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Clinical Presentation of Mucopolysaccharidosis Type II (Hunter's Syndrome)

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Abstract: We present a very rare case of mucopolysaccharidosis with atypical presentation such as severe mental retardation, dolicocephalic head, a coarse facial features, no corneal clouding with inguinal hernia. The purpose of presenting this case is to highlight the distinctive manifestation of Hunter Syndrome. Based on thorough clinical examination and radiological survey it is possible to diagnose a case of mucopolysaccharidosis. Multidisciplinary approach will go a long way to manage the patient holistically.
Keywords: Coarse facial features, Glycosaminoglycans, Hunter syndrome, Mucopolysaccharidosis.

INTRODUCTION

Mucopollysaccharidosis (MPS) is a group of autosomal recessive metabolic disorders caused by the absence or malfunctioning of lysosomal enzymes needed to break down molecules called glycosaminoglycans (GAGs). These are long chains of sugar carbohydrates in each cell that help to build bone, cartilage, tendons, corneas, skin and connective tissues. Glycosaminogycans are also found in the fluids that lubricate joints. Children with MPs either do not produce enough of one of 11 enzymes required to breakdown these sugar chains into proteins and simpler molecules or they produce enzymes that do not work properly. Over a long period, these GAGs collect in the cells, blood and connective tissues. They cause permanent progressive cellular damage which affects the appearance of individual, causing facial dysmorphisim, organomegaly, joint stiffness, airway obstruction, pulmonary dysfunction, myocardial enlargement, valvular dysfunction and neurological impairment. This could result in impaired intelligence. As there is no effective therapy for Hunter's syndrome, care has been predominantly palliative. However, enzyme replacement therapy (ERT) with recombinant human iduronate -2-sulfatase has now been introduced. We report this case of MPs type II because of rarity and the atypical features of severe mental subnormality, dolicocephalic head without 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 three years old male toddler presented to the pediatric outpatient department with abdominal distension without pain, had been gradual and progressive since he was one and half years and he had also swelling in right inguinal region. There was also history of abnormal increasement of head size and deformity of back and also history of not gaining height properly. On further inquiry he had history of recurrent upper respiratory tract infection, irritability and developmental delay. There was no history of constipation, diarrohea, vomiting, bleeding, jaundice, seizure, weight loss or loss of appetite or of consciousness. His bladder habit was normal. He was born of an uneventful pregnancy and he was immunizing as per national immunization programme.

On examination his head was dolicocephalic in shape with a circumference of 55cm and cephalic index 75%. He had a short stature (86cm), with low upper to lower segment ratio of 1.4:1(expected for age) and stunted without wasting. He had a depressed nasal bridge, short neck, coarse facial features, enlarged tongue, small stubby fingers and widening of wrist (Figure 1 & 2). His fundus appeared normal and no corneal clouding. His abdomen was soft, distended, nontender with right inguinal hernia. His liver was 10cm below the right costal margin in the mid clavicular line, with a firm, sharp margin and smooth surface with span of 11cm. His spleen was not palpable. He had grade 2 soft systolic murmur and Harrison sulcus with no adventious sound. Gait was noted to be clumsy and stiff. Range of motion in all extremities was limited. Intelligence quotient, as determined by "draw man test," was severe (mental retardation) range.

