CASE REPORT

Morquio Syndrome: A Report of a Rare Disease and Literature Review

Edwin M **DIM**[1]
Ifiok C **UDOMESIET**[1]
Michael E **UGBEYE**[2]
Uchenna E **DIM**[3]

[1]*Department of Orthopaedics and Traumatology*
Faculty of Clinical Sciences
University of Uyo/ University of Uyo Teaching Hospital
Uyo, NIGERIA

[2]*Arthroplasty Unit*
Department of Trauma and Orthopaedic Surgery
National Orthopaedic Hospital, Igbobi
Lagos, NIGERIA

[3]*Nursing Services Division*
National Orthopaedic Hospital
Lagos, NIGERIA

Author for Correspondence
*Dr Edwin M **DIM***
Department of Orthopaedics and Traumatology
Faculty of Clinical Sciences
University of Uyo/University of Uyo Teaching Hospital
Uyo, NIGERIA

Phone: +234703 753 4952
E-mail: maduakonamdim@yahoo.com

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ABSTRACT

Morquio syndrome is a rare multisystem disease that leads to severe functional impairment. Serious morbidities and potentially fatal conditions may be present following affectation of various organs. Musculoskeletal abnormalities, including short stature, spinal deformities, hip dysplasia, genu valgum, pectus carinatum, among other abnormalities, constitute the common mode of presentation. This is a case report of a 28-year old male Nigerian student with severe musculoskeletal deformities, who presented with a one- year history of right hip pain and inability to walk of 5 months duration. He was 1.16 metre (116cm) tall and weighed 27kg, with subluxed hips, absent femoral heads, spine deformities and dysplastic acetabula. All deformities observed in the patient fit into a clinical suspicion of Morquio syndrome.

Keywords: *Morquio, Musculoskeletal deformities, Rare disease, Nigeria*

INTRODUCTION

Morquio syndrome, also known as Morquio-Brailsford syndrome, was described in 1929 by Dr Luis Morquio, a Uruguayan Paediatrician, and by Dr James Fredrick Brailsford, a British radiologist. It is a rare, autonomic recessive and multi-systemic disorder due to deficiency of *N*-acetylgalactosamine-6 sulfatase, resulting in abnormal degradation of keratan sulphate and accumulation of mucopolysaccharides.[1,2]

The affectation of various organs presents the patient with serious morbidities and potentially fatal conditions. Morquio syndrome is recognized as one of the mucopolysaccharidoses (MPS IV), a chronic and progressive multi-systemic storage disease. MPS are a group of similar disorders characterized by the abnormal accumulation in the body of glycosaminoglycans (GAGs) which is caused by deficiency of lysosomal enzymes responsible for degradation of glycosaminoglycans (dermatan sulfate, heparan sulfate, keratan sulphate).[1] Skeletal abnormalities occur early and are prominent features of Morquio Syndrome, in addition to early growth arrest. Most patients have short statures, spinal deformities, hip dysplasia, genu valgum, pectus carinatum among other abnormalities.[1,2,3]

Despite the severe multisystem affectation, most patients have normal intelligence.[1] Urinary analysis of GAGs is useful as a preliminary investigative test for MPS. Excessive undegraded Keratan Sulfate (KS) released into circulation is an important biomarker for screening and assessing Morquio disorder.[2]

Although considered a rare disorder, there is a large database of the medical and surgical management of the various clinical manifestation of Morquio syndrome.[2] To the best of our knowledge, there is no documented report of Morquio syndrome in local literature within our nation, and the aim of this paper, therefore, is to report a case of a 28 year old Nigerian man with clinico-radiological features suggestive of Morquio syndrome who was seen at the Orthopaedic outpatient clinic of our hospital.

Case Report

A 28-year old Nigerian man presented to us with a one-year history of pain in the right hip and a five-month history of inability to walk. The hip pain was gradual in onset, but became progressively worse. Initially, the patient could ambulate with the help of a walking stick, but later became unable to ambulate five months prior to presentation. The pain was not relieved by non-steroidal anti-inflammatory agents. The left hip was also occasionally painful and there was a history of long standing low back pain. There was no history of trauma or chronic cough. He was not a known sickle cell disease patient.

He sought treatment at a Traditional bone setter's clinic to no avail. He had normal intelligence and was a Higher National Diploma student in a Nigerian Polytechnic, until five months prior to presentation when he could no longer go to school on account of inability to walk.

