Type IV Mucopolysaccharidosis (Morquio Syndrome) – a rarity in Ophthalmology

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Abstract

A 9 years male child who was born of consanguineous marriage was brought with a complaint of progressive painless diminution of vision in both eyes. Detailed ocular examination only revealed bilateral diffuse corneal stromal haze. Systemic evaluation showed coarse facial features, prominent chest and knock knees. Multiple digital X-rays revealed features of mucopolysaccharidosis. Genetic analysis with leucocyte lysosomal enzyme study showed reduced activity of N-acetylgalactosamine-6-sulfate sulfatase suggestive of a rare mucopolysaccharidosis, type IV A (Morquio syndrome). Parental counseling was done regarding the disease inheritance, need for follow up and long term prognosis.

Keywords: Morquio syndrome, mucopolysaccharidosis, corneal clouding

Introduction

Mucopolysaccharidosis (MPS) are lysosomal storage disorders caused by deficiency of enzymes required for the breakdown of glycosaminoglycans (GAGs), previously known as mucopolysaccharides. Fragments of partially degraded GAGs accumulate in the lysosomes, resulting in cellular dysfunction and clinical abnormalities.

MPS are rare, with an estimated incidence of approximately 1 in 20,000 live births.[1] MPS type IV (Morquio syndrome) is estimated to occur in 1 in 2,00,000 live births.[2] These are characterized by multiple skeletal deformities. Extra skeletal manifestations include neurosensory dea¬fness, aortic regurgitation, hernia, hepa¬tosplenomegaly, thinness of tooth enamel and caries. Medullary compression induced neuropathy may shorten the life to three to four decades. Intelligence remains normal.[3]

Type IV MPS (Morquio syndrome) is an autosomal recessive disorder characterized by the deficiency of either β-galactosidase or Galactosamine-6-sulphatase and consequent deposition of keratan sulfate and chondroitin sulfate in various tissues.

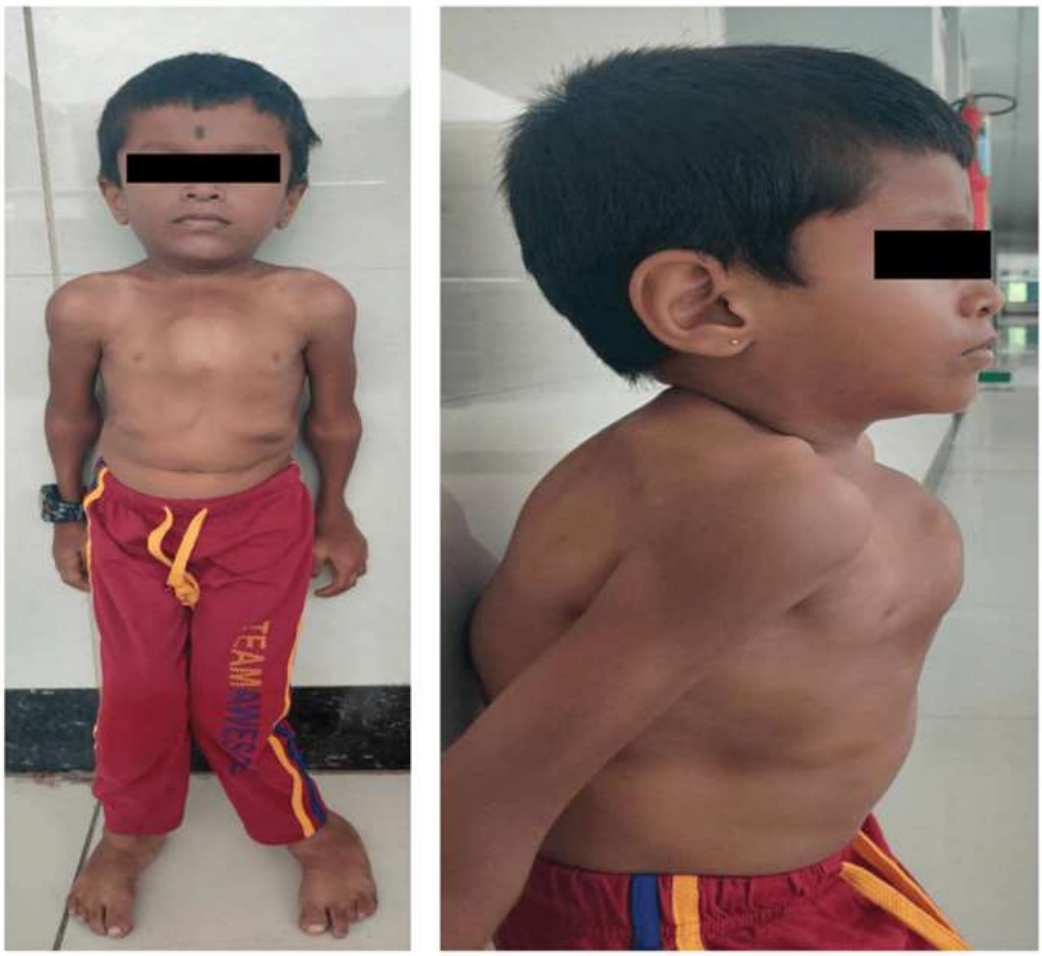
Ophthalmologically, such patients present with corneal clouding due to small dust like opacities dispersed in the stroma having little effect on vision, with most patients maintaining a visual acuity of 6/12 or better.[4] We report here a rare case of type IV MPS presenting to Ophthalmology OPD.