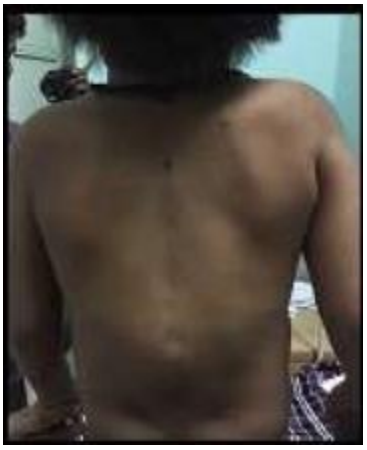

Fig-1: Showing gibbus at lumbosacral region

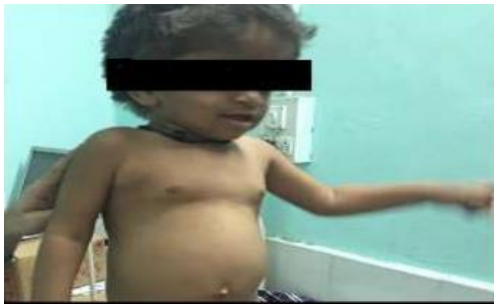

Fig-2: Showing Coarse facial feature

His investigation was revealed normal complete blood count, serum electrolytes, and blood urea and serum creatinine. Anteroposterior and lateral X ray of the skull showed thickening of clavarial bones, enlarged skull, small facial bone and J shaped sella turcica (Figure 3). Anteroposterior and lateral X ray of dorsolumbar spine showed kyphosis and anteroinferior breaking with convex superior and inferior surface resulting into ovoid shaped vertebrae (Figure 4). An anteroposterior X ray chest showed widened inferior ribs with tapered posterior ends (a paddle and/or spatulated appearance (Figure 5). X ray of both hands showed shortened metacarpals with pointed proximal ends and prominent trabecular pattern in forearm bones (Figure 6). X ray pelvis with both hips showed flaring of bilateral illia and acetabular roofs obliquely directed resulting coxa valga deformity (Figure 7). Glycosaminoglycans were present in urine and 24 hours urinary electrophoresis for mucopolysaccharidosis suggestive of type II MPS. Enzyme assay for iduronate sulfatase was not carried out because of non-availability in our lab and economic problem. Our diagnosis of MPS was confirmed from his history, clinical examination, skeletal survey and lab investigations.

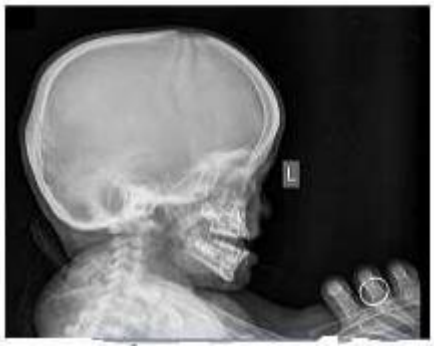

Fig-3: X ray skull showed J shaped sella turcica

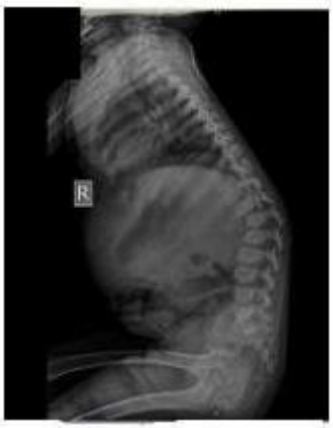

Fig-4: A lateral X ray of dorsolumbar spine shows kyphosis and breaking of vertebrae

