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Mucopolysaccharidosis Type 4 (Morquio Syndrome): A Case Report

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ABSTRACT:

Mucopolysaccharidosis type 4 (Morquio syndrome): a case report

Objective: Mucopolysaccharidoses, develop with genetic transmission which cause destructive changes in various organs as a result of glycasoaminoglycans deposition in lysosomes. Herein, we are presenting a case with Morquio syndrome so as to attract attention to this rarely seen disease.

Case: A 11-year-old male patient presented to our hospital with complaints of short stature, and bone deformities. The parents were not relatives, and he had 3 healthy younger siblings. On physical examination, coarse facial features, hypertelorism, disproportionate short stature, genu valgum, pectus carinatum, kyphoscoliosis, were detected. He demonstrated a waddling gait. His neuromotor development was normal for his age. On bone radiograms, kyphoscoliosis, flared iliac wings, coxa valga, flattening of femoral epiphysis, widened ribs, and narrowed iliac wings were detected. Urine tests were positive for glycosaminoglycans (keratan sulphate). Enzymatic analysis revealed low levels of glucose-6-phosphatase [15 pmol/mg/hr, (n:400-2000)], which made the final diagnosis.

Conclusions: Morquio syndrome has Aand B types with similar clinical manifestations which are transmitted as an autosomal recessive trait. Tip 4A is a disease due to a deficiency of galactosamine-6-sulfatase (GALNS) enzyme, which is encoded by the 16q24.3 gene, while Type 4B is characterized by deficiency of beta galactosidase. In both types of the disease, keratan sulphate, and chondrotin 6 sulphate accumulate. Also in our case manifestations became more prominent around age 1, and gradually progressed. Our patient without mental problems had typical skeletal signs on radiograms which is named dysostosis multiplex.

It is necessary to initiate enzyme replacement therapybefore the onset of gait disorders.

Keywords: Enzyme therapy, Morquio syndrome, mucopolysaccharidosis

ÖZET:

Bir olgu nedeni ile mukopolisakkaridoz tip 4 (Morquio sendromu)

Amaç: Mukopolisakkaridozlar, genetik geçişli ve lizozomlarda glikozamino glikan depolanması sonucu vücuttaki çeşitli organlarda hasara yol açan hastalıklardır. Burada nadir görülen bir tür olan Morquio sendromlu bu olguyu konuya dikkat çekmek amacı ile sunmaktayız.

Olgu: Onbir yaşındaki erkek hasta, hastanemize boy kısalığı ve kemik bozuklukları nedeni ile başvurdu. Anne baba akraba değildi ve olgumuzun üç sağlıklı küçük kardeşi vardı. Fizik muayenede kaba yüz, hipertelorizm, orantısız boy kısalığı, çarpık bacak, pektus karinatum, kifoskolyoz saptandı. Ördekvari yürüyüşü vardı. Nöromotor gelişimi yaşına uygundu. Kemik grafilerinde kifoskolyoz, iliak kanatlarda parlama, koksa valga, femoral epifizlerde düzleşme, genişlemiş kaburga kemikleri ve dar iliak kanatlar tespit edildi. İdrarda glikozaminoglikan (keratan sülfat) pozitif bulundu. Enzimatik analizde glukoz-6-fosfataz düşük bulunarak [15 pmol/mg/saat (n:400-2000)] kesin tanı kondu.

Sonuçlar: Morquio sendromunun benzer klinik tabloları olan ve otozomal resesif kalıtılan A ve B tipleri vardır. Tip 4A galactosamine-6-sulfatase (GALNS) enzim eksikliğine bağlı 16q24.3 geni ile kodlanan hastalık iken, Tip 4B beta galaktozidaz eksikliği ile ortaya çıkar. Her iki tip hastalıkta da, keratan sülfat ve kondrotin 6 sülfat birikmektedir. Bizim olgumuzda da bulgular 1 yaş civarında belirginleşmiş ve giderek ilerlemiştir. Zeka problemi olmayan hastamızın, dizostozis multipleks olarak adlandırılan kemik radyolojik bulguları tipiktir.

