

Images: Hurler's disease

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Hurler's disease is a severe form of mucopolysaccharidosis (MPS). The MPS constitute a group of hereditary disorders, having in common lysosomal accumulation of undegraded glucosaminoglycan (GAG) secondary to deficiencies in specific enzymes. All but one of the MPS is marked by the urinary excretion of GAG products—chondroitin sulfate, keratan sulfate, dermatan sulfate, and heparan sulfate.^[1,2] Hurler first described this disease, MPS 1H, in 1919, just two years after the Hunter syndrome (MPS II) was described.^[3] The associated skeletal abnormalities had been properly termed as dysostosis multiplex by Hurler in 1931.^[4] It has an autosomal recessive inheritance. The defect is due to the absence of lysosomal hydrolase α -L-iduronidase (IDUA). A specific diagnosis of any of the MPS is done on the basis of the distinctive clinical and radiological features.

Case Report

A 9-year-old girl presented with diminution of vision in both eyes and other systemic abnormalities.

On clinical examination, she was 105 cm in height with a moderate build. Her skull was large and she had a short neck. She had coarse facies [Figure 1]. Growth of hair on the scalp and eyebrows was abundant. The nose was saddle-shaped, with flared nostrils; she had mucoid rhinitis. The lips were thick. Examination of the oral cavity revealed a swollen alveolar ridge and gums with misaligned teeth. The tongue was large and the palate was high arched. On ocular examination, she had cloudy, opaque corneas. The auditory functions were normal. The abdomen was protuberant, with an umbilical hernia. The liver was 4 cm enlarged but the spleen was not palpable. Both her upper limbs were short. The scapulae were elevated and widely placed. The hands were broad. The thick fingers were held in semiflexion during rest. The lower extremities were also short. The second toes were overlapped by the third toes and she walked on her toes due to ankle stiffness. The movements of the elbow, hip, and knee joints were restricted. The cardiological examination revealed cardiomegaly and the presence of murmurs due to thickened mitral and tricuspid valves. The amount of mucopolysaccharides in a 24-h urine sample was assessed and showed 21 mg urinary aminoglycan (UA)/day (normal: 5–10 mg UA/day); 47%



Figure 1: Clinical photograph showed the coarse facies and clouding of the corneas (arrows).

was heparin sulfate, 32% was chondroitin sulfate, 10% was keratan sulfate, and the rest was dermatan sulfate.

There was premature union of the cranial sutures. The calvarium was thickened. The sella turcica was wide, deep, and J-shaped [Figure 2].

The cardio–thoracic ratio was increased. The ribs were narrowed at the vertebral ends and were widened at their sternal ends (oar-shaped). The clavicles were short and thickened medially. The shoulder joints showed shallow glenoid cavities, with irregular upper metaphyses. An area of constriction below the neck of the humerus was also seen [Figure 3].

Anterosuperior hypoplasia of the lumbar vertebral bodies was seen with prominent inferior beaks [Figure 4].

The hip joints showed shallow acetabulums. The femoral heads were small and there was coxa valga. The acetabular and supraacetabular portions of the iliac bones were hypoplastic, resulting in an apparent flaring of the iliac

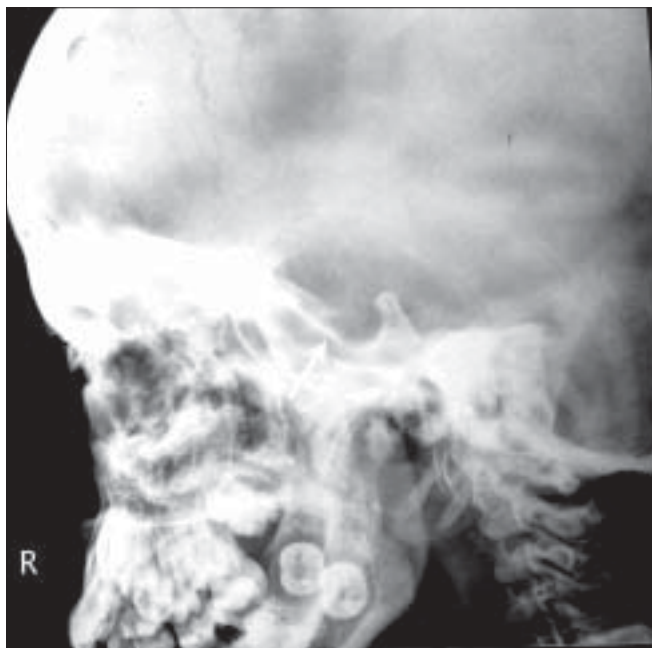


Figure 2: Lateral radiograph of the skull (magnified) showing 'J'-shaped sella turcica (arrow)



