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A Child Presenting with Mucopolysaccharidosis

Ntombizodwa Madi, Fatima Yakoub Moosa, Kebashni Thandrayen

Department of Paediatrics, Chris Hani Baragwanath Academic Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
Email: Ntombizodwa.Mahlaba2@wits.ac.za, fatima.moosa@wits.ac.za, Kebashni.thandrayen@wits.ac.za

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Abstract

The lysosomal storage disorders are a group of diseases that are typified by an accumulation of waste products in the lysosomes. Mucopolysaccharidoses are lysosomal storage disorders due to diverse lysosomal enzyme deficiencies. Ms HT was 2 years and 5 months old when she presented to our metabolic bone clinic with clinical features that were suggestive of a genetic syndrome that was associated with a metabolic bone disease. The urine GAG spot test was positive. The MPS screen identified a reduction in arylsulfatase B activity and sequencing of the ARSB gene detected a pathogenic variant, in keeping with Maroteaux-Lamy syndrome. The diagnosis of MPS is confirmed by urine GAG, enzyme activity analysis and genetic testing. The available treatments include hematopoietic stem cell transplantation, enzyme replacement therapy and surgery. MPSs are heterogeneous, progressive, multisystem diseases for which diagnosis is often delayed. Greater awareness of MPS will enable early diagnosis and treatment. Treatment is however costly and is frequently unavailable to patients in the public sector.

Keywords

Mucopolysaccharidosis, Lysosomal Storage Disorders, Maroteaux-Lamy Syndrome

1. Introduction

Lysosomes are formed by budding off from the membrane of the trans-Golgi network. Macromolecules are absorbed into the cell in vesicles formed by endocytosis. The vesicles fuse with lysosomes, which then break down the macromolecules using hydrolytic enzymes. The lysosomal storage disorders (LSD) are a group of approximately 70 diseases that are distinguished by an accumulation of waste products in the lysosomes resulting in the formation of large intracellular vacuoles [1] [2].

Mucopolysaccharidoses (MPSs) are a group of lysosomal storage disorders that are due to multiple lysosomal enzyme deficiencies, causing progressive storage of glycosaminoglycans (GAGs) in tissues and organs, and these GAGs cause multi-organ dysfunction [2].

There are seven types of MPSs that are known and are due to 11 different enzyme deficiencies. The inheritance pattern of MPSs is autosomal recessive, with MPS II being the only one with X-linked inheritance [3]. The incidence of MPS VI (the type of MPS present in our patient) is reported to be 1 per 320000 live births [4].

The aim of our case report is to raise awareness of this rare but important and potentially fatal disorder, so that its treatment may be made available to our South African patients, which would be both life-changing and lifesaving.

2. Background

2.1. Pathophysiology

MPSs are rare genetic bone disorders accounting for less than 1% of all genetic disorders. The incidence is low, but the disorder occurs throughout the world in various ethnic groups and demographic regions [2]. The pathophysiological causes as well as the pertinent clinical findings of the various MPSs have been summarized in **Table 1**.

MPS I, known as Hurler syndrome, was first described by Dr Gertrud Hurler in 1919. It is due to the mutation of the gene α-L-iduronidase (IDUA) and more than 100 different alleles of this gene can cause MPS I. There are three clinical subtypes, which are divided based on their clinical severity of MPS I; that is, Hurler syndrome (severe), Hurler-Scheie syndrome (intermediate) and Scheie syndrome (mild) [5].

MPS II, or Hunter syndrome, is caused by the mutation of the gene Iduronatesulfatase (IDS). MPS II is X-linked recessive, thus it primarily affects males, but females can be affected because of autosomal X-chromosomal translocation and non-random X-chromosome inactivation. It is divided into two subtypes due to its severity whereby MPS IIA is severe and MPS IIB is of moderate severity [6] [7].