Physical examination showed an anxious looking young man in pain and on a wheel chair. He was short-statured with a height of

1.16 meters and a body weight of 27 kilograms. The Body Mass Index (BMI) was 20kg/m^2. He had a short neck with prominent mandible, barrel chest, pectus carinatum and thoracolumbar kyphosis. There was good muscle bulk in both upper limbs with spindle shaped fingers and swan neck deformity of the fingers. Muscle power was normal in both upper limbs. Hand grip was normal.

The lower limbs were thin. There were fixed flexion deformities of the knees (30 degrees bilaterally), with a range of motion 30-120 degrees bilaterally. The right hip showed a fixed flexion deformity of 30 degrees and the left hip a fixed flexion deformity of 25 degrees.

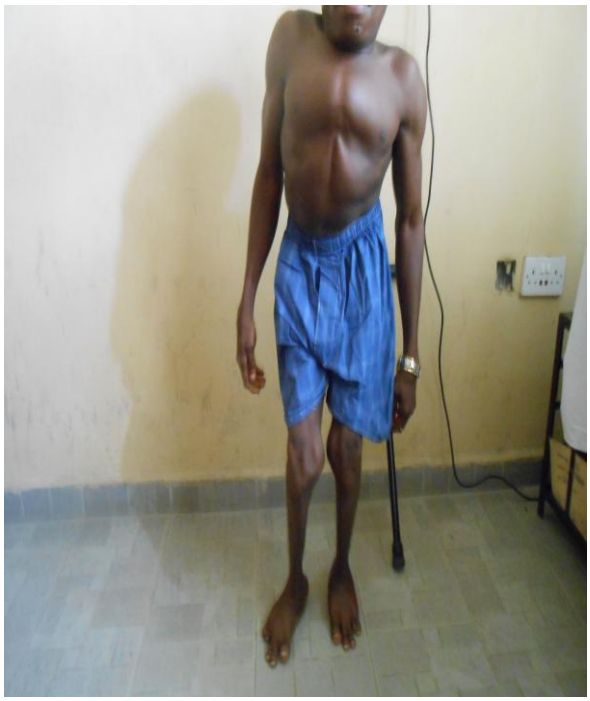
The range of motion on the right hip was grossly reduced, especially internal rotation. The left hip had normal range of motion. There was no limb length inequality, but patient had bilateral pes planus deformity. There was no significant abdominal finding (Figure 1). Other systems examination was not remarkable.

Radiographs of the thoracolumbar spine and pelvis showed vertebral osteopaenia, flattening of the vertebrae, thoracolumbar kyphosis, bilaterally dysplastic acetabula, absent femoral heads and bilateral hip subluxation (Figures 2a and b).

A clinical diagnosis of Morquio syndrome with bilateral secondary osteoarthritis of the hips was made. Biochemical assay of blood and urinary levels of glucosaminoglycans (GAGs) could not be arranged on account of financial constraints on the part of the patient on the one hand, and unavailability of the facilities for these investigations in our centre and elsewhere within the country where inquiries were made. There was the option to send the samples to outside the country but this was not acceptable to the patient on account of financial constraint.

Although he desired relief from his bilateral hip pain, he could not afford the suggested bilateral Total Hip Arthroplasty using customized prosthesis. Upon follow up on conservative measures, including wheel chair mobilization and analgesics, he has barely continued to cope with limited activities of daily living.

Figure 1. Front view in standing position showing severe pectus carinatum, truncal deformity, well developed upper limbs, and lower limb deformities.



DISCUSSION

A systematic review by Leadley *et al.* showed that the birth prevalence of Morquio Type A ranged from 1 per 71,000 to 1 per 500,000 live

Figure 2a. Image showing bilaterally dysplastic acetabula, absent femoral heads, bilateral hip subluxation and osteoarthritis

