

Atypical Presentation of Mucopolysaccharidosis. Morquio's Syndrome (Type IV-B): A Morbid Entity

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Abstract

Mucopolysaccharidosis (MPS) are a group of metabolic disorders of the lysosomal storage disease family caused by the absence or malfunctioning of lysosomal enzymes, which blocks degradation of mucopolysaccharides and leads to abnormal accumulation of heparan sulfate, dermatan sulfate, and keratan sulfate. Morquio's syndrome is a rare autosomal-recessive mucopolysaccharidosis. This syndrome is characterized by a reduced activity of N-acetylgalactosamine-6-sulfate-sulfatase (type A), or beta-galactosidase (type B). This deficiency leads to a lysosomal storage disease with accumulation of keratan sulfate and chondroitin-6-sulfate in connective tissue, skeletal system and teeth. The general phenotype includes coarse facies, corneal clouding, hepatosplenomegaly, joint stiffness, hernias, dysostosis multiplex, lower limb alignment problems, mucopolysaccharides excretion in the urine and metachromatic staining in peripheral leukocytes and bone marrow. Consequently, aortic valvular disease, gastrointestinal disease and dental abnormalities occur. Clinical manifestations of mucopolysaccharidosis depend on the type of disease. We report a case of morquio's syndrome in a child, solely diagnosed on the basis of history and physical examination of the case reported. The clinical features and complications of the case and review of the literature are discussed.

Keywords: Mucopolysaccharidosis, connective tissue, morquio's syndrome, lysosomal storage disease. (ASH & KMDC 19(2):109;2014).

Introduction

Mucopolysaccharidosis (MPS) are hereditary group of broad spectrum metabolic disorders due to deficiency or mutations of genes coding for lysosomal enzymes required to degrade a class of glycosaminoglycans (acid mucopolysaccharides). Glycosaminoglycans (GAG's) are a long-chain complex carbohydrate composed of uronic acids, amino sugars, and neutral sugars. The major GAGs are chondroitin-4-sulfate, chondroitin-6-sulfate, heparan sulfate, dermatan sulfate, keratan sulfate, and hyaluronan¹. GAG's help to build bone, cartilage,

tendons, cornea, skin and connective tissue. People with MPS either do not produce enough of one of the 11 enzymes required to break down these sugar chains into proteins and simpler molecules, or they produce enzymes that do not work properly². Over time, these GAG's collect 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.

On the basis of clinical and biochemical studies, these disorders have been designated as MPS I through MPS VII. They are classified into Hurler's syndrome (MPS I-H), Scheie's syndrome (MPS I-S), Hurler-Scheie's syndrome (MPS I-H/S), Hunter's syndrome A, B (MPS II-A, B), Sanfilippo's syndrome A,B,C,D (MPS II-A,B,C,D), Morquio's syndrome A,B,C (MPS IV-A,B,C), Maroteaux-Lamy's

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syndrome (MPS VI) and Sly's syndrome (MPS VII)³. The mucopolysaccharidosis incidence is around 0.04-0.3% of the newborn and they are 1.5% of all congenital disorders⁴. The general phenotype includes facial dysmorphism, corneal clouding, hepatosplenomegaly, joint stiffness, hernias, dysostosis multiplex, contractures, pulmonary dysfunction, myocardial enlargement, valvular dysfunction, neurological involvement and mucopolysaccharides excretion in the urine and metachromatic staining in peripheral leukocytes and bone marrow^{1,5-6}.

Mucopolysaccharidosis type IV (MPS IV) results from an inborn deficiency of lysosomal enzyme N-acetyl-galactosamine-6-sulphate sulphatase (type A) beta-galactosidase (type B), an enzyme that degrades keratan sulphate. The syndrome is estimated to occur in 1 of every 200,000 births⁴. We present this rare case of MPS (Morquio's syndrome) type IV B that came to Out Patients Department of Paediatrics Unit II, Abbasi Shaheed Hospital. The child had the atypical features of skeletal deformities short neck, pectus carinatum, no corneal clouding, normal intelligence and all other features suggestive of MPS type IV.

Case Report

A nine-year-old boy (84cm, 16kg) presented at the Out-Patients Department of Paediatrics Unit II, Abbasi Shaheed Hospital with the complaint of failure to gain weight, and abnormal shape of bones including spine. In early infancy it was noticed by parents that he had an abnormal shaped chest, broad ribs, and with age child did not grow and was of a small stature. During early childhood the skeletal deformities became increasingly evident and he walked with difficulty. However, his mental status remained normal. Mother said that the child could see well and had no problems in the vision.

He had never visited a general practitioner or local hospital for any other complaints. He has three siblings, none of which had a congenital or similar illness however; his first cousin suffers from a similar congenital disease. His parents were married in consanguinity. He was delivered at full term

via spontaneous vaginal delivery. There is no history of maternal illness or drug exposure or premature rupture of membranes. He was vaccinated according to EPI schedule. There was no developmental delay of milestone to this date.

On general examination, an active and responsive boy with occipito-frontal circumference between 60th and 70th centile, weight and length below 5th centile, temperature 100°F, respiratory rate 18/min, heart rate 100 beats/min. Child had a semi-crouching stance and appeared small for age with disproportionate dwarfism, thoracic deformity and a short neck. The dental enamel was defective, nose was stubby, the mouth broad and teeth widely spaced. His hands were mis-shapen and loose-jointed; nevertheless his features were not ugly.