There are four subtypes of MPS III (Sanfilippo syndrome) with subtypes IIIA, IIIB, IIIC and IIID; due to the deficiency of heparan-N-sulfatase (SGHS), α-N-acetylglucosaminidase (NAGLU), α-glucosaminidase acetyltransferase (HGSNAT) and N-acetylglucosamine 6-sulfatase (GNS) respectively. MPS IIIA and IIIB are more common than IIIC and IIID in clinical settings [8].

MPS IV also known as Morquio syndrome is due to the deficiency in N-acetylgalactosamine-6-sulfate sulfatase (GALN in MPS IVA) or β-galactosidase (GLB1 in MPS IVB). A deficiency in GALNS impairs the degradation of chondroitin-6-sulfate (C6S) and keratansulfate (KS) which contributes to severe clinical symptoms. GLB1 deficiency leads to a moderate phenotype with only accumulation of KS [9].

Table 1. Types of MPS.

MPS	Syndrome(s)	GAGs accumulated	Enzyme deficiency	Genetic mutation	Mode of inheritance	Main clinical presentation
I	Hurler's Scheie Hurler-Scheie	Dermatan, heparan sulphate	*α*-L-iduronidase deficiency	*IDUA* 4p16,3	Autosomal recessive	Progressive mental decline and loss of physical skills by 2-4 years of age. Hearing loss, enlarged tongue and corneal clouding Restricted joint movement Hurler's syndrome is the most severe form of MPS I. Scheie is the mildest form of MPS I. Children with Scheie syndrome have normal intelligence or may have mild learning disabilities Hurler-Scheie is less severe than Hurler syndrome alone
II	Hunter's	Dermatan, heparan sulphate	Iduronate sulfatase deficiency	IDS Xq28	X-linked recessive	Two clinical subtypes which are neuropathic (with CNS involvement) and non-neuropathic (without CNS involvement) No corneal clouding Hepatosplenomegaly Hydrocephalus Heart valve abnormalities
III	Sanfilippo (Subtypes A-D A = Most severe)	Heparan sulphate	A: heparan N-sulfatase B: alpha-N-acetylglucosaminidase C: acetyl-CoAlpha-glucosaminide acetyltransferase D: N-acetylglucosamine 6-sulfatase	A: *SGSH* 17q25,3 B: *NAGLU* 17q21.2 C: *HGSNAT* 8p11.21-p11.1 D: GNS 12q14,3	Autosomal recessive	Progressive dementia, aggressive behaviour, hyperactivity, seizures, some deafness and loss of vision, and an inability to sleep more than a few hours at a time Delayed mental, motor and language skill development
IV	Morquio (Subtypes A and B)	Keratan and chondroitin sulphate,	A: N-acetylgalactosamine-6-sulfatase B: beta-galactosidase	A: *GALNS* 16q24,3 B: GLB1 3p22,3	Autosomal recessive	Onset is between ages 1- and 3-years Neurological complications include spinal nerve and nerve root compression; progressive skeletal changes, particularly in the ribs and chest; conductive and/or neurosensory hearing loss and clouded corneas. Intelligence is normal unless hydrocephalus develops and is not treated
VI	Maroteaux Lamy	Dermatan, chondroitin sulphate	N-acetylgalactosamine 4-sulfatase	*ARSB* 5q13-14	Autosomal recessive	Skeletal abnormalities; macrocephaly; coarse facial features; macroglossia; contractures; Carpal tunnel syndrome; spinal stenosis; hepatosplenomegaly; umbilical hernia, clouded corneas; growth stops at age 8 years

Continued

VII	Sly	Dermatan/ heparan/ chondroitin sulphate	beta-glucuronidase	*GUSB* 7q11,21	Autosomal recessive	Hydrops fetalis (severe form); mild to moderate intellectual disability; communicating hydrocephalus, nerve entrapment, corneal clouding; short stature; joint stiffness and restricted movement, and umbilical and/or inguinal hernias.
IX	Natowicz	Hyaluronan	Hyaluronidase deficiency	*HYAL1* 3p21,3	Autosomal recessive	Periodically painful soft tissue masses around the joints, acquired short stature and erosion of the hip joint, although joint movement and intelligence are normal

