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Morquio A Syndrome Case Report and Literature Review

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Abstract **Case Report**

Morquio A syndrome is an autosomal recessive disorder, one of 50 lysosomal storage diseases (LSDs), and is caused by the deficiency of N-acetylgalactosamine-6-sulfate sulfatase (GALNS). Deficiency of this enzyme causes specific glycosaminoglycan (GAG) accumulation: keratan sulfate (KS) and chondroitin-6-sulfate (C6S). The majority of KS is produced in the cartilage, therefore, the undegraded substrates accumulate mainly in cartilage and in its extracelluar matrix (ECM), causing direct leads to direct impact on cartilage and bone development and leading to the resultant systemic skeletal spondyloepiphyseal dysplasia. Chondrogenesis, the earliest phase of skeletal formation that leads to cartilage and bone formation is controlled by cellular interactions with the ECM, growth and differentiation factors and other molecules that affect signaling pathways and transcription factors in a temporal-spatial manner. In Morquio A patients, in early childhood or even at birth, the cartilage is disrupted presumably as a result of abnormal chondrogenesis and/or endochondral ossification. The unique clinical features are characterized by a marked short stature, odontoid hypoplasia, protrusion of the chest, kyphoscoliosis, platyspondyly, coxa valga, abnormal gait, and laxity of joints.In spite of many descriptions of the unique clinical manifestations, diagnosis delay still occurs. The pathogenesis of systemic skeletal dysplasia in Morquio A syndrome remains an enigmatic challenge. In this review article, screening, diagnosis, pathogenesis and current and future therapies of Morquio A are discussed.

Keywords: The mucopolysaccharidoses, Morquio A syndrome; bone involvement.

INTRODUCTION

Type IV mucopolysaccharidosis (Morquio A syndrome; MPS IVA; OMIM 253000), is a multisystemic, severe and very disabling disease, also life-threatening; MPS IVA is due to a defi ciency of the enzyme N-acetylgalactosamine-6-sulfate sulfatase (GALNS), a lysosomal enzyme responsible for the degradation of keratan sulfate (KS) and chondroitin-6-sulfate (C6S). The disease is characterized by respiratory, pulmonary manifestations and also causes bone involvement with progressive spondyloepimetaphyseal degradation and mild and late-onset ophthalmologic, hearing and cardiac complications. These manifestations progressively impair the patients' physical mobility. Severe forms of the disease, diagnosed before the age of 1 year, can be distinguished from intermediary (diagnosed between 1 and 5 years old) and attenuated disease, diagnosed after the age of 5 years (occasionally far later) [1].

The main signs are bone deformities namely pectus carinatum, kyphoscoliosis and genu valgum, with early flattening of the growth curve, leading rapidly to almost complete growth arrest. Patients have normal cognitive development. The radiological signs are relatively specific with, in particular, platyspondyly, [2] shortening of the long bones and characteristic pelvic changes. The diagnosis is suggested by elevated urinary GAGs level and profile, and is confi rmed by GALNS enzymatic studies on molecular testing. Genetic counseling is important in this autosomal recessive disorder and enzymatic and/or molecular testing can be offered for prenatal diagnosis. Management is mostly symptomatic, based on early detection and orthopedic correction of spine and lower limb deformities, ENT and respiratory management and psychological, social and educational support for the child and his/her family.

Patient aged 7 years, having as antecedent a sister with Morquio disease, his record is also in favor of a Morquio disease, At the age of 3 years, the patient began developing subtle flexion contractures of his fingers and his mother noticed that he could not lift his arms above his head. He frequently asked for assistance with dressing and he tended to walk on his toes. General appearance of our patient with the deformation

of the anterior thorax, the micromelia, the short neck, the malposition of the feet and the elbow extension limitations. Left upper limb with shortening of the hand, elbow flexion and ulnar deviation of the hand. The patient was referred to Genetics and was found to have deficiency of the enzyme N-acetylgalactosamine-6-sulfate sulfatase (GALNS), and Morquio disease was confirmed.

