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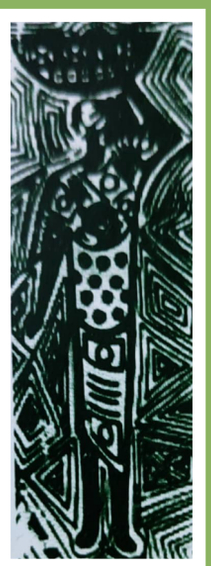

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CASE REPORT

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Challenges of Care in Mucopolysaccharidosis IVa (Morquio Syndrome Type A) in a Resource-Constrained Setting: A Case Report

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Abstract
Mucopolysaccharidosis type IVA (MPS IVA), also known as Morquio syndrome type A, is a rare inherited metabolic disorder resulting from the deficiency of the N-acetylglucosamine-6-sulfate sulfatase enzyme. A 5-year-old boy was referred to the Paediatric Endocrinology Clinic for evaluation and possible growth hormone therapy due to concerns about short stature. The patient was initially seen by the Orthopaedic Surgery team, who noted significant growth impairment and skeletal abnormalities. On examination, he had an abnormal gait. Radiological assessment revealed short and broad metacarpals, tapering phalanges, and hypoplastic, irregular carpal bones, which are classical features of mucopolysaccharidosis type IVA (MPS IVA). Enzyme analysis showed a markedly reduced level of N-acetylgalactosamine-6-sulfatase, confirming the diagnosis of MPS IVA. This case report highlights the challenges faced in diagnosing and managing this rare condition in a resource-constrained setting. This report underscores the importance of early diagnosis and access to enzyme replacement therapy (ERT), particularly in resource-limited regions.

Keywords: Enzyme replacement therapy, Morquio syndrome, Mucopolysaccharidosis Type IVA, Nigeria, Rare disease, Skeletal dysplasia.

Introduction

Mucopolysaccharidosis type IVA (MPS IVA), or Morquio A syndrome, is a rare autosomal recessive lysosomal storage disorder caused by a deficiency of the enzyme N-acetylgalactosamine-6-sulfate sulfatase (GALNS).[1] This deficiency results in the accumulation of specific glycosaminoglycans (GAGs), namely keratan sulfate and chondroitin-6-sulfate, predominantly within cartilage, leading to progressive skeletal dysplasia and systemic involvement.[2] It was first described in 1929 by Morquio and Brailsford. The incidence is unknown, but it is estimated to be between 1 in 75,000 of the population in Northern Ireland, 1 in 200,000 of the population in British Columbia, and 1 in 640,000 live births in Western Australia. Classic clinical features include short-trunk dwarfism, kyphoscoliosis, pectus carinatum, joint laxity, and genu valgum, often manifesting within the first few years of life.[3] Non-skeletal manifestations may include corneal clouding, cardiac abnormalities, hearing loss, and respiratory insufficiency, although intelligence is typically preserved.[4] To date, no cases of MPS IVA have been reported in Nigeria or other sub-Saharan African countries, though