MPS VI (Maroteaux Lamy) that has been diagnosed in our patient is characterized by a deficiency of N-acetylgalactosamine-4-sulfatase that results in the storage of Dermatan chondroitin sulphate (DS) and chondroitin-4-sulfate (C4S). It presents as a multi-system disorder due to accumulation of GAGs in numerous organs and progressive clinical deterioration with age [10].

MPS VII (Sly syndrome) is a rare type of MPS that is due to the lack of the β-D-glucuronidase enzyme that causes an accumulation of DS, HS (heparan sulphate), C4S, and C6S in tissues. There are multiple phenotypes and multisystemic involvement [11].

MPS IX (Natowicz syndrome) is a very rare type of MPS that is caused by the mutation in the gene HYAL1 that results in the lack of the enzyme hyaluronidase with accumulation of hyaluronan. Hyaluronan is required for cartilage formation and joint lubrication [12].

2.2. Clinical Findings

MPS I

Patients with MPS I presents with skeletal abnormalities termed dysostosis multiplex which result in joint immobility, restricted growth and immobility. Other symptoms and signs include umbilical and inguinal hernias, coarse facial features, chest deformity, gibbus deformity, recurrent upper respiratory tract infections, hearing and vision loss, organomegaly and cardiac disease. Developmental and cognitive impairment occur later in the disease process. Patients with severe disease die in the first year of life whilst those with milder disease survive till adulthood [13] [14].

MPS II

The presentation of MPS II is like MPS I with short stature, umbilical and inguinal hernias, coarse facial features, cardiac disease, hepatosplenomegaly and chronic upper respiratory tract infections. Early skeletal deformities include kyphosis, stiffness of joints and spinal cord compression. Affected patients may

develop chronic diarrhoea and communicating hydrocephalus. Neurological and cognitive impairment varies amongst patients. Developmental and speech delay is frequently diagnosed around 2 - 5 years of age. Patients with severe forms of disease die early in life similar to MPS I [15].

MPS III

All forms of MPS III present with cognitive and neurological impairment with little or no somatic involvement. This disorder may be recognized in childhood by developmental delays, behavioural difficulties, sleep disturbances and dementia. The mental retardation can be profound in patients with severe disease, with a lack of development of social or communicative skills in early childhood. There are 3 phases of the disease: Phase I is pre-symptomatic with normal development. In phase 2, there is progressive cognitive impairment, sleep disturbance and behavioural problems. The third phase begins in adolescence with the decline in motor function and loss of mobility [16].

MPS IV

MPS IV is characterized by a skeletal dysplasia which is distinct from the dysostosis multiplex; seen in MPS I, II and VI. Patients also present with joint hypermobility rather than stiffness, cervical spine instability and communicating hydrocephalus. Patients with mild forms of the disease can live past the third decade of life. Other common features are corneal clouding, hearing loss, respiratory obstruction and sleep apnoea [17].

MPS VI

Patients with MPS VI have normal neurology and development but CNS pathology such as communicating hydrocephalus, cerebral atrophy and low IQ have been documented. They present with signs and symptoms that are like MPS I, II and VII. Patients with severe disease present early between 2 and 3 years of age and those with milder disease present in the teenage years or early adulthood. Typical symptoms include coarse facial features and enlarged tongues, hepatosplenomegaly, cardiac valve problems, short stature, joint stiffness and hearing loss [17] [18].

MPS VII

Patients with MPS VII can present with hydrops fetalis and they may be stillborn, or they may die shortly after birth. The time of onset ranges from infancy to childhood but few patients survive into adulthood. Patients have the same clinical features as MPS I and II with coarse facial features, corneal clouding, skeletal deformities and hydrocephalus. The patients with MPS VI have a short life expectancy and they die due to heart diseases and airway obstruction [11].