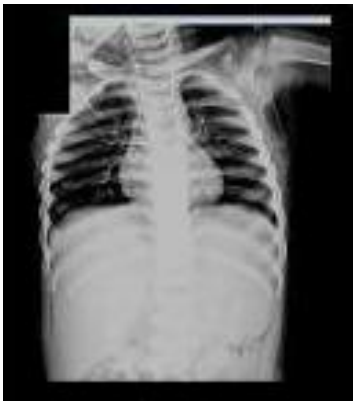

Fig-5: A chest X ray shows spatula shaped ribs

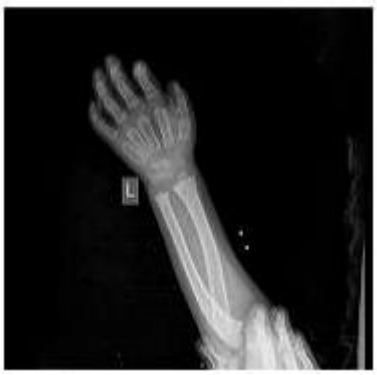

Fig-6: X ray hand show shortened metacarpals

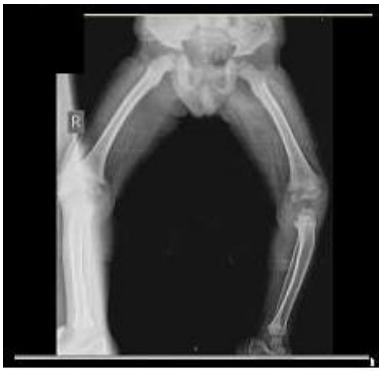

Fig-7: X ray pelvis shows coxa valga deformity

DISCUSSION

Mucopolysaccharidosis was first described by Charles Hunter, a Canadian physician, who in 1917 described a rare disease found in two brothers [1, 2]. Mucopolysaccharidosis is a group inherited diseases characterized by defective lysosomal enzymes responsible for the degradation of mucopolysaccharidosis, which are major components of intracellular connective tissues. This leads to an accumulation of incompletely degraded glycosaminoglycans and excreted in the urine. Deposition of GAGs leads to airway obstruction, cardiomegaly, cardiac valve dysplasia, hepatosplenomegaly, neurological decline and musculoskeletal deformities resulting into individual to have a characteristic appearance and are thus called "gargoyles" [3, 4]. All MPS are autosomal recessive except Hunter syndrome which is X linked recessive, it would not be expected to affect females. Despite this, a few girls have been reported with MPS II [5, 6].

Mucopolysaccharidosis type II or Hunter Syndrome is a rare and is a caused by a deficiency of iduronate -2 sulfatase. Data from the Netherlands and Germany indicate that the incidence is 1.3 per 100,000 male live births [1]. MPS type II is classified into mild (type II, HB) and sever (type II, A) and this classification is based on the length of survival and the presence or absence of neurological 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 mild form the clinical features appear in the second decade of life. In the severe form there is severe mental retardation and loss of skill. 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 [3, 7].

Diagnosis of the disease is usually made by the clinical presentation, skeletal survey and lab investigation. The common clinical presentations are a large head (dolicocephalic), short stature, mental retardation, coarse facial features, a proturbent abdomen, a broad nose with flared nostril, large tongue and musculoskeletal deformities. Other features include upper respiratory infections, valvular heart diseases, enlarged liver and spleen, umbilical as well as inguinal hernia, skin lesions, hypoplastic enamel and carious teeth [1, 3, 4, 6, 7, 8]. Most of the signs were present in our case. 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 (heparin and dermatan sulphates) in urinary electrophoresis is very valuable and cost effective screening test and rule out MPS disorder if the test can be accurately adjusted in laboratory. The presences of excess heparin and dermatan sulphates in the urine is evidence of MPS type I, MPS type II or MPS type VII [9, 10]. In our case urinary electrophoresis reveals excess of glycosaminoglycans. Confirmatory diagnosis is by enzyme assay in leukocytes, fibroblast, or dried blood spot and plasma sample, using substrates specific 12S. Absent or low activity in male is a diagnostic of Hunter syndrome, provided other sulfatase deficiency has been ruled out. Enzyme assay was not done in our case due to lack of facility and financial problem. But careful history, prudent physical examination backed with good radiological investigation and urinary electrophoresis for GAGs help in making a diagnosis.

Enzyme replacement therapy using idursulfase, a recombinant human 12S produced in the human cells has been recently approved. Weekly intravenous infusion is given over 3 hours at a dose 0.5mg per kg, diluted in saline [1, 7]. Bone marrow transplantation and umbilical cord blood transplantation 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 Hunter syndrome.

CONCLUSION

Mucopolysaccharidosis is a multisystem disorder which present with constellation of clinical finding. Thorough clinical examination and radiological evaluation with the help of urinary screening test for GAGs is needed to diagnose the exact type of MPS in a low income country as enzymatic study facilities are costly and not available. Again multidisciplinary approach will go a long way to manage the patient wholistically.

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