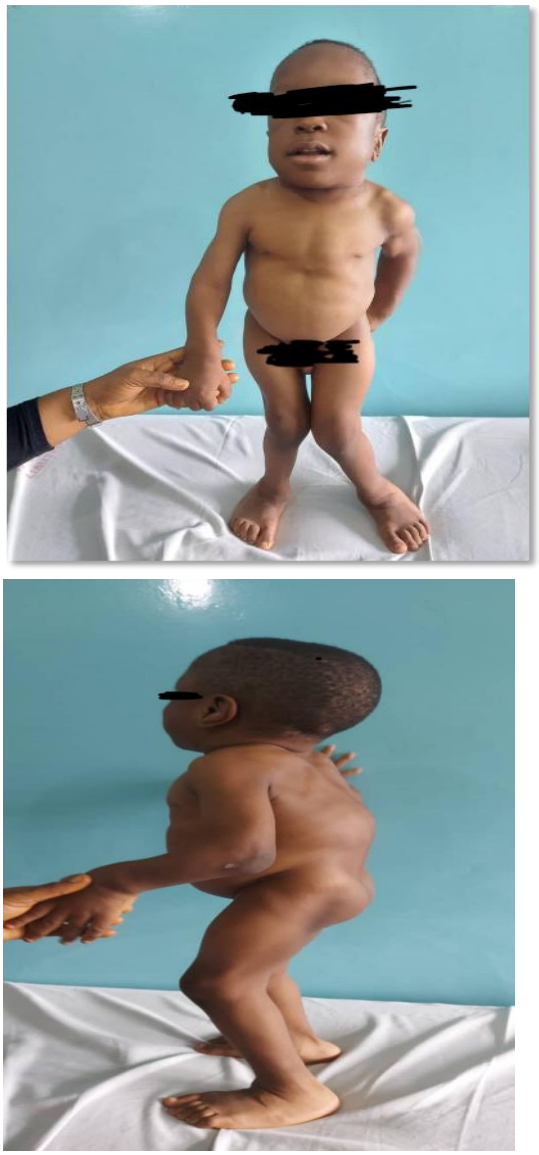
limited surveillance and diagnostic challenges may contribute to underrecognition. Isolated reports from North or South Africa, if any, remain unconfirmed or unpublished.

Case Presentation

A 5-year-old male was referred to the Paediatric Endocrinology Clinic at the Lagos University Teaching Hospital for evaluation and possible growth hormone therapy due to concerns about short stature. The patient was initially seen by the Orthopaedic Surgery team, who noted significant growth impairment and skeletal abnormalities. His primary concerns included delayed growth, joint deformities, and pain during movement. There was no known family history of similar conditions, and no significant psychosocial or genetic history was initially reported. The child had not undergone any significant medical intervention before this referral, aside from routine paediatric care. The parents are not related.

On examination, the patient had abnormal gait and coarse facial features. He had a short neck and a disproportionate short trunk with widened wrists and ankles. He also had bilateral genu valgum (knock knees), as shown in Figs 1 and 2, and experienced significant pain with movement. His anthropometry revealed a weight of 14kg (-2.06 z-score), a height of 81.7cm (-6.12 z-score), and a body mass index (BMI) of 21kg/m² (+3.35 z-score) for his age and gender.

Skeletal radiographs (Figures 4 and 5) of our patient revealed classic findings associated with MPS IVA, including bilateral genu valgum, short and wide metacarpals, tapered phalanges, and hypoplastic, irregularly ossified carpal bones, as well as anterior central vertebral body beaking (Figure 6).



Figures 1 and 2: Anterior and lateral views of a child with Morquio A syndrome (MPS IVA) showing characteristic features including short trunk dwarfism, prominent forehead, pectus carinatum, genu valgum (knock-knees), and joint laxity.

Figure 3: Short, broad hands with stubby fingers.

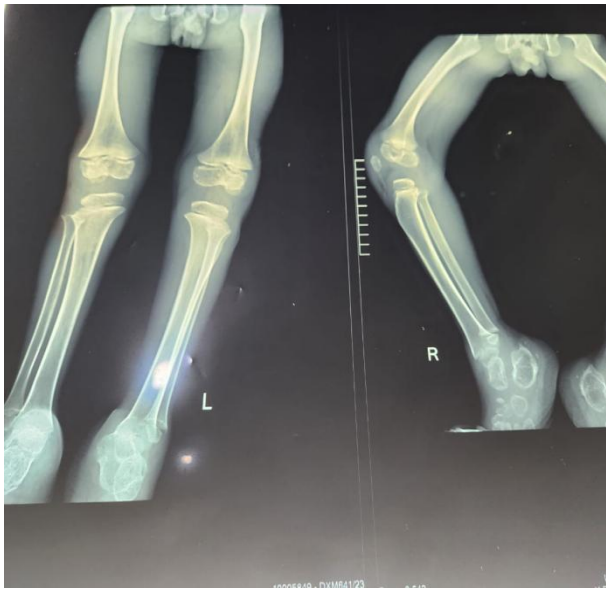


Figure 4: X-ray of the Legs showing bilateral genu valgum.