MPS IX

MPS IX was first described in 1996 with periarticular soft-tissue masses and nodular hyperplasia, short stature and acetabular erosions. Other symptoms may include cysts, frequent ear infections and a cleft palate. MPS IX should be considered in patients who are diagnosed with polyarticular juvenile idiopathic arthritis who fail to respond to conventional treatment [11] [19].

2.3. Diagnosis

The medical history and examination of patients and their family members is important for the diagnosis as MPSs are inherited diseases. The age of onset, the rate of clinical progression and the sequence with which the symptoms occur, can help to elucidate the type of MPS. X-rays, computed tomography (CT) and magnetic resonance imaging (MRI) are frequently used diagnostic methods for skeletal, cardiac, and intracranial involvement [12].

A valuable screening test for MPSs is the urine GAG spot test, but false negative results can occur due to assays that lack adequate sensitivity, dilute samples and GAG accumulates in tissues over time and thus will not be eliminated in the urine. Enzyme activity assays based on cultured fibroblasts, leucocytes, plasma, or serum, cultured from chorionic villus or amniocytes are definitive for a specific MPS disorder and are considered the gold standard for diagnosis. Gene sequencing can identify the type of gene mutation causing the enzyme deficiency and help for genetic counselling of the patient and their families and to facilitate family planning [3] [20].

2.4. Treatment Options

Enzyme replacement therapy (ERT) is given intravenously and indicated for patients with MPS I, II, IVA, VI, and VII. ERT does improve soft tissue complications and improve the patient's quality of life. ERT does not cross the blood brain barrier and thus will not improve central nervous system effects and it also has no effects on avascular bone lesions and cartilage. ERT is expensive and requires weekly injections. Hematopoietic stem cell transplantation (HSCT) and ERT can slow the progression of disease. HSCT is more cost effective compared to ERT. HSCT requires matched donors and there is a risk of graft versus host disease [21].

SRT (substrate reduction therapy) aims to reduce an excess of a substrate thus slowing GAG synthesis. These small molecules that inhibit substrate synthesis are administered orally. These facilitate SRT and penetrate the blood-brain barrier. Genistein, a soy-derived isoflavone, was first identified as a potential drug for SRT; it acts as a tyrosine kinase inhibitor and alleviates neurological manifestations. However, a subsequent clinical trial of SRT failed to find any significant neurological benefit because of a decline in urinary GAGs [22].

Gene therapy can be in vivo which is when a gene product is delivered directly into the body systemically or is administered in-situ. Gene therapy can also be ex vivo whereby the patients' stem cells are modified externally and infused back into the patient's system. An immune reaction can occur to a vector or gene product. Gene therapy is still in development, its long-term effects are still unknown and clinical trials are still in progress [23].

3. Case Presentation

Ms HT presented to our metabolic bone clinic at 2 years 5 months of age with

short stature. She was under-weight for age and had relative macrocephaly. She had clinical features which were suggestive of a genetic syndrome with underlying metabolic bone disease.

Her mother reported that she had a normal pregnancy, with no history of exposure to any known teratogens. There were no antenatal scans performed on the baby. Ms HT was born via normal vaginal delivery, with normal Apgar scores and her anthropometrical measurements were normal at birth. She required nasal prongs oxygen for transient tachypnoea of the neonate. She had no other admissions. In terms of her development, her mother noticed an unusual curvature of her spine at 14 months of age, but all her milestones were attained at the appropriate age. The parents were non-consanguineous. They had a son who demised at 1 year from acute gastroenteritis and he too had a same spinal deformity.