Enzim replasman tedavisinin yürüme fonksiyonunu kaybetmeden başlanması önemlidir.

Anahtar kelimeler: Enzim tedavisi, Morquio sendromu, mukopolisakkaridoz

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INTRODUCTION

Mucopolysaccharidoses (MPS) are metabolic diseases that develop due to enzyme deficiency, genetically transmitted and seen in one of 20,000 births in society, resulting in damage to various organs in the body with the accumulation of glycosaminoglycan (GAG) in lysosomes (1). Mucopolysaccharidoses have 7 [1,2,3,4,6,7,9] types according to the affected enzyme. Type 4 is also divided into A and B types. In mucopolysaccharidosis, bone, joint, heart, lung, gastrointestinal system and central nervous system can be affected (2). In this article, we aim to present a case of Morquio syndrome (Type 4) which doesn't involve mental problem, but a rare type with extensive bone involvement, to draw attention to the issue.

CASE

A 11-year-old male patient presented to our hospital with complaints of short stature, and bone deformities. We received the approval form from the patient's father with the condition that only the radiograms would be published. The parents were not relatives, and he had 3 healthy younger siblings. We learnt that one of his cousins had a similar disease. The birth anamnesis was normal. He had hip dislocation operation when he started walking.

Physical examination: Weight: 27.2 kg (3-10 p), hegiht 111.4 cm (<3 p), coarse facial features, hypertelorism, bulbous nose, small and rounded ears, curly and brown hair, flat and wide nasal root, wide mouth, short neck, short body, disproportionate short stature, genu valgum, pectus carinatum, kyphoscoliosis, ulnar deviation in the wrists, short forearm, joint hypermobility, hand joint ankle disorders. Abdominal examination: 3 cm liver, 2 cm spleen palpated. It was seen that the upper and lower permanent cutting teeth have been rotted and spitted. He demostrated a waddling gait. Neuromotor development was appropriate for the age, and he was successful at school.

The patient's biochemistry and hemogram values were normal. Mild aortic insufficiency was detected on echocardiography. On bone radiograms,

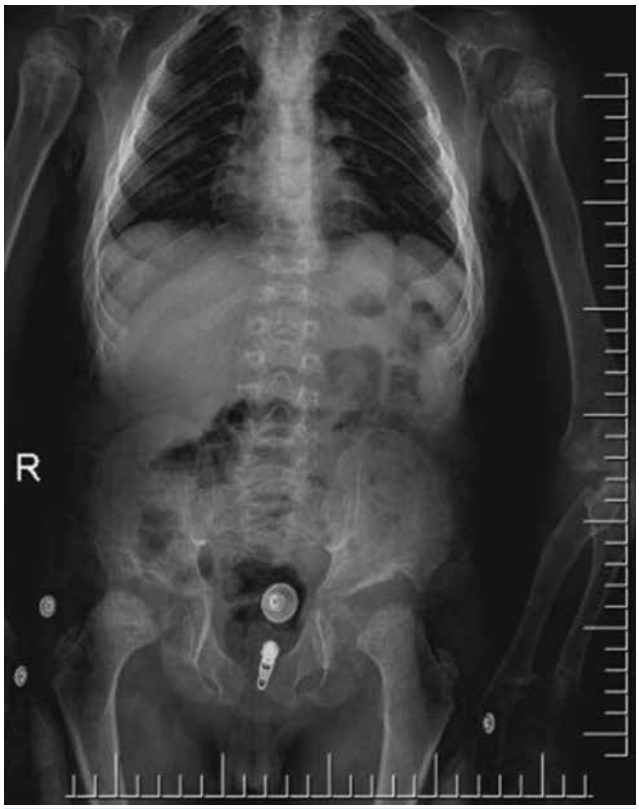

Figure-1: The bone radiograms of our patient with extensive involvement

odontoid hypoplasia, kyphoscoliosis, flared iliac wings, coxa valga, flattening of femoral epiphyses, widened rib bones and narrowed iliac wings were detected (Figure-1). Keratan sulfate, a kind of glycosaminoglycan was found positive in the urine. Enzymatic analysis revealed low levels of glucose-6-phosphatase [15 pmol/mg/hr, (n:400-2000)], and normal levels of beta galactosidase [148 mikromol/gr/saat (100-400)] which made the definitive diagnosis of MPS Type 4A.

