A Rare Encounter: Cardiac Manifestations in a Patient with Maroteaux-Lamy Syndrome (MPS VI)

Dr. Hershavardhini K[1], Dr. Veeresh Manvi[2], Dr. Shaila Pachapure[3]
[1]*MBBS, Junior Resident, Jawaharlal Nehru Medical college, Belagavi*
[2]*MBBS, MD pediatrics, F.N.B, Professor, pediatric cardiology, Jawaharlal Nehru Medical college, Belagavi*
[2]*MBBS, MD pediatrics, Assistant Professor, Department of Pediatrics, Jawaharlal Nehru Medical college, Belagavi*

Abstract: -
Background: Mucopolysaccharidosis type VI (MPS VI), or Maroteaux–Lamy syndrome, is a rare lysosomal storage disorder caused by *ARSB* gene mutations, leading to deficient arylsulfatase B enzyme activity and the accumulation of dermatan sulfate. This results in progressive multi-system involvement, with skeletal abnormalities, corneal clouding, and cardiovascular complications being prominent features.

Case Presentation: We report the case of a 2.8-year-old female, born to consanguineous parents, who presented with excessive sweating, frequent falls, poor appetite, delayed dentition, and skeletal deformities. She had a prior history of respiratory distress requiring hospitalization and diuretic therapy. On examination, she exhibited characteristic dysmorphic features, including coarse facies, frontal bossing, corneal clouding, widened wrists, and an umbilical hernia. Anthropometric assessment revealed severe growth failure (weight: 7.43 kg, Z-score: -3.97; height: 75.5 cm, Z-score: -4.34).

Cardiac evaluation detected a grade 3 systolic murmur, and echocardiography revealed mitral regurgitation, global left ventricular hypokinesia, and a significantly reduced ejection fraction of 25%. Radiographic findings showed dysostosis multiplex, including ovoid vertebral bodies, widened ribs, and bullet-shaped metacarpals. Whole exome sequencing confirmed a homozygous pathogenic *ARSB* mutation, consistent with MPS VI.

Conclusion: This case highlights the significance of early recognition of MPS VI, especially in patients with cardiac involvement. While enzyme replacement therapy remains the standard treatment, a multidisciplinary approach is crucial for optimizing outcomes and improving the patient's quality of life.

Keywords: **MPS VI, Cardiac complications, lysosomal storage disorder**

INTRODUCTION

Mucopolysaccharidoses (MPS) are a group of rare inherited metabolic disorders caused by the abnormal accumulation of glycosaminoglycans (GAGs) due to defective lysosomal enzyme function [1]. The global birth prevalence of MPS is estimated to be 0.77 per 100,000 live births [2], though this is likely an underestimation, as diagnosis is primarily based on clinical presentation. Early identification through newborn screening programs may provide more accurate prevalence data [2]. In India, comprehensive statistics on the incidence and prevalence of MPS remain limited [3].

Maroteaux–Lamy syndrome (MPS VI) is a rare autosomal recessive disorder caused by pathogenic mutations in the ARSB gene, which encodes the lysosomal enzyme N-acetylgalactosamine 4-sulfatase (arylsulfatase B) [4]. This enzyme deficiency leads to the accumulation of dermatan sulfate and chondroitin sulfate, causing progressive multi-system involvement. The classical features of MPS VI include skeletal abnormalities such as dysostosis multiplex, short stature, and motor dysfunction. Other commonly observed manifestations include corneal clouding, ENT complications, and orodental anomalies such as hypoplastic condyles, malpositioned teeth, and open bite [4].

The diagnostic process for MPS VI typically begins with the recognition of clinical features indicative of a metabolic disorder followed by quantitative glycosaminoglycan (GAG) analysis which detects elevated total urinary GAG levels. Qualitative analysis further identifies increased dermatan sulfate (DS), a hallmark of MPS VI. Confirmation of the

diagnosis is achieved through molecular genetic testing of the *ARSB* gene to identify disease-associated variants. However, newborn screening for MPS VI is available in only a few countries.[4] The primary treatment for MPS VI is enzyme replacement therapy (ERT) with galsulfase, which helps reduce glycosaminoglycan (GAG) accumulation and improve mobility and organ function[5]. Allogenic hematopoietic stem cell transplantation (HSCT) is considered a potential treatment for select patients with mucopolysaccharidoses (MPS) VI. Supportive care, including physical therapy, surgical interventions, and symptom management, is essential. Early treatment improves outcomes but does not prevent all disease complications [6]

Although cardiac involvement in MPS VI is rare, various forms of cardiovascular abnormalities, including valvular defects, myocardial hypertrophy, thickened chordae tendineae, and coronary artery narrowing, have been reported in other MPS types [4,7,8]. Mitral and aortic valve involvement, often associated with left ventricular hypertrophy, is the most frequently observed cardiac abnormality [4]. While cardiomyopathy is well-documented in MPS I [8,9], there is limited literature describing cardiac manifestations in MPS VI. Here, we present a rare case of a 2-year-old female diagnosed with MPS VI, exhibiting significant cardiac involvement. Here, we present a rare case of a 2.8 year old female diagnosed with MPS VI, exhibiting significant cardiac involvement.