On clinical examination, her growth measurements plotted on the weight for age Z-score of -2, a height for age Z score of -2 and head circumference plotted on the +1.5 Z score. She is under-weight and stunted for age and has relative macrocephaly. She had the following facial dysmorphic features: a prominent forehead, bitemporal narrowing, flattened facial profile, epicanthic folds, depressed nasal bridge with mild midface hypoplasia, prominent lips and fleshy ear helices (**Figure 1**).

Her chest examination revealed a pectus carinatum deformity. The lower ribs were flared with the left being more prominent than the right. She had limited extension at the elbow joints with a wide carrying angle and her fingers were slightly tapered, with prominent proximal interphalangeal joints. She had bilateral clinodactyly and the small joints of the hands were exhibiting decreased range of movement. There was limited supination at the forearms (**Figure 2**).

She had pes planus and genu valgum of left knee with limited extension at the knee joint. On examination of her back a thoracolumbar kyphosis was noted. She had patchy hyperpigmentation over the skin of the shoulders, upper and lower back. She had a large congenital melanocytic nevus (>15 cm in diameter) over the lower back, sacrum, and buttocks (**Figure 3**). She had normal neurodevelopmental, ophthalmologic, audiology, abdominal and cardiac examinations.

Prominent forehead, bitemporal narrowing, flattened facial profile, epicanthic folds, depressed nasal bridge with mild midface hypoplasia, prominent lips and fleshy ear helices

Figure 1. Facial features of Ms HT.

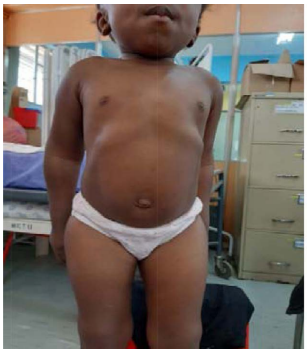

Figure 2. Ms HT chest and musculoskeletal examination findings.

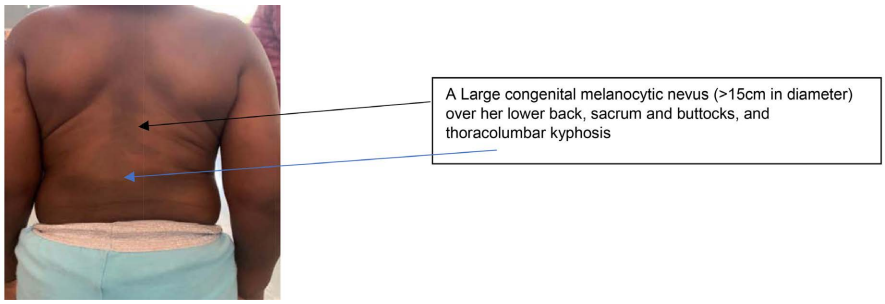

Figure 3. Ms HT examination findings of her back and skin.

On further investigations, her biochemistry, which included, renal function, calcium, phosphate, parathyroid hormone, and alkaline phosphatase were within normal ranges. Her echocardiogram showed a tri-leaflet aortic valve and mild aortic regurgitation (**Figure 4**). The skull radiograph showed caput quadratum, a rounded prominence of the frontal and parietal bones often seen in children with rickets (**Figure 5**). The chest radiograph was normal. The MRI of her spine showed an L3/L4 spondylolisthesis and dural ectasia of unknown cause (**Figure 6**). In view the above clinical features and initial investigations, a urine glycosaminoglycans screening test for MPS was sent, which was confirmed to be positive. Finger prick blood spot samples to assess enzyme activity were sent to North-West University to the Centre for Human Metabolomics. This would aid in identifying specific deficiencies, thus assist with classifying the type of LSD and guide further management. This expanded MPS screen identified a significant reduction in arylsulfatase B activity. This is in keeping with MPS VI (Maroteaux-Lamysyndrome) and sequencing of the *ARSB* (Arylsulfatase B) gene detected a homozygotic variant (c.905G>A; p. Gly302Glu) that was classified as likely pathogenic according to the American College of Medical Genetics and Genomics [24].

