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Mucopolysaccharidosis: A Case Report

KEYWORDS: Glycosaminoglycans, Metabolic diseases, Lysosomal storage diseases, Dysostoses, Magnetic resonance imaging.

Dr. Neeru Assudani
Associate Proffesor, Department of Radiodiagnosis and Imaging, Bharati Hospital and Research Center, Pune

Dr. Priscilla Joshi
Professor and Head,Department of Radiodiagnosis and Imaging, Bharati Hospital and Research Center, Pune

Dr. Nagesh Seth
Associate Professor,Department of Radiodiagnosis and Imaging, Bharati Hospital and Research Center, Pune

Dr. Wasim Siddiqui
Resident, Department of Radiodiagnosis and Imaging, Bharati Hospital and Research Center, Pune

ABSTRACT *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). Glycosaminoglycans (formerly called mucopolysaccharides) help build bone, cartilage bone, cartilage, tendons, corneas, skin and connective tissues .These are also found in the fluid that lubricates joints. In MPS absence or malfunctioning of enzymes results in accumulation of GAGs in the cells, blood and connective tissues. This results in permanent, progressive cellular damage which affects the appearance, physical abilities, organ and system functioning and, in most cases, mental development. The typical symptoms include organomegaly, dysostosis multiplex, mental retardation and developmental delay. Definitive diagnosis is usually possible through enzymatic assays of the defective enzyme in cultured fibroblasts or leukocytes Skeletal radiograph and MRI may show specific features in MPS patients, although it is not possible to accurately differentiate between MPS types based on skeletal and neurological characteristics. The evaluation of these imaging findings is useful for suggesting and supporting MPS as a possible diagnosis.*

Introduction:
Mucopolysaccharidosis (MPS) is a group of autosomal recessive metabolic disorder in which the accumulation of undegraded glycosaminoglycans (GAGs) leads to progressive damage of affected tissues.

The radiological findings include abnormal signal intensity in the white matter, dilatation of periventricular spaces, widening of cortical sulci, brain atrophy, enlargement of extraventricular spaces and spinal cord compression. With reference to the skeletal system, most important radiological findings include multiplex dysostosis, which is represented by several bone malformations found in the skull, hands, legs, arms and column. The abnormal storage of GAGs leads to liver and spleen enlargement; it also damages cartilage layers and synovial recesses in the joints.

Case Report:
A three years-old boy presented to the Pediatric Out-Patients Department with delayed development and inability to walk since he was two. There was no history of constipation, diarrhea, vomiting, bleeding, jaundice, seizure, weight loss or loss of appetite or of unconsciousness. His bladder habit was normal.

On examination his head was acrocephalic in shape. He had a depressed nasal bridge, a short neck and coarse facial features.

Anteroposterior and lateral radiographs of the skull showed an enlarged and J-shaped sella turcica (Figure 1). The bones of the skull and sutures appeared normal for his age. Anteroposterior and lateral radiographs of the dorso-lumbar spine showed anterior beaking (Figure 2). Vertebral bodies appeared ovoid due to convexity of the superior and inferior surfaces. There was acute kyphosis at C4- 6 level with bony spinal canal stenosis at the same level. Radiographs of both hands showed that the phalanges and metacarpals were widened with proximal tapering (Figure 3). The remaining bones and joints under view appeared normal. An anteroposterior radiograph of the chest showed that the ribs were wide with tapered posterior ends (a paddle and/or spatulated appearance).

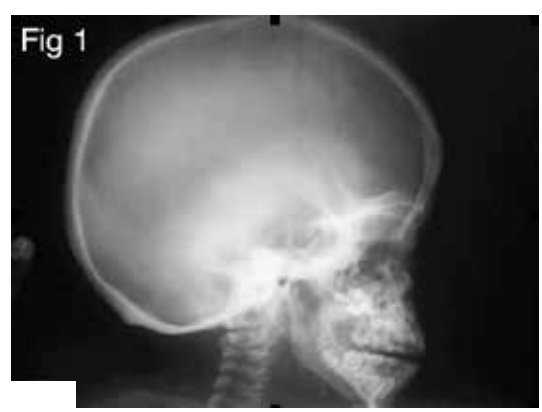

Figure (1): Lateral radiograph of the skull showing J shaped sella.