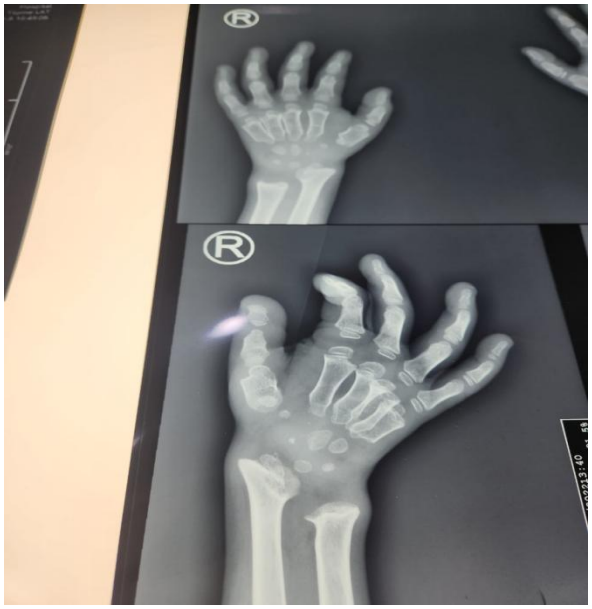


Figure 5: X-ray of the hand (AP) showing Short and broad tubular metacarpals, tapering phalanges, and hypoplastic, irregular carpal bones.

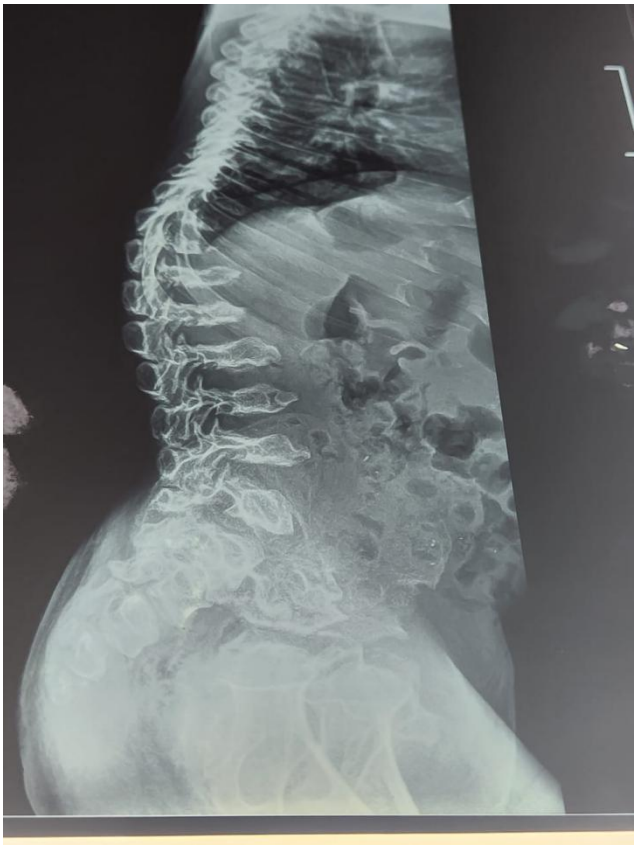


Figure 6: Thoracolumbar and sacral radiograph showing exaggerated thoracic kyphosis. Also seen is a reduction in vertebral body heights, anterior central vertebral body beaking and posterior vertebral body scalloping.

Diagnostic Assessment

Initial laboratory tests, including serum calcium, phosphorus, alkaline phosphatase, albumin, thyroid function, and insulin-like growth factor-1 (IGF-1) levels, were all within normal ranges. Radiological assessment revealed classical features consistent with mucopolysaccharidosis type IVA (MPS IVA), including short and broad metacarpals, tapering phalanges, and hypoplastic, irregular carpal bones as shown in Figure 5. The bone age was estimated to be 4.5 years, which is slightly behind the chronological age. Definitive enzyme analysis revealed a markedly reduced level of N-acetylgalactosamine-6-sulfatase, confirming the diagnosis of MPS IVA (Morquio Syndrome Type A). The limited availability of advanced biochemical and genetic tests within the local healthcare setting challenged the diagnostic process. Fortunately,

enzyme analysis was facilitated through an external partnership with Sanofi-Aventis Ltd in South Africa.