Chest was clear on auscultation; his liver and spleen were not palpable. On more detailed examination main signs of bone deformities namely pectus carinatum, ligamentous laxity, atlanto axial instability, flat feet as shown in Fig. 1 & 2 were present. Joints were very loose and hyper-mobile with early flattening of the growth curve, leading rapidly to almost complete growth arrest.

Patient has normal cognitive development. Bone scan revealed that skull with reduced bone density, prominent maxilla, short vertical height of cervical vertebra, increased AP diameter of chest, dorsolumbar lordosis, ovoid vertebral bodies with central anterior beaking, widened intervertebral disc spaces, narrow pelvis, hypoplastic acetabulum with broad flared iliac wings. Limbs showed short radius with hypoplastic ends of radius and ulna and humerus as shown in Fig. 3 & 4, widening of femoral neck with coxa valga, proximal pointing and shortening of metacarpal and metatarsal phalanges.

On laboratory investigations the complete blood picture, serum calcium, phosphorus, alkaline phosphatase and all other bio-chemical markers were in the normal range for age.

Discussion

The eponym Morquio's syndrome (mucopolysaccharidosis type IV; MPS IV) is a rare autosomal-recessive mucopolysaccharidosis that exists in two forms (Morquio syndromes A and B) and occurs because of a deficiency of the enzymes N-acetyl-galactosamine-6-sulfatase and beta-galactosidase, respectively⁶. A deficiency of either enzyme leads to an abnormal accumulation of certain complex carbohydrates (mucopolysaccharides or glycosaminoglycans) in the arteries, skeleton, eyes, joints, ears, skin, and/or teeth. These accumulations may also be found in the respiratory system, liver, spleen, central nervous system, blood, bone marrow and eventually causes progressive damage to cells, tissues, and various organ systems of the body. In most cases, individuals with Morquio syndrome have normal intelligence, as in our patient.

The clinical features of MPS IV-B are usually fewer and milder than those associated with MPS IV-A⁷. In people with MPS IV, the clear covering of the eye (cornea) typically becomes cloudy, which can cause vision loss⁸. Some affected individuals have recurrent ear infections and hearing loss. The airway may become narrow in some people with MPS IV, leading to frequent upper respiratory infections and short pauses in breathing during sleep (sleep apnea).

Other common features of this condition include mildly "coarse" facial features, thin tooth enamel, multiple cavities, heart valve abnormalities, a mildly enlarged liver (hepatomegaly), and a soft out-pouching around the belly-button (umbilical hernia) or lower abdomen (inguinal hernia)⁷. Unlike some other types of mucopolysaccharidosis, MPS IV does not affect intelligence. All of these findings were present in our case except corneal clouding, hearing loss, respiratory tract infections, heart disorders, hepatosplenomegaly and umbilical hernia. The major orthopedic manifestations include shortening of the trunk and limbs, spinal curvature, odontoid hypoplasia with upper cervical instability, and lower-limb alignment problems.

Patient suffering of MPS, usually, don't show clinical sign from their birth in fact the signs develop gradually, later in life with characteristic appearance². Genu valgum and paraplegia of slow onset due to spinal cord compression are common complications which may bring children with the true Morquio's syndrome⁴. The average survival of these patients is around 20-30 years⁵, and the exitus is due to cardiac failure or to infections to the gastrointestinal tract or to instability of atlantoaxial joint⁸.

All mucopolysaccharidosis are autosomal recessive disorders, except for Hunter's syndrome that is X-linked and recessive form⁹. Genetic counseling is important in this autosomal recessive disorder and enzymatic and/or molecular testing can be offered for prenatal diagnosis. Although no routine laboratory findings are present in MPS. The diagnosis is suggested by elevated urinary GAG's level and profile, and is confirmed by GALNS enzymatic studies on molecular testing. Plain radiography (to detect dysostosis multiplex), Computed tomography (CT) of the cranium (to help diagnose hydrocephalus), Echocardiography (to monitor ventricular function and size in MPS patients with cardiovascular disease), Electroretinography, Audiologic assessment⁵. Medical treatment modalities includes Laronidase, Idursulfase, Elosulfasealfa enzyme replacement therapy⁹. No specific treatment exists to this date in order to prevent the disease progression. Management is mostly symptomatic, based on early detection and orthopedic correction of spine and lower limb deformities, ENT and respiratory management.

In our patient, keeping the above prognosis in mind the parents were counseled and reassured about mild form of mucopolysaccharidosis type (IV-B) and physical rehabilitation of child was done. Psychological, social and educational support for the child and his/her family was advised. Follow up was recommended to the parents for any future anticipated complications.

This case has been highlighted so that the physicians and pediatricians are aware of children presenting with such systemic deformity and disability, with the objective of counselling the parents regarding future children and hence avoidance of consanguineous marriage.



Fig. 1 & 2 : Nine year old boy with Morquio's Syndrome showing coarse facies, short neck, pectus carinatum, spatulated ribs, and swollen knee joints and limb deformities.



Fig. 3 and Fig. 4 : shows Radiographs of Nine year old boy with Morquio's Syndrome. Chest Xray PA-view with dorsolumbar lordosis and Radiographs of wrist and hands shows hypoplastic, flaring and cupping ends of radius and ulna.

Conclusion

In our patient, there was a mild presentation of Morquio's Syndrome (type IV-B). Diagnosis of Morquio syndrome is important because the frequent odontoid hypoplasia can lead to a deadly atlanto-axial instability, hypoplasia of ends of long bones, if not treated. Mucopolysaccharidosis is a rare entity with limited number of cases reported locally. The sole principle of managing such patients is to counsel their parents and treat them symptomatically.

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