Case Report

A 9 years male child, born of consanguineous marriage, was brought with a complaint of painless progressive diminution of vision in both eyes. He had a history of diagnosis of skeletal scurvy and kyphosis at the age of 6 months. His parents had 4 children, 2 sons and 2 daughters, among whom the 1st male child had died at the age of 5 years.

The child had coarse facial features with a prominent chest and knock knees. (Figure 1)

Figure 1: Body profile images showing prominent chest and knock knees



His best corrected visual acuity was 6/12 in right eye with +5.0 Dsph/+1.0 Dcyl at 90^{o} and 6/9 in left eye with +4.50 Dsph/+1.0 Dcyl at 100^{o}. Detailed slit lamp examination revealed bilateral diffuse corneal stromal haze. (Figures 2 and 3)

Figure 2: Diffuse illumination of right eye showing corneal clouding

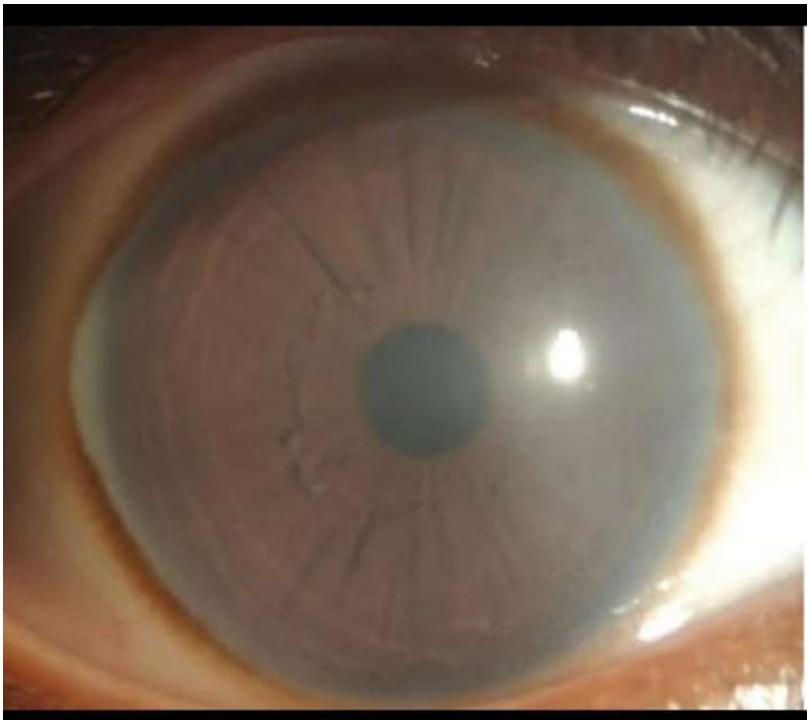
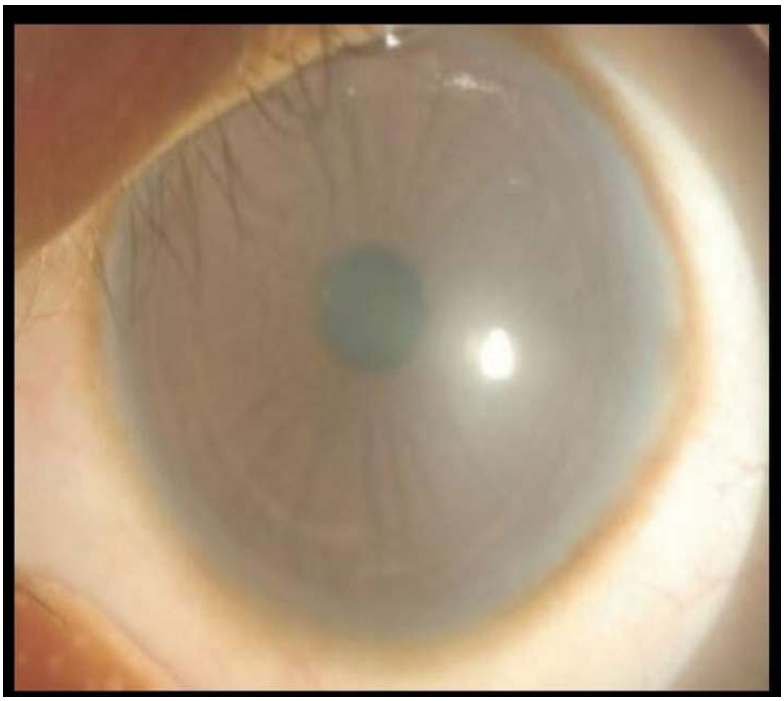
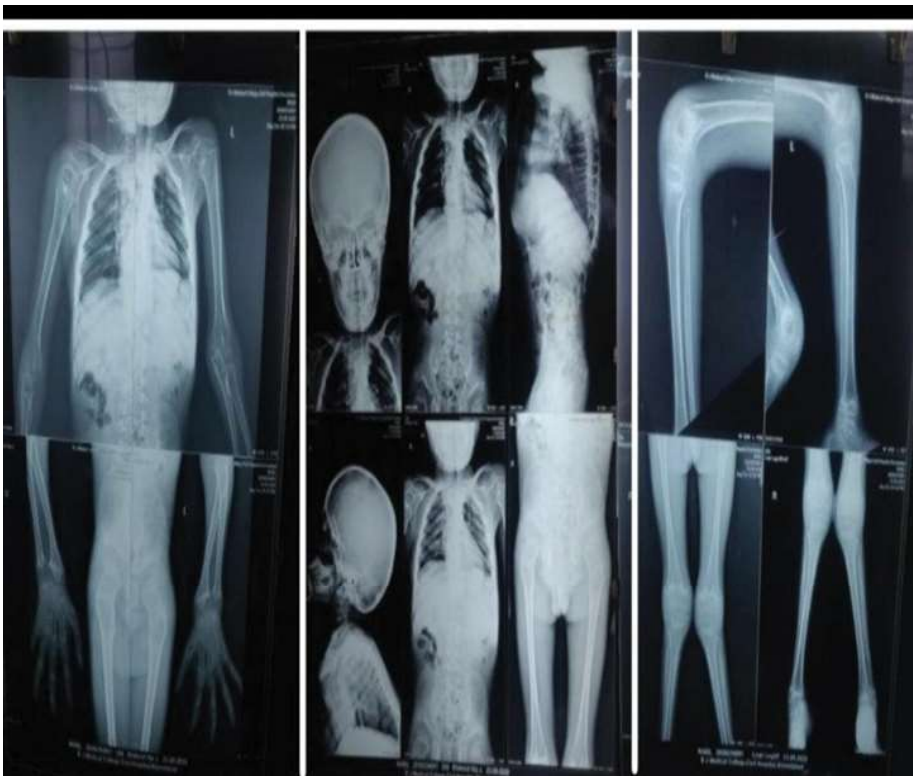