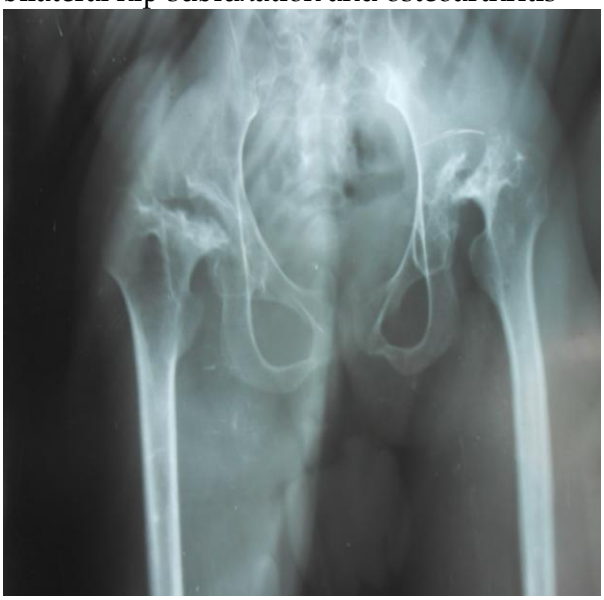
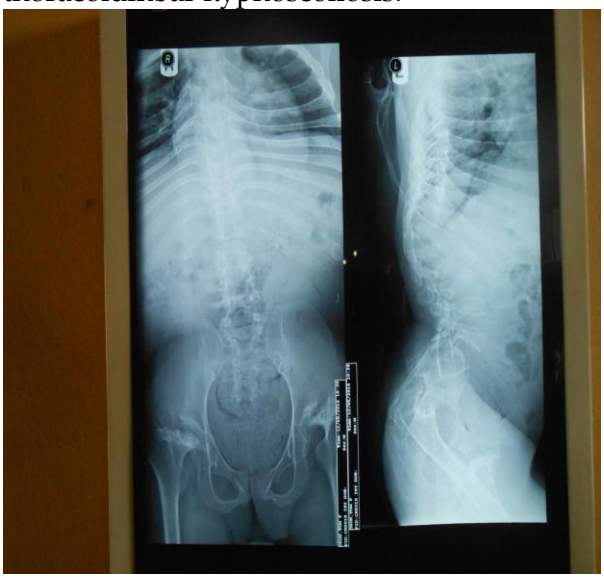


Figure 2b. Image showing vertebral osteopaenia, flattening of the vertebrae, thoracolumbar kyphoscoliosis.



births in studies with recommended diagnostic methods.[3] For all unclassified Morquio, birth prevalence ranged from 1 per 28, 000 to 1 per 208, 000 live births for studies with recommended diagnostic methods. Leadley *et al*. also found that birth prevalence was reported by such countries as Australia, Brazil, Canada, Germany, Japan, Netherlands, Saudi Arabia, Taiwan, UAE and UK. No data were found for prevalence of Morquio A in France, Italy, Mexico, Poland, Portugal, Qatar, Spain, South Korea, Turkey or United States of America (USA).[3] Morquio syndrome shows no racial predilection and both genders are equally affected.

Two phenotypes of Morquio syndrome have been described.[3] In type A, the lysosomal enzyme N-acetylgalactosamine-6-sulfatase (GALNS) is deficient. In type B, the enzyme beta-galactosidase is deficient. These lysosomal enzymes are needed to break down complex carbohydrates known as mucopolysaccharides or glycosaminoglycans (GAGs). Their deficiency results in excessive accumulation of GAGs in lysosomes of bone, cartilage, and ligaments and in the extracellular matrix of these tissues. This in turn causes a cascade of events leading to the progressive damage of cells, tissues and organs. The deficiency of N-acetylgalactosamine-6 sulfatase (GALNS) results in accumulation of chondroitin-6-sulfate (C6S) and keratan sulfate (KS) in many tissues and organs. In addition, beta-galactosidase deficiency leads to accumulation of ganglioside, causing the neurodegenerative disease gangliosidosis. The accumulation of these mucopolysaccharides or

galactosaminoglycans (GAGs) results in multi-systemic clinical impairments including musculoskeletal abnormalities, short stature, pulmonary and cardiac dysfunction, hearing loss and corneal clouding.[3] Morquio type A is the more common and more severe variant of the disorder. Our patient could not be conclusively classified, from biochemical point of view, due to lack of facility for these lysosomal enzymes assay. However, from clinical assessment, the absence of neurodegenerative symptoms in the patient suggests that our patient may be Morquio type A.

A number of deformities have been described as clinical entities found in Morquio syndrome.[1,2,4,5] At birth patients with Morquio generally appear healthy, but abnormal radiographs of the spine are observed prior to other clinical manifestations. Diagnosis is often made in the first two or three years of life, when features of spondyloepiphysio-metaphyseal dysplasias are first noted. There may be delayed motor milestone, but after a period of normal development, features of the disorder become apparent and growth retardation is noted. The reported average adult height is about 115cm.[4] Our patient is 116cm tall.