Ms HT has continued to follow up at our metabolic bone clinic. She is receiving physiotherapy and occupational therapy for joint stiffness and her mobility limitations. She has had a repeat echocardiogram that has shown worsening of the cardiac disease, with mild to moderate mitral and tricuspid valve regurgitation and trivial aortic valve regurgitation (**Figure 7**). She is on enalapril to reduce

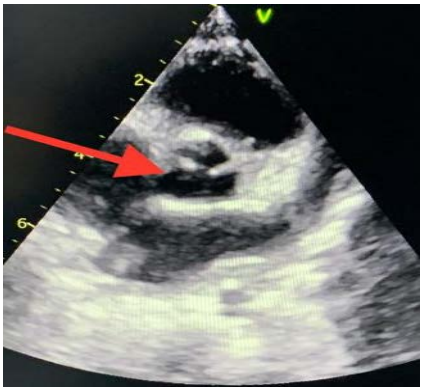

Figure 4. Echocardiogram showing a tri-leaflet aortic valve.

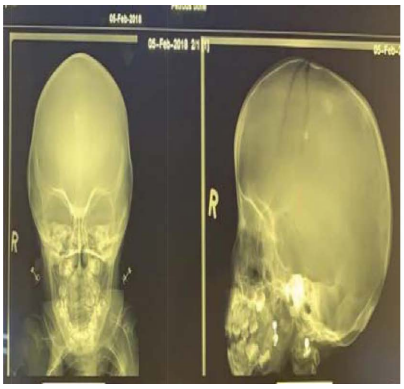

Figure 5. The skull radiograph showing caput quadratum.

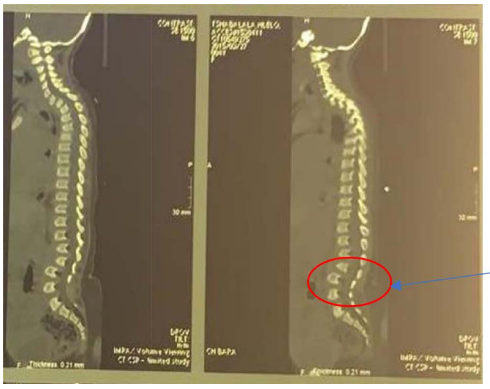

Figure 6. Ms HT's MRI spine: L3/L4 spondolisthesis and dural ectasia of unknown cause.

the mitral regurgitation. She has recurrent upper respiratory and ear infections, which we have had to treat with antibiotics and antipyretics. She is following up with the ear, nose, and throat specialists; ophthalmologists; speech therapists and the audiologist.

In terms of Ms HTs current outcome, her hearing is worsening and awaits hearing aids. She has corneal clouding that is compromising her vision. The thoracolumbar kyphosis has worsened but the spondylolisthesis that was discovered on the initial MRI of the spine has not worsened with no spinal compression. Her cardiac function has deteriorated thus she is less active.

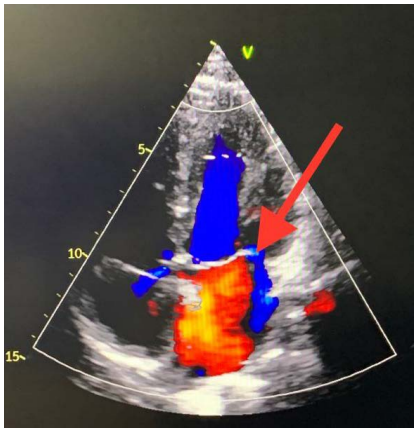

Figure 7. Echocardiogram showing mild to moderate mitral valve regurgitation.

Ms HT a 6-year-old female patient, whose current condition is that: she can mobilize unassisted; she complains of painful joints at the knees, elbows, and wrists. She has developed corneal clouding and the spinal deformity is worsening. Her audiology tests show progressive hearing loss. She is on treatment for aortic regurgitation, but we have not been able to obtain ERT for the treatment for confirmed MPS VI.