Figure 3: Diffuse illumination of left eye showing corneal clouding



Perkin's applanation tonometry revealed an IOP of 20 mm Hg in right eye and 18 mm Hg in left eye. Ultrasonography and ultrabiomicroscopy revealed no abnormal findings. Fundoscopy and gonioscopy were not possible due to the corneal clouding. Pachymetry was 0.65 mm in both eyes. Digital whole body X-Rays showed multiple skeletal abnormalities in the form of J shaped sella, depressed nasal bridge, scoliosis in dorsal spine, kyphosis in lumbar spine, spatulate configuration of ribs, short thick proximal bones with Chevron deformity of distal growth plates, reverse madelung deformity of ulna, bowing of forearm bones, poor ossification of carpal bones, short thick phalanges, tapered proximal ends of all metacarpal bones, coxa valga, genu valgum, fragmented margins of proximal femoral epiphyses, hypoplastic lateral aspect of proximal tibial plateau and metaphyseal widening involving the femur and tibia. (Figure 4)

Figure 4: Digital X-Rays of various body parts showing features of Morquio syndrome



Pediatric evaluation did not reveal any further abnormalities. A Lysosomal Enzyme study from Leucocytes was performed which showed significantly reduced activity of N-acetylgalactosamine-6-sulfate sulfatase (0.5 nmol/17 hrs/mg protein, the normal value being 3.9 - 42.6 nmol/17 hrs/mg protein) with normal activity of Beta galactosidase enzyme confirming Morquio-A disease (MPS-IVA).
The parents were counseled about the prognosis, inheritance pattern and need for regular follow up.

Discussion:

MPS are a group of rare autosomal recessive lysosomal storage diseases caused by genetic deficiency of enzymes involved in degradation of GAGs, which function in cell adhesion and cellular signaling.[5] Storage of GAGs can lead to secondary effects in cells such as autophagy, apoptosis and mitochondrial dysfunction.[5] MPS are currently classified into six well defined syndromes based on their genetic, clinical and biochemical characteristics.[6] These account for less than 0.1% of all genetic diseases.[7] In Asia, most patients suffer from MPS type II. In a Chinese study, 506 patients with MPS were identified; in whom type II accounted for nearly

50% of all cases, type I for 13.7%, type III for 7.9%, type IV for 24%, and type VI for 2.6% cases.[8]
MPS IV is further subdivided into types A and B depending on deficiency in N-acetylgalactosamine-6- sulfate sulfatase (GALNS) or β-galactosidase (GLB1). Deficiency of GALNS impairs the degradation of chondroitin-6-sulfate and keratan sulfate (KS), which contributes to severe clinical symptoms while GLB1 deficiency leads to a moderate phenotype with only KS accumulation. Unlike the other types, MPS IV involves mild cognitive impairment but more obvious skeletal dysplasia, usually starting at the age of 1-3 years.[9] Other features include corneal clouding, hearing loss, respiratory obstruction and sleep apnea.[9] In our patient, multiple skeletal abnormalities were present along with corneal clouding.
Patients of MPS have a shorter life expectancy with a poorer quality. The diagnosis is usually delayed till irreversible clinical features manifest.[10] Radiographic findings are frequently used but a definitive diagnosis relies on molecular tests such as identification of the type of GAG. An enzyme assay and genetic testing of prenatal samples can also be done.
Management focuses on slowing the disease progression and improving the quality of life of the patient through palliative treatment, surgery and disease-specific treatments like hematopoietic stem cell transplantation and enzyme replacement therapy (ERT). Novel treatments include intrathecal ERT, gene therapy and combined therapy. Genetic counseling of parents is of importance considering the recessive inheritance pattern.

Conclusion:

Although MPS are rare inherited multisystem disorders and ocular involvement is not significant, their suspicion is essential in presence of other gross skeletal deformities so that appropriate and timely referral and investigations can be done. High mortality and expensive treatment make these a major medical and social problem. Genetic counseling plays a major role in preventing further inheritance. Visual and systemic rehabilitation may improve the quality of life of the affected.

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