Following diagnosis, the child was yet to commence enzyme replacement therapy (ERT), which is the standard of care for MPS IVA. The treatment presently costs $380,000 (NGN 608,000,000) per year, making it an extremely expensive treatment option that is inaccessible and unaffordable for the patient.[2] Efforts were underway to secure access to ERT, which is both expensive and not available in Nigeria. The current treatment being provided includes supportive care through physiotherapy and pain management. Growth hormone therapy was deemed inappropriate given the underlying aetiology of the short stature.

The patient has been under close follow-up in the paediatric endocrinology and orthopaedic units. While awaiting ERT, multidisciplinary care is being provided to manage his skeletal symptoms and monitor disease progression. He is undergoing physiotherapy, one hour per session, three times a week, which helps improve his muscle strength and joint stability. He has undergone Adenotonsillectomy, which improved his airway obstruction. Intervention adherence and tolerability have been assessed through regular clinic visits and parent reports. No adverse events have been reported to date. The lack of access to definitive therapy remains a significant challenge.

Ethics

Informed consent was obtained from the child's parents for publishing this case. They willingly provided permission for the use of clinical data and images, with an understanding of the educational and advocacy value of the case in highlighting the challenges of managing rare diseases in resource-constrained settings.

Discussion

Patients with MPS IVA (Morquio A syndrome) often appear normal at birth, but initial presenting symptoms typically manifest between the first and third years of life, primarily through skeletal abnormalities.[5] In our case, the child was referred for evaluation of short stature at the age of five years. However, careful clinical examination revealed hallmark musculoskeletal features, including abnormal gait, coarse facies, short neck, widened wrists and ankles, bilateral genu valgum, and significant pain with movement—findings that strongly raised suspicion for MPS IVA. Similar to other reported cases, the index patient exhibited short stature, joint laxity, and progressive skeletal dysplasia, which are among the most frequent initial manifestations of MPS IVA.[6]

Skeletal radiographs revealed classic features associated with MPS IVA, including bilateral genu valgum, short and wide metacarpals, tapered phalanges, hypoplastic and irregularly ossified carpal bones, and anterior central vertebral body beaking. These findings are consistent with prior literature, where platyspondyly, anterior vertebral beaking, coxa valga, and odontoid hypoplasia are well-described radiologic hallmarks.[7] The index patient's bone age was slightly delayed, in keeping with reports of delayed skeletal maturation in MPS IVA. However, it is essential to note that bone age assessment may be confounded by reduced bone mineral density, a frequently observed finding in individuals with Morquio A syndrome. This reduction in bone mineral density can limit the reliability of bone age estimations, especially when using standard radiographic techniques. Moreover, advanced imaging techniques such as dual-energy X-ray absorptiometry (DEXA), which could offer more accurate assessment, remain expensive and largely inaccessible in many low-resource settings. This represents a significant gap in care, underscoring the need for future research to develop cost-effective and accessible diagnostic tools for evaluating bone health in this population.

While delayed bone age is commonly reported, the possibility of normal bone age readings in MPS IVA patients cannot be entirely excluded. To date, there is a lack of robust data on the full

range of bone age findings in these patients. We recommend that future studies include a broader literature review to examine whether cases with normal bone age have been documented and to determine the frequency of this occurrence. This would help refine diagnostic approaches and avoid over-reliance on bone age as a marker of disease progression.

Extra-skeletal manifestations are critical in MPS IVA, including restrictive lung disease, cardiac valve abnormalities, hearing loss, and corneal clouding.[8] Although we did not observe overt cardiac or respiratory symptoms in the index patient at the time of diagnosis, these complications may emerge with disease progression and require longitudinal monitoring. Early recognition and multidisciplinary surveillance are crucial for enhancing quality of life and outcomes.[9,10] One notable feature in this patient is the level of pain and movement restriction, which was significant during examination. While skeletal abnormalities are expected, the extent of pain in the index patient was pronounced. Painful ambulation and joint discomfort have been reported in MPS IVA but are not always as prominent early in the disease course. This suggests possible early joint instability or secondary nerve compression due to skeletal abnormalities.

