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Case Report

Typical presentation of mucopolysaccharidosis type IVA: a case report

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ABSTRACT

Mucopolysaccharidosis (MPS) IVA, or Morquio syndrome, is a rare lysosomal storage disorder characterized by skeletal dysplasia. It is caused due to deficiency in the enzyme N-acetylgalactosamine-6-sulfatase (GALNS), which results from an autosomal recessive mutation in the GALNS gene. The frequency of this mutation is equivalent in men and women. Here in, we present the case of Morquio syndrome, in a male child of twin gestation with poor antenatal and natal history. The peculiar presentations are those of skeletal deformities, coarse facial features, recurrent respiratory tract infections, and a history of NICU admission for meconium aspiration syndrome. This case is unique because, despite a negative family and prenatal history, and one of the twins being unaffected which adds to its appeal. Later, on biochemical and radiological investigations, he was diagnosed with mucopolysaccharidoses IVA and ultimately managed him supportively.

Keywords: Mucopolysaccharidosis, Morquio syndrome, Skeletal dysplasia

INTRODUCTION

Mucopolysaccharidosis are a group of genetic disorders caused by deficiency of enzymes involved in the metabolism and breakdown of glycosaminoglycans (GAGs) chondroitin sulfate, dermatan sulfate, heparan sulfate, keratin sulfate, resulting in their accumulation in various tissues of the body causing peculiar symptoms. There are eleven different types of enzyme deficiencies, which are associated with seven different types of MPS (MPSI, II, III, IV, VI, VII, IX).[1] Type IV MPS, also known as Morquio syndrome is a rare lysosomal storage disorder which consists of MPS IV A, which results from mutations in galactose-6-sulfatase genes, and MPS IV B, which results from beta-galactosidase deficiency.[2,3] This enzyme defect is acquired in an autosomal recessive mannerdue to the mutation in GALNS gene. According to researches, the incidence of MPS ranges from 0.144 to 0.22 per 100,000 births.[4] MPS consists of a wide constellation of symptoms and a significant overlap between the various types. The type IV MPS involves organs systems like bone, joint, heart, lung, gastrointestinal system and central nervous system.[5]

CASE REPORT

A 3-year-old male child, fourth in birth order, born in twin gestation, born out of 3rd degree consanguineous marriage, was brought by mother with the chief complaints of- not gaining height since one year, abnormality in chest shape observed particularly since 1 year. There was a history of snoring present in the baby since one year. There was a past history of recurrent upper respiratory tract infections since the age of 6 months, occurring at a frequency of almost 2 episodes per month. There was no significant antenatal and natal history. However, post-natal history revealed NICU admission for 15 days in view of meconium aspiration syndrome with respiratory distress with persistent

pulmonary hypertension (PPHN), treated with surfactant administration and sildenafil.

Table 1: The anthropometry of the child with Morquio syndrome.

Anthropometry	Measurement	Percentile according to WHO growth charts
Weight (kg)	13.1	15th to 50th percentile
Height (cm)	83	<3rd percentile
Mid upper arm circumference (cm)	15	50th to 75th percentile
Head circumference (cm)	51	85th to 97th percentile
Weight for height	-	87th to 99th percentile
Upper segment to lower segment ratio	1.07:1	disproportionate

The other twin was completely normal and asymptomatic and there was no significant family history. Head to toe examination revealed a large head, hypertelorism, short nasal bridge, wide nose, short neck, pectus carinatum, wrist widening, short stubby fingers, and genu valgum.

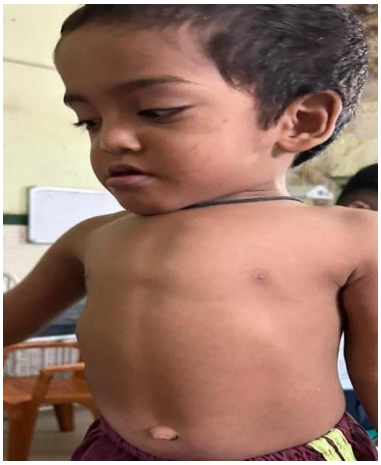

Figure 1: Showing large head, coarse facial features and abnormal shape of the chest of the affected child.

