

Mucopolysaccharidosis Type IVA (Morquio A Disease) in a Girl

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Abstract: Morquio A syndrome (Mucopolysaccharidosis type IVA is an autosomal recessive lysosomal storage disorder (LSD) caused by deficiency of Nacetylgalactosamine-6-sulfate sulfatase (GALNS) causes systemic skeletal spondyloepiphyseal dysplasia presenting as short stature, pectuscarinatum, knock-knee, kyphoscoliosis hypermobile joints, and an abnormal gait with an increased tendency to fall. We present 7 years old female patient presented with history of increase outward curvature of the spine and bowing of leg and arm. Noticed when the patient was at 1 years old. Diagnosis was confirmed by a significant increase in keratan sulfate in urine and marked deficiency of galactosamine-6-sulfate activity in her her blood samples and positive genetic testing and the patient was started on enzyme replacement therapy.

Keyword: Morquio A syndrome, Mucopolysaccharidosis type IVA, acetylgalactosamine-6-sulfate.

INTRODUCTION

Morquio A syndrome (Mucopolysaccharidosis type IVA is an autosomal recessive lysosomal storage disorder (LSD) caused by deficiency of Nacetylgalactosamine-6-sulfate sulfatase (GALNS). This enzyme deficiency leads to progressive accumulation of excessive glycosaminoglycans (GAGs), keratan sulfate (KS) and chondroitin-6-sulfate (C6S) primarily in the lysosomes of bone, cartilage, and ligaments [1].

We present 7 years old female patient presented with history of increase outward curvature of the spine and bowing of leg and arm. Noticed when the patient was at 1 years old. Diagnosis was confirmed by a significant increase in keratan sulfate in urine and marked deficiency of galactosamine-6-sulfate activity in her blood samples and positive genetic testing

CASE REPORT

7 years old female patient present with history of increase outward curvature of the spine and bowing of leg and arm. These symptoms noticed by the mother when the patient was 1 years old. It Started by the spine then involve the leg and arm. These symptoms were progressive, increasing in severity every year affecting her daily functioning like walking and handling objects by hands. She was product of full term normal spontaneous vaginal delivery.

Vaccination was up to date. Developmental parameters were appropriate for age. She was on family diet with average appetite. There was no consanguinity between parents. Her parents and siblings are healthy with unremarkable family history of similar disease.

On examination vitally stable. Her height was below 3rd centile for age and sex. she was Concious, alert, oriented, she has flat nasal bridge, flared nose, and a large mouth with broad lips with intact neurological examination she was Found to have coarse face wide space teeth, proment sternum ,abnormal walk ,kyphosis, pectus exacavatum, short neck, genua valga and hypermobile joints. On Chest examination there was good air entry bilaterally, no added sounds, audible first and second heart sound with no murmur, Abdomen was soft, lax, with no organomegaly and distension. There was No corneal clouding

Investigation revealed that complete blood count was within normal limit, Blood urea nitrogen, sodium, potassium, blood sugar, liver function and bone profile all were normal. Keratan sulfate was high in urine and there was marked deficiency of galactosamine-6-sulfate activity in her blood samples

Skeletal survey done and showed Sella is enlarged with prominent convolucional markings (Figure 1)



Fig-1: Sella is enlarged with prominent convoluted markings

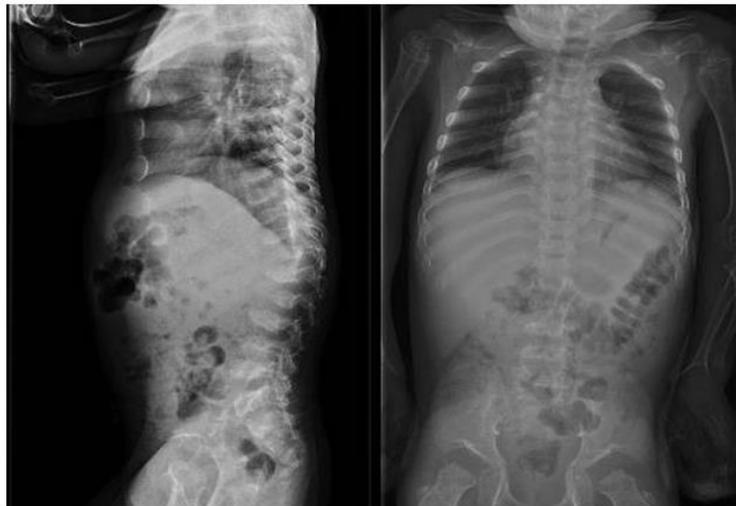


Fig-2: Hypoplasia of T11 and L2 vertebrae noted with platyspondyly of lower thoracic and lumbar vertebrae having anterior beaking

Hypoplasia of T11 and L2 vertebrae noted with platyspondyly of lower thoracic and lumbar vertebrae having anterior beaking. (figure2).



Fig-3: Simian pelvis with maldeveloped femoral capital epiphysis, shallow acetabulum
Simian pelvis with maldeveloped femoral capital epiphysis, shallow acetabulum (figure3)



Fig-4: Bones have decreased density with Radius and Ulna is angulated proximally. Metaphyseal ends are irregular Metacarpals are pointed proximally

Bones have decreased density with Radius and Ulna is angulated proximally. Metaphyseal ends are irregular. Metacarpals are pointed proximally (figure4)

Epiphysis are irregular. Tibia and fibula are positioned out wards. Decreased density of bones with irregular borders of calcaneum. Metatarsals are pointed proximally (figure 5). Echo cardiography revealed mild mitral valve prolapse. Hearing test was normal. Abdomen ultrasound done and show normal size intrabdominal organ with no abnormality.

Genetic testing by next-generation sequencing assay showed

A homozygous variant of GALNS (GALNS: NM_000512:exon8:c.860C>T: p. S287L) was identified in this patient. Missense variants of GALNS are suggestive of Mucopolysaccharidosis IVA, 253000 (3), Autosomal recessive. Patient was started on Enzyme Replacement Therapy with no drug reaction

DISCUSSION

Patient of Morquio A presented with systemic skeletal spondyloepiphyseal dysplasia seen as striking

short trunk stature, pectus carinatum, knock-knee, hypermobile joints, kyphoscoliosis and an abnormal gait with an increased tendency to fall [2].

Patients with Morquio A appear healthy at birth, but abnormal radiographs of the spine are observed prior to other systemic manifestations. Diagnosis of Morquio A patients are often not made until two - three years of age with more prominent skeletal dysplasia [3]. Urinary analysis of GAGs is useful as a preliminary investigative test for MPS [4-5]. Enzyme Replacement Therapy (ERT)

ERT is an established and approved treatment for MPS including MPS I [6], MPS II [7] and MPS VI [8]. Clinical trials with ERT in MPS I, II, and VI show limited improvement in joint pain, stiffness, or joint range of motion. Skeletal dysplasia is irreversible by conventional ERT [9] since there is little or no evidence that the current ERT directly delivers the enzyme to cartilage and bone lesions in MPS patients. The effectiveness of treatment could be greater if it is introduced early in life [10].



Fig-5: Epiphysis is irregular, Tibia and fibula are positioned outward Decreased density of bones with irregular borders of calcaneum. Metatarsals are pointed proximally

CONCLUSION

Morquio A syndrome is an autosomal recessive lysosomal storage disorder caused by deficiency of N-acetylgalactosamine-6-sulfate sulfatase (GALNS) causes systemic skeletal spondyloepiphyseal dysplasia. ERT is an established and approved strategy of treating Morquio A syndrome especially in early stage.

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