Bone mineral density is significantly reduced in patients with MPS IVA, as evidenced by DXA studies showing whole-body Z-scores around −2 and lumbar spine scores as low as −3.4 in ambulators and non-ambulators alike.[5] However, when adjusted for short stature and bone geometry, HAZ-adjusted BMD scores often normalise (e.g., mean lumbar-spine HAZ-adjusted $Z \approx -0.1$). This reduction in BMD confounds bone age assessment; standard radiographic bone age readings may underestimate actual skeletal maturation, as low mineralisation alters maturation markers and ossification patterns. Notably, technical and financial limitations restrict access to DXA or lateral distal femur measurements, particularly in low-resource settings, thereby further impeding the accurate evaluation of skeletal maturation and fracture risk.[10] While delayed bone age is common, there are sparse reports of normal bone age in MPS IVA (e.g., two cases with unaffected carpal ossification despite typical radiologic dysostosis), highlighting heterogeneity that warrants systematic investigation.

Enzyme replacement therapy with **elosulfase alfa** (Vimizim), a recombinant form of human GALNS, has demonstrated long-term stabilisation of endurance, pulmonary function, and urinary keratan sulfate levels in children and adults with MPS IVA, with mean 6-minute walk distances increasing by ≈32 m after 120 weeks, and stability maintained over 5–6 years of follow-up in real-world registry data, without new safety concerns apart from infusion-related hypersensitivity in 2–3% of patients. Patients also report a clinically meaningful reduction in chronic musculoskeletal pain over the first 52 weeks of therapy. The mechanism of action involves the uptake of exogenous GALNS enzyme via mannose-6-phosphate receptors, facilitating the lysosomal degradation of accumulated glycosaminoglycans and reducing inflammation in joint cartilage. However, penetration into avascular skeletal/cartilage tissue is limited, and severe dysostosis remains largely unresponsive.

The annual cost of therapy ranges from approximately US$380,000 to over US$2 million in some countries. Health technology assessments in the UK, Ireland, and other regions have concluded that its cost-effectiveness remains below accepted thresholds yet, studies from Colombia suggest that ERT may reduce long-term complications and associated healthcare costs Importantly, patient registry and qualitative data from MorCAP show sustained functional benefits, quality-of-life improvements, and caregiver-reported daily living gains over multiple years, with no novel adverse events identified beyond manageable infusion reactions. Thus, while elosulfase alfa offers meaningful clinical and

patient-centred benefits and is mechanistically aligned with treating the underlying enzymatic defect, its high cost and limited skeletal impact underline the need for ongoing research into adjunctive therapies and more affordable delivery models.

Diagnosis of MPS IVA is based on clinical suspicion, radiological features, and confirmation via biochemical or genetic testing. In our case, diagnosis was confirmed by demonstrating significantly reduced N-acetylgalactosamine-6-sulfate sulfatase activity through enzyme assay—a standard diagnostic method.[1] Access to enzyme replacement therapy (ERT) remains a challenge in many low-resource settings like ours, but efforts are ongoing to initiate therapy for the child. ERT with elosulfase alfa (approved by the FDA in 2014) has shown promising results in slowing disease progression and improving endurance, although long-term outcomes are still under evaluation.[5]

Conclusion

Mucopolysaccharidosis IVA is a rare and challenging condition that requires early diagnosis and access to specialised treatment. While diagnosis during infancy may be delayed due to nonspecific early symptoms, many cases exhibit distinct phenotypic features—particularly skeletal abnormalities—that become more apparent in early childhood, facilitating clinical recognition and diagnosis. Enzyme replacement therapy (ERT) significantly improves patient outcomes; however, its availability remains limited in resource-constrained settings. This case underscores the need for greater awareness and resources for managing rare metabolic disorders.

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Authors' Contributions: All authors were involved in the clinical management of the case and conceived the report. BFO and OEE drafted the manuscript. All authors revised the draft of the manuscript for sound intellectual content and approved the final version of the manuscript.

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