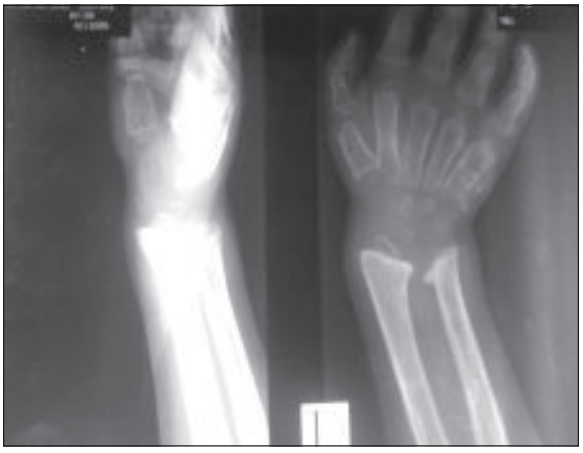

Fig.-3: *X-ray of wrist and hand showing pointing of metacarpal bones, with inferior breaking of radius and ulna.*

X-ray of wrist joint and hand showed pointing of metacarpal bones, inferior breaking of both radius and ulna, three carpal bones were ossified and epiphysis for lower ulna yet not appeared. (Figure 3). An antero-posterior chest X-ray view showed no parenchymal lesions were seen in visualized lung fluids and cardiac shadow also normal (Figure 4). CT scan of brain showing communicating hydrocephalus (Figure 5).

However in our patient there was atypical presentation such as an macrocephalic head, severe mental retardation, and no corneal clouding,

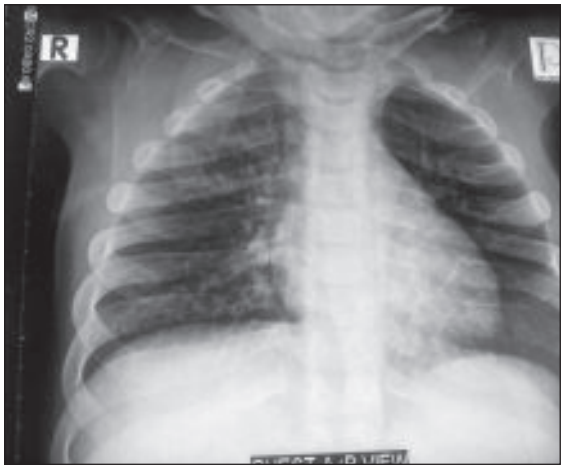

Fig.-4: X-ray of chest in P/A view showing normal findings.

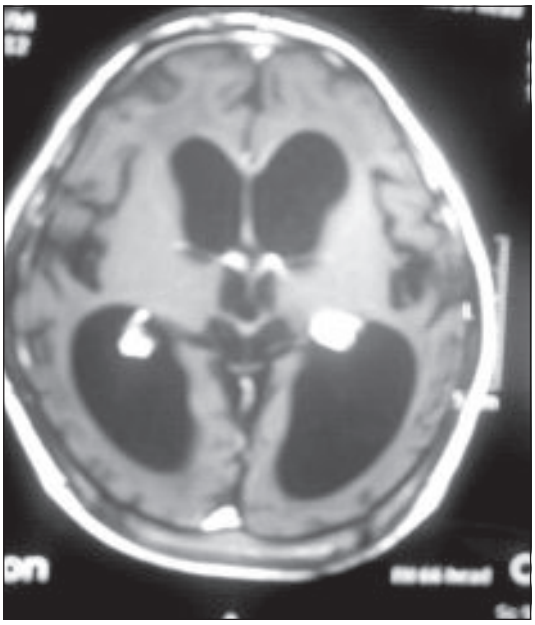

Fig.-5: *CT scan of brain showing communicating hydrocephalus.*

which are important features of MPS type II. We could perform measurement of GAG, keratan and heparan sulphates, in his urine and it was positive. Although the golden standard for diagnosing hunter syndrome is enzyme iduronate sulfatase analysis. We could not do enzyme analysis as it is not available in Bangladesh. Our diagnosis of MPS was confirmed from history, clinical examination, skeletal survey and urinary screening test positive.

Discussion:

Mucopolysaccharidosis was first described by Charles Hunter, a Canadian physician, who in 1917 described a rare disease found in two brothers[1-3]. Mucopolysaccharidoses are a group of inherited diseases characterized by defective lysosomal enzymes responsible for the degradation of mucopolysaccharides, which are major components of intercellular connective tissue. Hunter syndrome caused by deficiency of enzyme, iduronate- 2-sulphatase.[1] This leads to an accumulation of incompletely degraded mucopolysaccharides in the lysosomes which affect various body systems through enzymatic activity[4]. All MPS are autosomal recessive, except Hunter syndrome which is X-linked recessive. In affected individuals, undegraded or partially degraded GAG accumulates within the lysosomes and is excreted in excess in the urine. The accumulation of GAG within the lysosomes is responsible for the clinical manifestation of this disorder[5].