Figure 4: Lateral radiograph of the dorsolumbar spine showing pronounced inferior beaks in the lumbar vertebral bodies (arrows)



Figure 3: Radiograph of the chest and upper limbs showing increase in the cardio-thoracic ratio, oar-shaped ribs (white arrows), short and deformed clavicles (black arrows), shallow glenoid cavities, and irregular upper humeral metaphyses, bilaterally

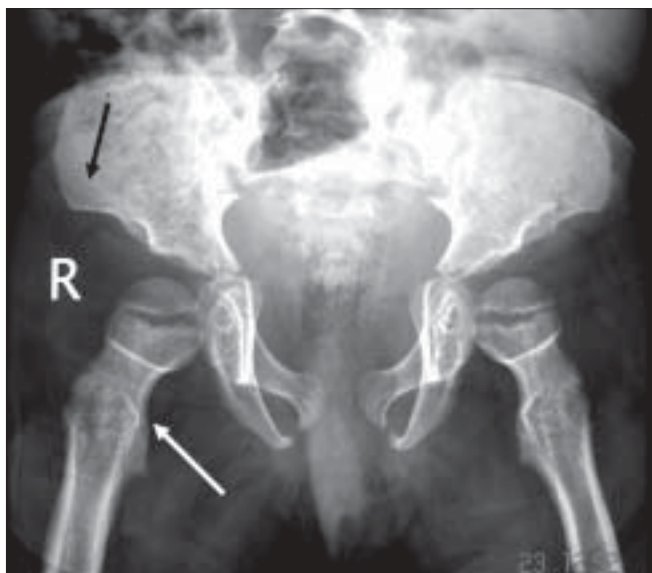


Figure 5: Radiograph of the pelvis (AP View) showing shallow acetabulums, coxa valga (white arrows), and flaring of the iliac wings (black arrows)

wings [Figure 5].

The distal ends of the radius and ulna were tilted toward each other. The appearance of only two carpal epiphyses suggested a delay in the development of the carpal bones. The metacarpals and the metatarsals were short, thickened, and stubby with undertubulation and demineralization. The metacarpals were characteristically tapered proximally. The proximal and middle phalanges of both the hands and feet were short and were wider proximally than distally, resulting in a bullet-like configuration. The distal phalanges were hypoplastic. There was overlapping of the third toe on the second toe. Hallux valgus was present [Figures 6 and 7].

Discussion

Almost all the cells of the body are involved in MPS. These include the chondrocytes and osteocytes as well as the cells within tendons, fascia, blood vessel walls, cardiac valves, meninges, muscles, and cornea. Similar deposits are found in the Kupffer cells of the liver, reticular cells of the spleen and lymph nodes, and the epithelial cells in the kidney and several endocrine organs.^[4]

The main radiographic features of dysostosis multiplex



Figure 6: Radiograph of both hands (AP view) showing short and stubby metacarpals with proximal tapering (black arrows) and bullet-shaped phalanges (white arrows).



Figure 7: Radiograph of both feet (AP view) showing short metatarsals (black arrows), bullet-shaped phalanges (white arrows), overlapping of the 3rd toe over the 2nd, and hallux valgus

are shown in Figures 2–7. In the long bones, the diaphyses are enlarged, the metaphyses have irregular appearances, and the epiphyseal centers are not well developed.

Characteristically, the metaphyseal changes are slight.^[1] In the shaft of the long bones, the classical changes are due to disturbed modeling which, in the initial stages, produces increased girth of the shaft, with thick cortical walls and narrow medullary cavities. Later, the cavities of the marrow dilate and the cortical walls become thin. These changes are more marked in the upper limbs. The infiltration of meninges with GAG products results in thickening, which can give rise to subarachnoid cysts and may lead to the development of a deformed, J-shaped sella turcica.^[4]

The main pathological consequences of Hurler's disease are due to the accumulation of mucopolysaccharides in parenchymal and mesenchymal tissues and the storage of lipids within neuronal tissues.

The disease is progressive. Patients with Hurler's syndrome appear normal at birth. They have accelerated growth during the first year of life, which is followed by slowing of both mental and physical growth. The developmental delay appears between 12 and 28 months.^[1,2] The radiological images are very characteristics of Hurler's disease.

References

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