CASE REPORT

A 2.8-year old female, born to a consanguineous marriage, presented to a tertiary care hospital with complaints of excessive sweating and frequent falls since she began walking at one year of age. She had a prior hospital admission at six months for respiratory distress and sweating, leading to a diagnosis of cardiac insufficiency and initiation of oral loop diuretics. Additionally, she had a history of poor appetite, delayed dentition, and bone deformities upon ambulation.

On examination, the child exhibited characteristic features, including coarse facial features, frontal bossing, widened wrists, lower chest indrawing, an umbilical hernia, an upturned nose, and corneal clouding (Figure 1). The child's anthropometric measurements revealed a weight of 7.43 kg (-3.97 Z-score) and a height of 75.5 cm (-4.34 Z-score), indicating severe undernutrition and stunting. Cardiac evaluation revealed a grade 3 systolic murmur, while a chest radiograph showed Ovoid or hypoplastic vertebral bodies, widened ribs with spatula-shaped ends and thoracolumbar kyphosis (Figure 2). Hand X-ray demonstrated bullet-shaped and irregular metacarpals, along with joint space widening and abnormal carpal bone development, consistent with mucopolysaccharidoses (MPS).(Figure 3). Echocardiography revealed mitral regurgitation, global left ventricular hypokinesia, and a significantly reduced ejection fraction of 25%.

Suspecting mucopolysaccharidosis (MPS), whole exome sequencing was performed. It confirmed a homozygous missense variant c.430G>A (p.Gly144Arg) in Exon 2 of *ARSB* gene, which was found to be pathogenic and consistent with MPS Type VI. The child was further evaluated for additional comorbidities, which were ruled out. She is currently managed conservatively with oral furosemide and is thriving well.

DISCUSSION

Mucopolysaccharidosis type VI (MPS VI), also known as Maroteaux–Lamy syndrome, is a rare lysosomal storage disorder caused by pathogenic mutations in the *ARSB* gene, leading to deficient arylsulfatase B enzyme activity. This deficiency results in the accumulation of dermatan sulfate, contributing to progressive multi-system involvement. The characteristic clinical features of MPS VI include skeletal abnormalities, corneal clouding, and orodental anomalies, with varying severity among affected individuals [4].

Cardiac manifestations, though less common in MPS VI compared to other MPS subtypes, remain a significant cause of morbidity. Valvular thickening, primarily affecting the mitral and aortic valves, along with myocardial hypertrophy and coronary artery narrowing, have been reported in literature [4,7,8]. In this case, the child presented with mitral regurgitation, global left ventricular hypokinesia, and a notably reduced ejection fraction of 25%. While valvular disease is frequently associated with MPS VI, substantial ventricular dysfunction, as observed here, is less commonly documented. This highlights the importance of cardiac monitoring in MPS patients, as cardiovascular complications may progress silently before clinical symptoms appear.

Radiographic findings play a crucial role in diagnosing MPS VI. The presence of dysostosis multiplex, including ovoid vertebral bodies, widened ribs with spatula-shaped ends, and bullet-shaped metacarpals, are hallmark skeletal abnormalities consistent with MPS [4]. The confirmation of MPS VI through whole exome sequencing, identifying a homozygous pathogenic variant in the ARSB gene, further reinforced the diagnosis.

The mainstay of treatment for MPS VI is enzyme replacement therapy (ERT) with galsulfase, which has been shown to improve mobility and slow disease progression by reducing glycosaminoglycan accumulation [5]. However, ERT does not fully prevent all disease complications, necessitating a multidisciplinary approach to care, including orthopedic, cardiac, and respiratory management [6]. In this case, the child is currently managed conservatively with diuretics for cardiac insufficiency and remains under close clinical monitoring.

This case contributes to the limited body of literature on significant cardiac involvement in MPS VI and underscores the need for early diagnosis and comprehensive management to improve long-term outcomes in affected patients.

CONCLUSION

MPS VI is a rare but progressive disorder requiring early diagnosis and comprehensive management. This case underscores the significance of recognizing early clinical signs, particularly cardiac involvement, to initiate timely interventions. While enzyme replacement therapy improves outcomes, it does not halt disease progression. A multidisciplinary approach, including regular cardiovascular monitoring and supportive care, is crucial in enhancing the patient's quality of life and addressing long-term complications effectively.