DISCUSSION

MPS can affect different tissues and organs. While the brain is usually affected in Types 1,2 and 7, it is commonly associated with accumulation in soft tissue and bone. Type 6 is characterized by affecting soft tissue and bone, type 4 affecting bone only, and type 3 affecting only the brain (2).

There are similar clinical findings in both two

types of Morquio syndrome; Type A and B. They are inherited as autosomal recessive. Type 4A is a disease encoded by the 16q24.3 gene, associated with galactosamine-6-sulfatase (GALNS) enzyme deficiency, whereas Type 4B occurs due to lack of beta galactosidase. In both types of disease, keratan sulphate and chondrotin 6 sulphate accumulate (3). Morquio syndrome is characterized by short stature, short neck, and joint loosening and bone involvement, which are evident at around one year of age (4). Pectus carinatum and genu valgum are present in the majority of patients. Dysostosis multiplex, a characteristic bone finding, is seen at early ages. Spondyloepiphyseal dysplasia and flattened vertebral bodies are seen (5,6).

The lack of adequate ossification causes atlanto axial loosening and odontoid dysplasia resulting from subluxation. This situation shows up in patients as fatigue and progressive muscle weakness due to slow cervical cord compression. Sudden respiratory arrest with small traumas in severe forms may happen. Patients lose their gait function in the second or third decades if no enzyme replacement is done (7).

Mild corneal opacities, hepatosplenomegaly and heart valve diseases may be seen. Progressive hearing loss and dental anomalies may be seen in some patients. Both types of patients with Morquio syndrome have mild and severe symptoms due to residual enzyme activity. In severe forms, there is a minimal height growth after 7-8 years of age and they are lost with respiratory insufficiency at 3rd-4th decades. Mild forms can live up to the age of seventies (8).

In our case, the findings became evident around the age of one and progressed gradually. Bone radiographic findings of our patient with no mental problem had disease-specific radiographic bone images called dysostosis multiplex. Muscle weakness suggests odontoid dysplasia, and the patient was followed by neurology and orthopedics clinics. The patient's coarse facial feauture was typical for MPS. Mild corneal haze was detected on the eye examination, but the patient's visual acuity was normal. Our patient had heart valve involvement, and mild aortic insufficiency.

Given the frequency of consanguineous marriages in our country, urine GAG should be checked in cases where symptoms and findings suggest an autosomal recessive disorder such as MPS 4A, and it should not be forgotten that even if this result is normal, examining the enzyme level would provide a definite diagnosis. Findings and clinical course of the disease can be slowed down by enzyme replacement therapy. Especially treatments prior to the impairment of respiratory system and gait functions give more successful results. Gene therapy for this disease is also actual, and studies are ongoing (9). In 2014, the recombinant human GALNS enzyme (Elosulfase alpha) was started to be used. It stops the progression of respiratory and skeletal findings and provides growth. Its use is suggested under the age of five in the literature (10). However in our patient, despite the fact that he was 11 years old, Elosulphase Alpha treatment was planned with the objective of preventing progression of bone symptoms and providing the height growth with the reasons that he could walk without support and had no respiratory problems.

As a result, starting the enzyme treatment soon after the patient is identified will reduce morbidity and mortality. In addition, identification of carriers and avoidance of new patients by genetic counseling in new pregnancies is crucial as the high treatment costs are considered and treatment is currently only causing the clinical progression of the disease to slow down.

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