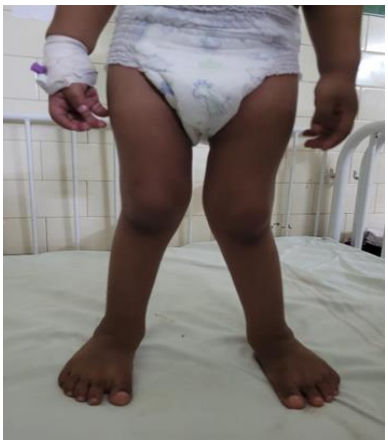

Figure 2: Showing genu valgum in the limbs of the child.

A 3-year-old male child, fourth in birth order, born in twin gestation, born out of 3rd degree consanguineous marriage, was brought by mother with the chief complaints of- not gaining height since one year, abnormality in chest shape observed particularly since 1 year. There was a history of snoring present in the baby since one year. There was a past history of recurrent upper respiratory tract infections since the age of 6 months, occurring at a frequency of almost 2 episodes per month. There was no significant antenatal and natal history. However, post-natal history revealed NICU admission for 15 days in view of meconium aspiration syndrome with respiratory distress with persistent pulmonary hypertension (PPHN), treated with surfactant administration and sildenafil.

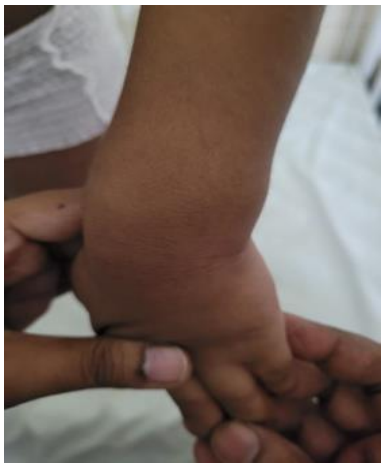

Figure 3: Showing widened distal end of forearm.

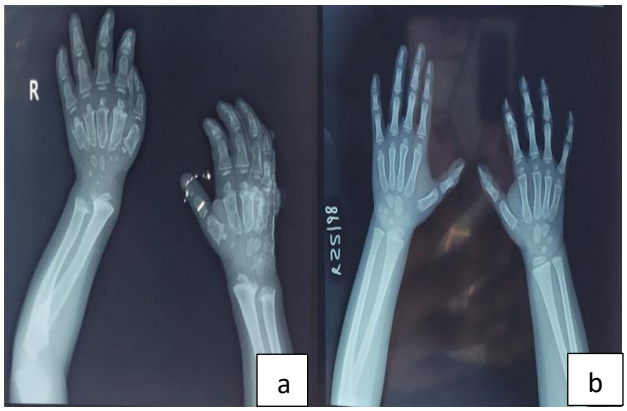

Figure 4: a) X ray of forearm and wrist with phalanges shows bullet shaped phalanges, broad metaphysis & proximal narrowing of the metaphysis, b) X-ray forearm and wrist with phalanges of the normal twin which shows no abnormalities.

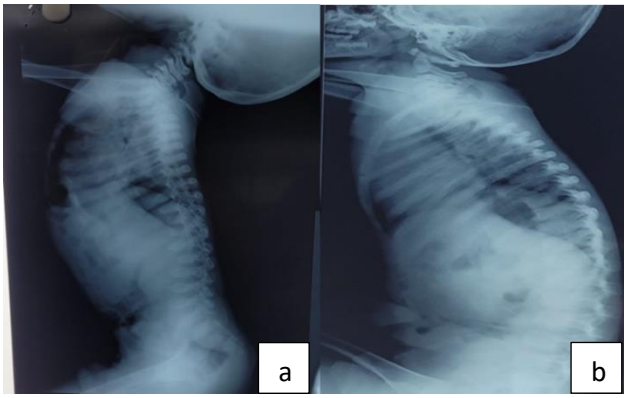

Figure 5: a) X-ray spine revealed anterior beaking of vertebral bodies, b) X-ray spine of the unaffected twin reveals a normal finding.