4. Discussion

The lysosomal storage disorders (LSD) are a group of approximately 70 diseases that are characterized by an accumulation of waste products in the lysosomes, resulting in the formation of large intracellular vacuoles. MPS are a group of lysosomal storage disorders typified by diverse lysosomal enzyme deficiencies, causing progressive storage of glycosaminoglycans (GAGs) in tissues and organs that culminates in multi-organ failure. GAG accumulation is progressive; thus, signs and symptoms of the disease worsen with age. Seven types of MPS are known and are due to 11 different enzyme deficiencies [1] [2] [3] (**Table 1**).

MPS VI is rare autosomal recessive disorder that is a result of mutations in the *ARSB* gene which leads to a deficient activity of the lysosomal enzyme N-acetylgalactosamine 4-sulfatase (ASB) [25]. Children with MPS VI, Maroteaux-Lamy syndrome, usually have normal intellectual development but share many of the physical symptoms found in Hurler syndrome (which is the most severe form of MPS, MPS type 1) [26].

Our patient had normal intellectual development, with normal growth initially. However, with ongoing follow-up it is noted that she is now underweight and stunted for her age, but still had preserved intelligence.

Maroteaux-Lamy syndrome is characterized by a spectrum of severe symptoms. The neurological complications include clouded corneas, deafness, thickening of the dura around the brain and spinal cord and pain caused by compressed or traumatized nerves and nerve roots [27]. Ms HT had normal vision and hearing initially, but she has developed corneal clouding and progressive

hearing loss. The MRI of her spine did show dural ectasia. The most common complication of MPS VI is spinal cord compression due to thickening of the dura around the brain and spinal cord [28].

Growth is normal in the beginning but stops suddenly at about 8 years of age. By age 10 children have developed a shortened trunk, hunched posture and restricted joint movement. In more severe cases, children also develop a protruding abdomen and forward curving of the spine. Skeletal changes (particularly in the pelvic region) are progressive and limit movement [29]. Our patient is still able to ambulate without assistive devises, although she is developing progressive ankylosis of her large joints. Many children also have umbilical or inguinal hernias which Ms HT did not have. Nearly all children have some form of heart disease, as seen in our patient. She had mild Aortic valve regurgitation for which she is following up with the paediatric cardiologists and receiving treatment. The accumulation of dermatansulfate and chondroitin sulfate (GAGs) leads to corneal clouding, deafness, restricted joint movement, bone dysplasia, thickening of the dura, organomegaly and heart disease [29] [30].

MPS VI is diagnosed by a combination of clinical symptoms, raised urine GAG, a deficiency of ASB enzyme activity and genetic sequencing that reveals *ARSB* gene mutation variants [31]. The GAGs are unbranched polysaccharide chains containing repeated disaccharides with uronic acid, galactose or hexosamine. ASB enzyme activity can be performed on dry blood spots, on leukocytes or fibroblasts. Leukocytes and fibroblast are considered as the gold standard for demonstrating ASB enzyme activity [32]. The ARSB gene was discovered in 1990 and is mapped on chromosome 5q 13-14. This gene has a wide genetic heterogenicity and numerous mutations and polymorphisms have been described. There are more than 200 pathogenic variants of the ARSB gene reported on ClinVar, EmvClass, ClinVitae databases [25]. **Table 2** is an illustration of some of these pathological variants, including the variant that was described on our patient (c.905G>A; p. Gly302Glu) highlighted in yellow.