REFERENCES

[1] Ribeiro EM, Brusius-Facchin AC, Leistner-Segal S, da Silva CAB, Schwartz IV. Cardiac disease as the presenting feature of mucopolysaccharidosis type IIIA: A case report. Molecular Genetics and Metabolism Reports [Internet]. 2014 Sep 29 [cited 2020 Nov 12];1:422–4.

[2] Tulebayeva A, Mukhambetova G, Sharipova M, Tylki-Szymanska A. The Birth Prevalence of Mucopolysaccharidosis Types I, II, III, IVA, VI, and VII in the Republic of Kazakhstan Between 1984 and 2023. *Diagnostics*. 2025; 15(6):679.

[3] Ali, M. A., Maheshwari, S., Mohapatra, M. D., & Dash, D. K. (2025). A case of mucopolysaccharidosis type VI in Indian family: importance of clinical characteristics, urinary GAG and enzyme assay in diagnosis of mucopolysaccharidosis. International Journal of Contemporary Pediatrics, 12(3), 512–516.

[4] D'Avanzo F, Zanetti A, De Filippis C, Tomanin R. Mucopolysaccharidosis Type VI, an Updated Overview of the Disease. *Int J Mol Sci*. 2021;22(24):13456. Published 2021 Dec 15.

[5] Harmatz, P., Ketteridge, D., Giugliani, R., et al. (2006). Enzyme replacement therapy in mucopolysaccharidosis VI (Maroteaux–Lamy syndrome). J Pediatr, 148(4), 533–539.

[6] Giugliani, R., Harmatz, P., Wraith, J. E. (2007). Management guidelines for mucopolysaccharidosis VI. Pediatrics, 120(2), 405–418.

[7] V. Fesslova, P. Corti, G. Sersale, A. Rovelli, P. Russo, S. Mannarino, G. Butera, R. Parini

[8] The natural course and the impact of therapies of cardiac involvement in the mucopolysaccharidoses Cardiol. Young, 19 (2009), pp. 170-178

[9] E.A. Braunlin, J.M. Berry, C.B. Whitley Cardiac findings after enzyme replacement therapy for mucopolysaccharidosis type I Am. J. Cardiol., 98 (2006), pp. 416-418

FIGURES :

FIGURE 1- clinical features suggestive of MPS - coarse facial features, upturned nose and frontal bossing

FIGURE 2- Chest radiograph showing Ovoid or hypoplastic vertebral bodies, widened ribs with spatula-shaped ends and thoracolumbar kyphosis

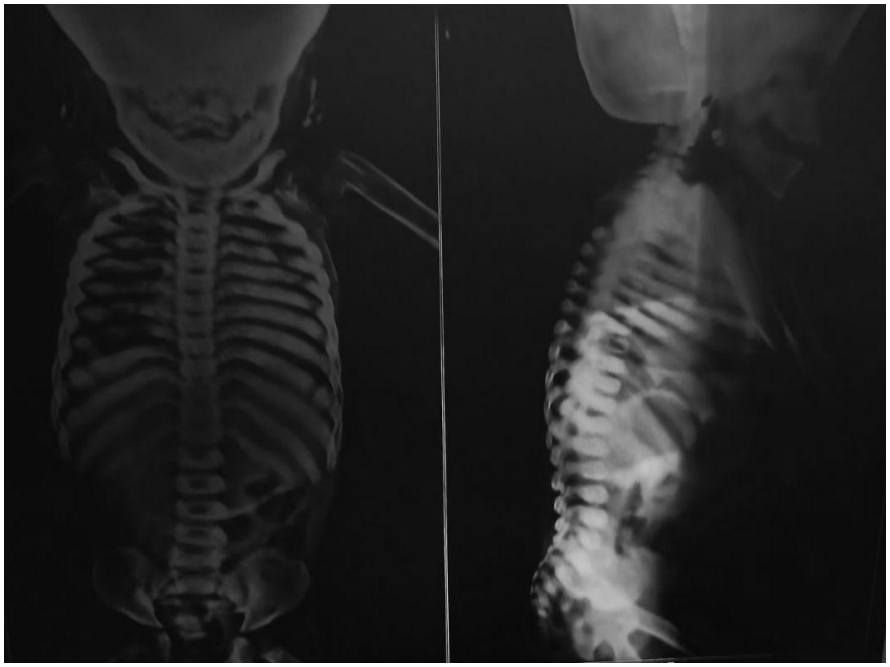

FIGURE 3- Hand X-ray showing bullet-shaped and irregular metacarpals, along with joint space widening and abnormal carpal bone development