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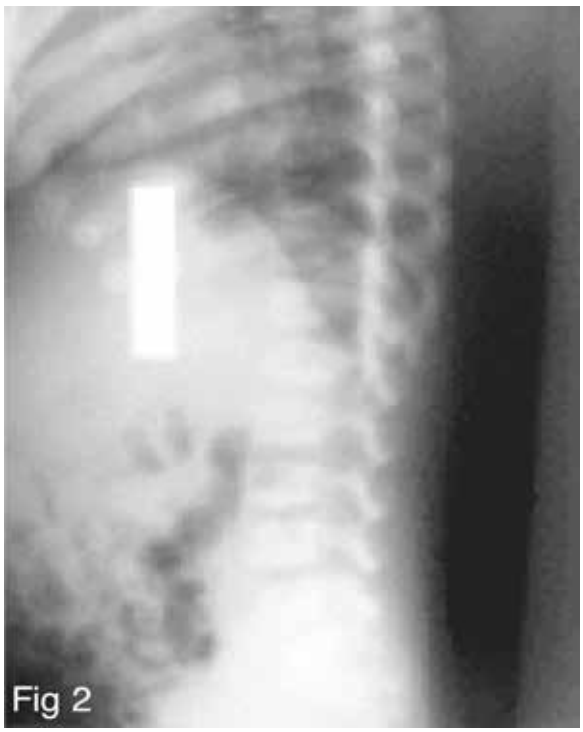

Figure (2): Lateral radiograph of dorso-lumbar spine showing flattened vertebrae with anterior beaking.

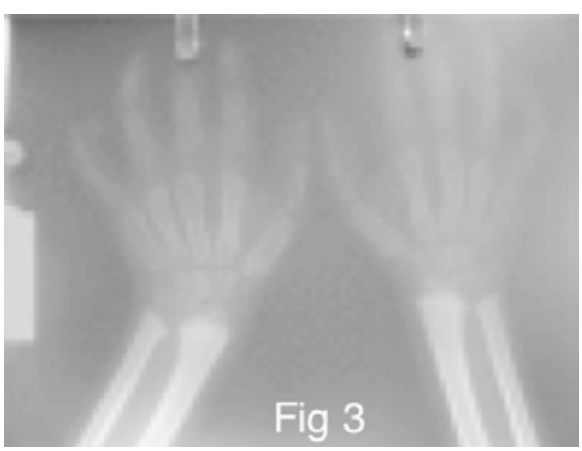

Figure (3): X-ray of the hands showing phalanges and metacarpals are widened with proximal tapering of metacarpals.

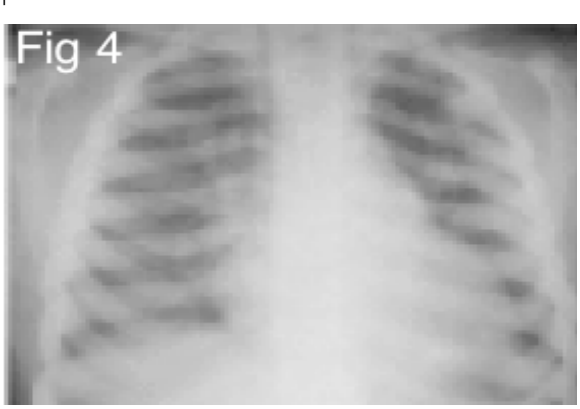

Figure (4): Anteroposterior chest X-ray showing paddle and/or spatulated ribs.

MRI Brain showed no significant abnormality. Cervical spine showed acute kyphosis at C4-C6 level attenuating the anterior thecal space and indenting the spinal cord. Spinal cord was seen draped along the kyphotic curve. Cord was thinned and exhibited abnormal signal intensity representing cord ischemia.

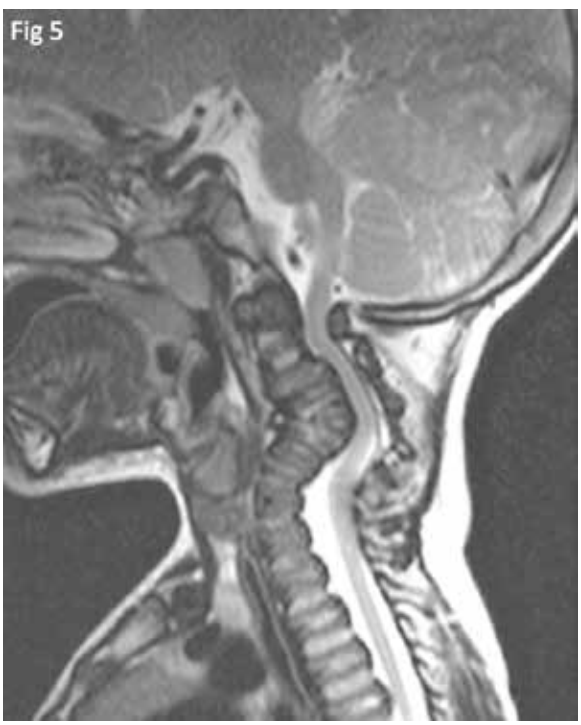

Figure (5): MR T2W image of the cervical spine showing acute kyphosis at C4-C6 level attenuating the anterior thecal space and indenting the spinal cord. Spinal cord is draped along the kyphotic curve. Cord is thinned and showing abnormal signal intensity representing cord ischemia.

On radiological investigation diagnosis of MPS was made. Unfortunately we could not perform any measurement of GAG, keratan and heparan sulphates, in his urine because of the lack of test kits. Enzyme assay for iduronate sulfatase is not carried out in our laboratory therefore it was not performed either. Our diagnosis of MPS was confirmed from his history, clinical examination and skeletal survey.