The presently available treatments for MPS VI are enzyme replacement therapy (ERT), with palliative surgeries for joint and skeletal deformities and spinal cord decompression (spinal cord compression is a major complication of MPS VI), ear-nose- and throat (ENT), neurosurgical, ophthalmic, and cardiac treatments [25] [33]. These treatments have been effective in ameliorating the lives of affected individuals but are far from assuring a complete return to normality. Hematopoietic stem cell transplantation (HSCT) or Bone marrow transplant for MPS VI has shown limited efficacy. HSCT is thought to deliver the cells required to produce the lacking enzyme to the tissues that are deficient of the enzymes and thus eliminating the symptoms. HSCT has been shown to be effective in MPS VI with the limitations of finding a suitable donor and transplant rejection [2] [34]. ERT is available for patients with MPS VI in many countries and is a safer option than HSCT [27]. ERT replaces the missing enzyme in the tissues and thus ameliorates the symptoms by decreasing the number of GAGs which

Table 2. ARSB gene pathological variants associated with MPS VI.

ARSB variant Location	Clinical significance
c.*905G>A (p.Gly302Glu)	Likely pathogenic
c.*3181T>A	Uncertain significance
c.*3181T>G	Benign
c.*3174T>G	Uncertain significance
c.1577del (p.Thr526fs)	Pathogenic
c.1601A>C (p.Ter534Ser)	Likely pathogenic
c.1558del (p.Arg520fs)	Pathogenic
c.1493T>C (p.Leu498Pro)	Likely pathogenic
c.1325C>T (p.Thr442Met)	Conflicting interpretations of pathogenicity
c.1261G>T (p.Glu421Ter)	Pathogenic
c.899-1337_1142+1055del	Pathogenic
c.284G>A (p.Arg95Gln)	Pathogenic/Likely pathogenic
c.238del (p.Val80fs)	Pathogenic (severe type of MPS VI)
c.215T>A (p.Leu72Gln)	Conflicting interpretations of pathogenicity (severe type of MPS VI)
c.200T>A (p.Ile67Asn)	Likely pathogenic

This table illustrates just a few of the ARSB variants for a complete representation see: https://www.ncbi.nlm.nih.gov/clinvar.

cause the disease [35] Galsulfase (Naglazyme), a purified human enzyme (rhASB), has been shown to improve walking capacity, stair-climbing capacity, pulmonary function, hepatosplenomegaly, cardiac function and survival in individuals with MPS VI [35] [36]. The importance of early ERT cannot be over-emphasized, as early ERT is effective in preventing the permanent effects of MPS that occur with disease progression. Thus, early diagnosis and treatment is crucial [36]. The reported side effects of ERT are hypersensitivity reactions and ERTs are unable to cross the brain blood barrier, thus central nervous system symptoms are not ameliorated [37] [38]. Future therapy in the form of gene therapy has also been tested in animal models of MPS VI and different types of viral vectors have shown promising results in delivering a correct version of the ARSB gene and achieving high levels of enzyme activity [39].

We have attempted to obtain ERT treatment for our patients at Chris Hani Baragwanath Academic Hospital with MPS VI, but it has proven unsuccessful due to the cost of treatment and lack of availability of ERTs in our country.

5. Conclusion

MPSs are heterogeneous, progressive, multisystem diseases. MPS may have a delayed diagnosis because of manifestations that mimic other disorders. The greater awareness of MPS will enable early diagnosis. The treatment for MPS VI

is currently unavailable to our patients at Chris Hani Baragwanath Academic Hospital South Africa. The reason for writing this case report is to raise awareness and initiate discussions or collaborations to provide a solution to our dilemma of non-availability of ERT, with the hope of improved patient outcomes.

Acknowledgements

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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List of Abbreviations

MPS: Mucopolysaccharidosis
GAG: Glycosaminoglycans
LSD: Lysosomal storage disorders
ASB: N-acetylgalactosamine 4-sulfatase
ARSB: Arylsulfatase B gene
ERT: Enzyme replacement therapy
HSCT: Hematopoietic stem cell transplantation
HS: Heparansulfate
DS: Dermatansulfate
KS: Keratansulfate
C4S: Chondroitin-4-sulfate
HA: Hyaluronic acid
SRT: Substrate reduction therapy