The mean life expectancy for patients with Morquio syndrome has been quoted as 25.3 years, but our patient is 28 years old at presentation.[3,6] Despite the severe multisystem affectation, most patients have normal intelligence.[1] Our patient has normal intelligence, evidenced by the fact that he was student of a Polytechnic at the time of presentation. The general features observed in these patients include short stature, short neck, coarse face, mid face hypoplasia, broad mouth with protuberant tongue, short anteverted nose, widely spaced teeth, tooth enamel hypoplasia and corneal clouding. The deformities in the trunk include barrel shaped chest, pectus carinatum, short trunk and kyphoscoliosis.

The upper limbs may be thin and short with features of wrist subluxation, ligamentous laxity, muscle weakness and carpal tunnel syndrome. The lower limbs may show deformities of the hips and knees with reduced range of motion, genu valga, prominent buttocks and pes planus. Other features may include corneal opacity, early onset of coronary heart disease, aortic or mitral valve dysfunction, pulmonary hypertension, hearing loss, groin hernia and hepato-splenomegaly.

Notwithstanding the general features observed in these patients, the musculoskeletal system is usually severely affected. Therefore, the orthopaedic surgeon may be the first to appreciate the skeletal findings culminating in a diagnosis of Morquio syndrome, particularly in the patient who presents with a lumbar gibbus deformity and a short stature.[5] Atlanto axial instability from odontoid hypoplasia poses a major orthopaedic and anaesthetic risk to the patient. There is the danger of cervical myelopathy, quadriparesis and death from chronic pulmonary failure. Cervical cord compression has historically been postulated to be the most common cause of death in Morquio syndrome.[7,8] The hips are usually dysplastic at birth. As the patient begins to bear weight, the

hip gradually dislocates. This dislocation is asymptomatic initially, and does not impair function. In adulthood, patients develop symptomatic osteoarthritis that can be debilitating. This is the mode in which our patient (the index case) presented to the hospital. Most patients develop genu valgum from around the age of 3 years. Ligamentous laxity plays a part in this deformity and patient may require corrective osteotomy.[9]

Morquio syndrome is a progressive disorder and severity increases over time. Clinical manifestations and severity are dependent on the level of enzyme deficiency. Patients with mild symptoms of the disease (type A or B) have been reported to live into the 7th decade, whereas those with severe disease do not survive that long.[4]

Numerous radiological anomalies have been noted in these patients, some of which are pathognomonic. Cervical spine odontoid hypoplasia (with the potential for atlanto – axial instability), platyspondyly in the thoraco-lumbar spine, thoraco-lumbar kyphosis and scoliosis are notable features. The long bones are short and curved with irregular trabeculations, as well as metaphyseal widening and irregularity. The femoral head may be flattened with associated coxa valga or vara deformity. There may be flaring of the iliac crest and the acetabulum is consistently dysplastic.[5]

The identification of GAG fragments (keratan sulfate and chondroitin sulfate) in urine using spectrophotometric assay with dimethylene blue provide more diagnostic aid, but these fragments may be absent in mild forms of the disease. Direct enzymatic assay in leucocytes or fibroblasts confirms the diagnosis, but prenatal diagnosis is also possible by measuring enzymatic activity in amniocytes or chorionic villi.[2,5,7] Level of blood and urine Keratan Sulfate is correlated with clinical severity at an initial stage, and therefore represent a good prognostic biomarker.[2]

Although these patients may present with complications requiring surgery, as seen in our patient, it must also be borne in mind that they generally constitute anaesthetic risks, especially on account of odontoid hypoplasia with subluxation, which calls for adequate precaution and preparation prior to anaesthetic intubation.[5,10]

From Orthopaedic view point, a patient with Morquio syndrome is a potential candidate for multiple surgeries, depending on presenting complications of the disease.[5] Individualized approach is recommended based on specific needs of individual cases. For cervical or thoracolumbar spine deformities associated with myelopathy, surgical fusion is advocated. Genu valgum, carpal tunnel syndrome, trigger digits, hip dysplasia and osteoarthritis may all require surgical intervention.[5] Our index case was counseled for bilateral Total Hip Arthroplasty with customized prosthesis on the advice of an Arthroplasty Surgeon, but was limited by non availability of fund.

Although he appreciated the need for continual follow up on his case, he was lost to follow up about a year. We have re-established contact with the patient, but he still has significant financial challenge and cannot afford surgery. He is, however, coping with the pain of osteoarthritis of the hips. This work is a preliminary report on the case. It

will be worthwhile to be able to conduct requisite diagnostic biochemical assays in urine and blood for GAGs and for lysosomal enzymes, and to observe the outcome of Total Hip Arthroplasty using customized prosthesis in this patient.

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