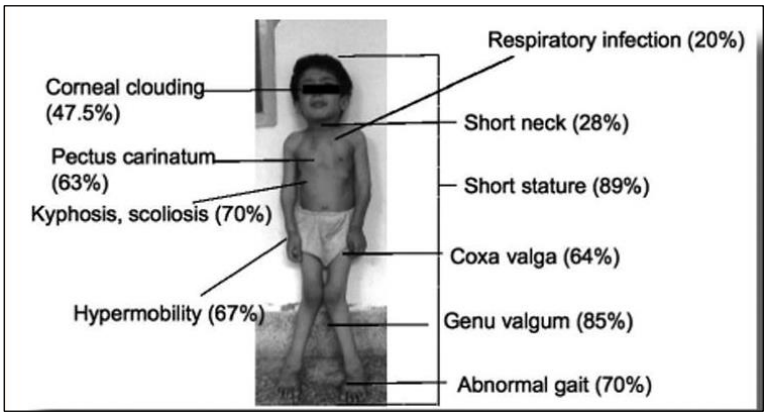
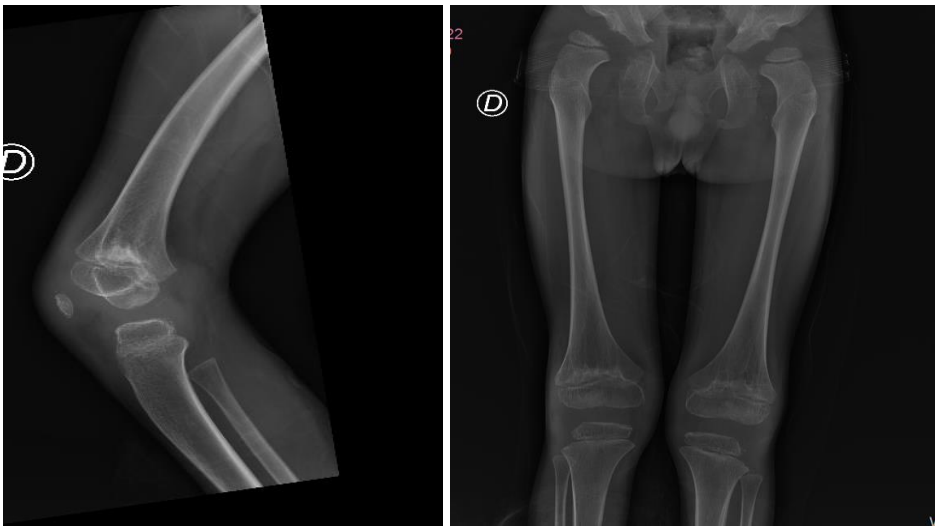


Figure 1: Clinical manifestations of Morquio A disease. Percentage of present symptoms based upon Morquio A database (photo; permitted by Morquio family)

Figure 2: General appearance of our patient with the deformation of the anterior thorax, the micromelia, the short neck, the malposition of the feet and the elbow extension limitations. Left upper limb with shortening of the hand, elbow flexion and ulnar deviation of the hand



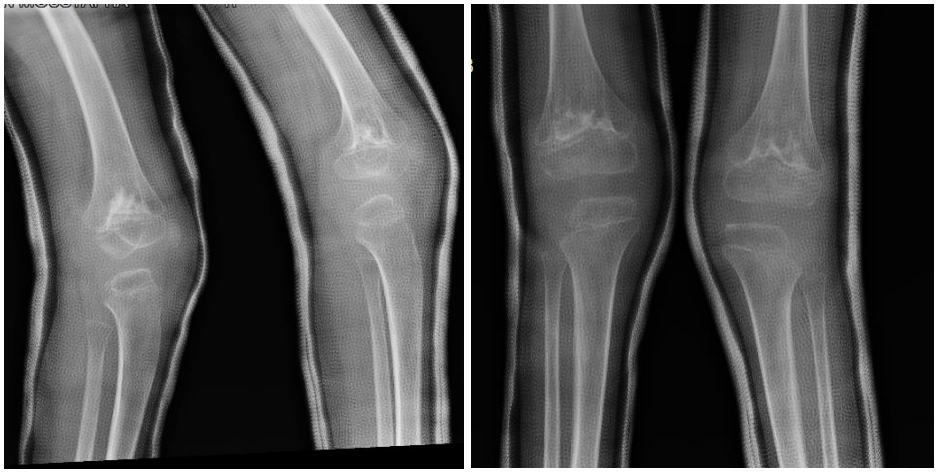


Figure 3: Enlargement of the acetabulum and abnormalities of the femoral epiphyses, superior, The diaphyses of the long bones, shorten, and the metaphyses are often irregular. The epiphyseal-metaphyseal abnormalities will increase over time