Mucopolysaccharidosis type II or Hunter syndrome is rare and is caused by a deficiency of iduronate-2-sulfatase. Hunter syndrome is one of the most common MPS with a prevalence of one in 170,000 male live births. MPS type II is classified into mild (type II, HB) and severe (type II, A) and this classification is based on the length of survival and the presence or absence of central nervous system (CNS) disease. Patients typically appear normal at birth in both types. In the severe form the clinical features appear between two and four years of age while in the mild form the clinical features appear in the second decade of life. In the severe form there is severe mental retardation and loss of skills. Death usually occurs in the first or second decade of life and the main cause of death is obstructive airway disease or cardiac failure. In the milder form there is mild mental retardation but intelligence is normal, stature is near normal, and clinical features are less obvious and progress very slowly. Diagnosis is usually made in the second decade of life. Death usually occurs in the fourth decade and the main cause of death is cardiac failure.

Diagnosis of the disease is usually made by clinical presentation and skeletal survey. The common clinical presentations are a large head (dolichocephalic), short stature, mental retardation, coarse facial features, a protuberant abdomen, a broad nose with flared nostrils, large jaws, hypotonia and a large tongue which becomes apparent between two and four years of age, and these clinical features were present in our case. Other clinical features include upper respiratory tract infection, valvular heart disease leading to right and left ventricular hypertrophy and heart failure, chronic diarrhea, enlarged liver and spleen, umbilical as well as inguinal hernia, corneal clouding with poor vision and hearing loss caused by both connective and sensorineural deficits. A communicating hydrocephalus is a common finding and can lead to severe manifestation of neurological signs which were not present in our case.

Analysis of GAGs (heparan and dermatan sulphates) is a screening test for MPS type II. The presence of excess heparin and dermatan sulphates in the urine is evidence of MPS type I, MPS type II or MPS type VII. Confirmatory diagnosis is by enzyme assay in leukocytes, fibroblasts or dried blood spots and plasma sample, using substrates specific for 12S. Absent or low 12S activity in males is diagnostic of Hunter syndrome, provided other sulfatase deficiency has been ruled out.

Enzyme replacement therapy using idursulfase (Elaprase), a recombinant human I2S produced in the human cell line, has been recently approved in the United States and the European Union for the management of MPS type II. Weekly intravenous infusion is given over three hours at a dose of 0.5 mg/kg diluted in saline. Bone marrow transplantation (BMT) and umbilical cord blood transplantation (UCBT) are definitive treatments for MPS. Apart from these, supportive management is very important. Physical therapy and daily exercise may improve mobility of joints. Blood transfusion, infection and nutritional management are also important in the management of MPS type II[6].

Conclusion:

Based on clinical findings and radiological features it is possible to diagnose a case of mucopolysaccharidosis. Urinary glycosaminoglycans (heparin and keratan sulphate) estimation and genetic studies confirms the diagnosis and its type, which will help in offering enzyme replacement therapy to the given individual.

References:

1. Wraith JE, Scarpa M, Beck M, Bodamer OA, Meirleir LD, Guffon N, Ploeg AT, Zemen J. Mucopolysaccharidosis Type II (Hunter syndrome): A clinical review and recommendations for treatment in the era of enzyme replacement therapy. Eur J Pediatr 2008;167: 267–77.
2. Martin R, Beck M, Eng C, Giugliani R, Harmatz P, Mufioz V, Muenzer J. Recognition and diagnosis of mucopolysaccharidosis II (Hunter syndrome) Pediatrics 2008;121: 377–86.
3. Hunter C. A rare disease in two brothers. Proc R Soc Med 1917;10:104-16.
4. Kliegman RM, Behrman RE, Jenson HB, Stanton FB. Nelson Textbook of Pediatrics. 18th ed. Philadelphia: Saunders; 2007. 620-26.
5. Tuschl K, Gal A, Paschke E, Kircher S, Bodamer OA. Mucopolysaccharidosis Type II in females: Case report and review of literature. Pediatr Neurol 2005;32:270-72.
6. Patil R, Waseka N , Jadhav SG, Zore R, Sangoi P, Vishwanath D. Clinical Presentation and Diagnosis of Mucopolysaccharidosis Type 2 (Hunter Syndrome). Journal of the association of physicians of india. 2013; 61: 54-56.