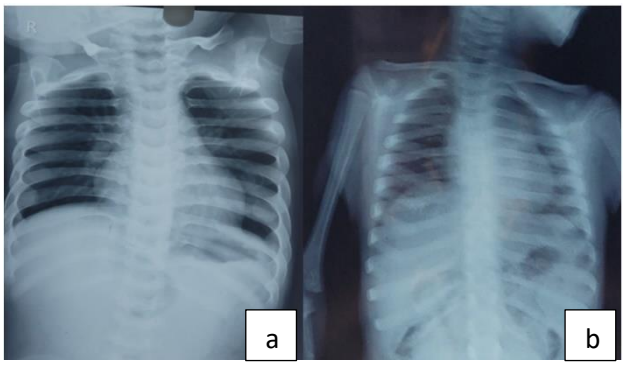

Figure 6: a) X-ray chest showed broad oar shaped ribs, b) X-ray chest of the unaffected twin showing normal findings.

The other twin was completely normal and asymptomatic and there was no significant family history. Head to toe examination revealed a large head, hypertelorism, short nasal bridge, wide nose, short neck, pectus carinatum, wrist widening, short stubby fingers, and genu valgum.

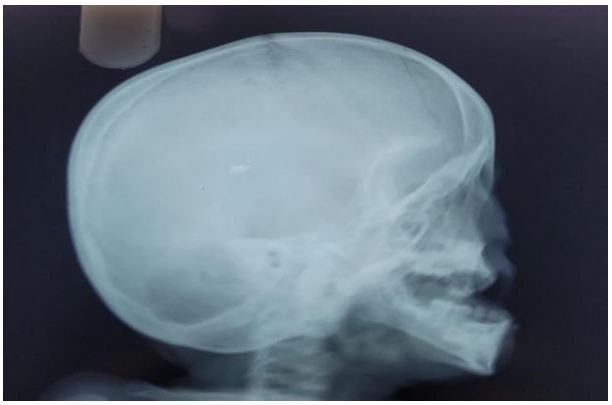

Figure 7: Thickened calvarium: A large skull with thickened calvarium.

All the developmental milestones are achieved normally according to the corresponding age (developmental quotient=100%). Differential diagnosis of the above condition includes- Rickets, Mucopolysaccharidosis, Mucolipidosis, Achondroplasia. Investigations reveal mild anaemia, normal LFT, RFT. Serum levels of vitamin D, ALP are normal, which rules out rickets. Bilateral fundus examination, 2D Echo, USG abdomen are normal. The skeletal findings of dyostosis multiplex were noted on multiple radiographs. The above findings point towards mucopolysacharidosis, which was confirmed by the enzyme assay of α-L-iduronidase, i.e.,0.84 nmol/hr/ml (normal range was 2.4-12 nmol/hr/ml).

DISCUSSION

MPS are a rare group of disorders which carry a significant morbidity. Consanguineous marriage is thought to be one of the significant risk factor in acquiring this genetic condition, although there can be many. The symptoms of type IV MPS result due to accumulation of keratan sulphate and chondroitin 6 sulphate.[6] The diagnosis of MPS can be made through symptomatology and clinical findings, however, reduced serum enzyme levels and urinary excretion of GAGs can be used as confirmatory tests. The detection of mutations in the GALNS or GLB1 genes helps to distinguish between a type A or type B Morquio syndrome. These children appear normal at birth. It is only by the age of 3-4 years that the symptoms come to notice, the major ones being that of skeletal abnormalities in type IVMPS.A significant morbidity of this disease can be that of pneumonia and nerve compressions as shown in a study conducted in 2021.[7,8] A multidisciplinary attention to Respiratory and Cardiovascular complications, Carpal Tunnel Syndrome, Spinal Cord Compression, Hearing Loss, Hydrocephalus and other problems can greatly improve the quality of life for patients and their families.

CONCLUSION

Enzyme deficiency disorders are difficult to diagnose at the onset due to wide range of overlapping symptoms they present with. Hence, learning and knowing the peculiar presentations and possible associations helps us to recognize the syndrome at an early onset, thereby reducing the mortality and morbidity for the child and providing the child with a better life by individualized treatment approach. The scope of this disease is far beyond just the symptomatic therapy and ranges from enzyme replacement therapy to hematopoietic stem cell transplant. Furthermore, recognizing the disease in the family helps to prevent further gene load of the disease by genetic counselling and genetic testing. The scope of the disease is not just limited to the patient care and extends to the field of medical research. Few researchers found that the ability of the mutations in MPS genes in cultured cells produced symptoms and cell hybridization techniques would reveal such defects at the earliest. Decoding the enzyme deficiency disease lays foundation to develop tools to detect and screen for the disease, even if the mutation load is less severe and symptoms are not classic.

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