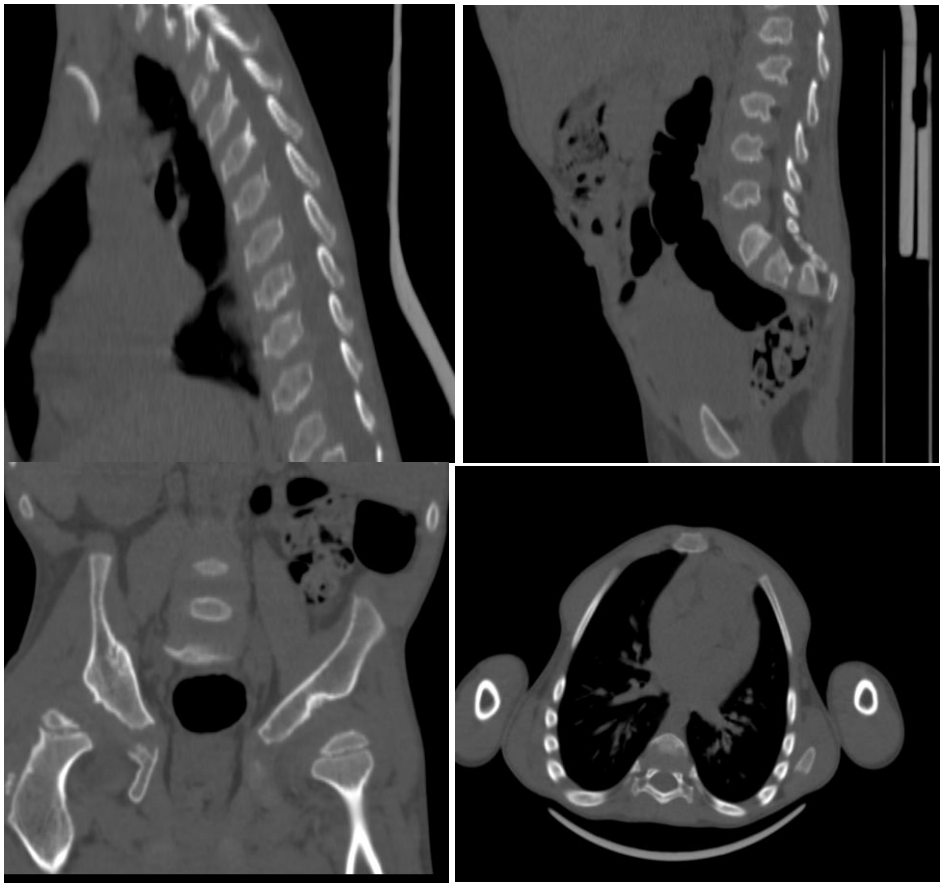


Figure 4: Flattened and elongated stepped aspect of the vertebral bodies more marked at the cervical level realizing the appearance of the short neck in relation to platyspondyly. • Rethrolistesis of the D9/D10 vertebral body with reduction of the anteroposterior diameter of the D9 leading to an accentuation of the dorsal kyphosis giving an arched back appearance. • Aspect of the thorax in carena with bilateral anterior prominence of the 3rd and 4th chondro-sternal joint

DISCUSSION

Morquio syndrome is a genetic disease caused by the lack of the enzyme responsible for the degradation of the mucopolysaccharide keratin sulfate. The resulting buildup of keratin sulfate causes a specific pattern of abnormalities. Affected children have normal intelligence and usually survive into adulthood. Two forms are recognized: type A, a deficiency of the enzyme galactosamine-6 sulfatase; and Type B, a deficiency of the enzyme beta-galactosidase.

A genetic defect has been identified in N-acetyl-galactosamine-6-sulfate sulfatase (GALNS gene) in Morquio syndrome type IVA or beta-galactosidase (GLB1 gene) in Morquio syndrome type IVB. Chondroitin 6-sulfate catabolism is also affected by the defect in the GALNS gene [3]. Metabolism of heparan and dermatan sulfate is normal in Morquio syndrome, which is why patients with Morquio syndrome do not have mental retardation. Patients with Morquio syndrome appear healthy at birth. Marked dwarfism, abnormal curvature of the spine (kyphoscoliosis), and decreased tone and weakness are prominent manifestations of early childhood. Also seen is a coarse facies, short nose, wide mouth, and widely spaced teeth with thinned enamel. The patient may have a waddling gait. Pectus carinatum (horizontal and protruding sternum) and a shortened neck with clouding of the cornea, ligament laxity and joint stiffness are also observed. Mental capacity is generally intact.