Discussion:

Mucopolysaccharidosis was first described by Charles Hunter, a Canadian physician, who in 1917 described a rare disease found in two brothers [1]. Mucopolysaccharidosis is an autosomal recessive diseases characterized by defective lysosomal enzymes responsible for the degradation of mucopolysaccharides, which are major components of intercellular connective tissue. This leads to an accumulation of incompletely degraded mucopolysaccharides in the lysosomes which affect various body systems through enzymatic activity [2]. Seven distinct clinical types of MPS have been identified and described in the literature, caused by 11 different enzymatic deficiencies. Even if each type of MPS presents a rare incidence, the overall incidence is not negligible (1 in 25,000 live births). A com-

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bination of clinical picture and analysis of urinary GAGs is usually performed to achieve the diagnosis of MPS

Radiographic features of skeletal changes of MPS have been comprehensively described by Langer and Carry [3]. The characteristic radiographic features include an abnormal "J-shaped" conformation of the sella turcica, seen on the lateral view of the cranium, paddle-shaped ribs, thick clavicles, wedge-shaped vertebral bodies with anterior beaking, odontoidhypoplasia, platyspondyly, lumbar gibbus, dorsal kyphosis, wide disc spaces and spinal canal stenosis. In the pelvis, characteristic features include long pelvis with narrowing at the acetabulae, widening of pubic symphysis and flaring of the ilia. In patients with MPS, the femoral head epiphyses appear normal in early life, however, dysplastic features develop in later life and include disappearance of the femoral head, widening of the femoral neck and a coxa valga deformity. Characteristic features also develop in the hands and include shortening of the metacarpals, small carpal bones (often with some absent) and the inclination of the distal portions of the radius and ulna toward each other(Madelung's deformity).

At the craniovertebral junction level, the most important abnormalities are odontoid process dysplasia-hypoplasia, atlantoaxial instability or subluxation, periodontoid tissue and ligaments thickening, spinal stenosis. These features represent a critical aspect in MPS (particularly in MPS IV), because if the spinal cord is compressed, cervical myelopathy may result. MRI is more appropriate for the evaluation of spinal cord alterations.

Other features that can be found are the notching of the proximal part of the humerus, the long and narrow aspect of the femoral neck, and the hypoplasia of the lateral tibial hemiplate, resulting in genu valgum.

The otorhinolaryngological manifestations are chronic otitis media and conductive hearing loss [4]. A thickened, retracted tympanic membrane and an increased attenuation of the tympanic cavity and mastoid cells can be observed on multidetector computed tomography (MDCT).

Neurological symptoms can be present at both early and late course of disease due to abnormal accumulation of mucopolysaccharides within perivascular spaces and neuroaxonal units with an adversely affected myelin turnover [6]. In MPS patients with myelopathy, the signs and symptoms do not always correlate with the degree of cord compression. Instead, in most circumstances, the neurological deficits manifesting clinically are usually less severe than suggested by MRI

On the basis of MRI findings a large spectrum of severity can be recognized, from negligible to severe. Neuroradiological features are abnormal signal intensity in the white matter and in the basal ganglia, dilatation of periventricular spaces, widening of cortical sulci, brain atrophy and enlargement of extra-ventricular spaces, and spinal cord compression. Few cases of closed cephalocele have been reported in the literature. Honeycomb-like" appearance is a typical imaging feature seen in the brain of in the basal ganglia and thalami ; this imaging finding has been observed in patients with MPS I, II and IIIB [7].

Other neurological features are Ventricular enlargement, with or without involvement of the subarachnoid spaces, atrophy of brain. Compression of the spinal cord most frequently occurs at the atlanto-axial (C1-C2) joint as seen in our case. Many of these patients suffer from several craniocervical junction abnormalities due to structural defects involving the spine. The most important one is atlanto-axial subluxation; Compressive cervical myelopathy is a critical problem since the involvement of the bulbar-spine junction may lead to central respiratory failure.

Finally, another imaging features reported in literature is the closed encephalocele; regarding this point, the presence of parenchymal/meningeal herniation at the level of the anterior or middle cranial fossa has been described as a characteristic neuro-radiological feature of patients affected by MPS II. CT and MRI reveal a variable-sized pouch filled with brain parenchyma and cerebrospinal fluid, delimited by a bone wall and usually located in the anterior cranial fossa at the level of the lamina cribrosa as a weak area of the skull. The radiologist should look out for the presence of a closed cephalocele because it may interfere with rhino-surgery and cause epilepsy [8]. With the recent advances in therapeutic interventions and prolonged life expectancy in MPS patients, the characteristic radiological features are expected to be more frequently encountered by radiologists during daily practice. Knowledge of radiological and neuro-radiological appearances of MPS is essential for radiologists. The evaluation of these imaging findings is useful for suggesting and supporting MPS as a possible diagnosis, usually obtained by laboratory analysis, for monitoring the chronic and progressive course of the disease, for surgical and medical planning and for assessing the impact of therapy.

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