Examination and tests may reveal short stature (flat vertebrae resulting in a short trunk), short neck, kyphosis or scoliosis with pectus carinatum (pigeon chest) and, in the cervical spine, odontoid hypoplasia; atlanto-axial instability may be associated with myelopathy with progressive loss of ability to walk [4]. Joint laxity, dysostosis multiplex, dysplastic hips, unsteady knees, wide elbows and wrists, and flat feet are other skeletal features. There may be heart abnormalities with enlarged liver and spleen. Surveys include spot urine tests which are readily available to screen for mucopolysaccharides but are associated with false positive and false negative results. Heparan, keratan, and dermatan sulfate can be distinguished by electrophoresis techniques to differentiate mucopolysaccharidosis. Diagnosis is confirmed by direct leukocyte enzyme assay, or fibroblast enzyme activity can be measured in amniocytes or chorionic villi.

The radiographic findings were reviewed by Langer and Carry [5]. Compared to other forms of MPS, Morquio syndrome tends to have more skeletal manifestations and spinal involvement such as scoliosis, kyphosis, hyperlordosis, severe gibbus, flare of the lower ribs as well as platyspondylia, pectus carinatum metacarpals and small carpal bones (often with some absent). Characteristic findings included hypoplasia of the odontoid ankle, universal platyspondylia humpback, and kyphosis of the dorsal region with widening of the disc spaces. A long pelvis with narrowing at the acetabulum, widening of the symphysis pubis, and flare of the ilia are also characteristic. There may be a shortening of the metacarpals and a tilting of the distal parts of the radius and ulna towards each other may also be observed (as in our case).

Complications develop later and include breathing problems, heart problems, spinal cord damage which can lead to paralysis, vision problems, walking problems related to abnormal curvature of the spine and other problems bony. Most patients survive until their third or fourth decade. The treatment is currently only palliative. Possible future treatments include enzyme replacement, gene therapy and allogeneic bone marrow transplantation.

CONCLUSION

All patients with Morquio's disease develop potentially serious chronic clinical manifestations, for some in a time-shifted way (slowly progressive form). The characterization of these manifestations, through large international observational studies carried out in recent years, improves understanding of the disease and facilitate its symptomatic management. Longitudinal studies will make it possible to better define the natural history of Morquio disease and to study the impact future specific treatments, and more particularly enzyme replacement therapy.

RÉFÉRENCES

1. Morquio, L. (1929). Sur une forme de dystrophie osseuse familiale. *Bull Soc Pediatr Paris*, *27*, 145-152.
2. Brailsford, J. F. (1976). Chondro-osteo-dystrophy: Roentgenographic and Clinical Features of a Child with Dislocation of Vertebrae. *Clinical Orthopaedics and Related Research (1976-2007)*, *114*, 4-5.
3. Nelson, J. (1997). Incidence of the mucopolysaccharidoses in Northern Ireland. *Human genetics*, *101*, 355-358.
4. Nelson, J., Crowhurst, J., Carey, B., & Greed, L. (2003). Incidence of the mucopolysaccharidoses in Western Australia. *American journal of medical genetics Part A*, *123*(3), 310-313.
5. Tomatsu, S., Fukuda, S., Masue, M., Sukegawa, K., Fukao, T., Yamagishi, A., ... & Orii, T. (1991). Morquio disease: isolation, characterization and expression of full-length cDNA for human N-acetylgalactosamine-6-sulfate sulfatase. *Biochemical and biophysical research communications*, *181*(2), 677-683.
6. Sukegawa, K., Nakamura, H., Kato, Z., Tomatsu, S., Montaño, A. M., Fukao, T., ... & Kondo, N. (2000). Biochemical and structural analysis of missense mutations in N-acetylgalactosamine-6-sulfate sulfatase causing mucopolysaccharidosis IVA phenotypes. *Human molecular genetics*, *9*(9), 1283-1290.