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Mucopolysaccharidosis and valvular heart disease

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Abstract

Mucopolysaccharidosis type I (MPS I) is a rare autosomal recessive lysosomal storage disorder caused by deficiency of α-L-iduronidase, leading to progressive accumulation of glycosaminoglycans in multiple organ systems. Cardiac involvement, particularly valvular heart disease, is a major determinant of morbidity and may be the initial manifestation prompting medical evaluation. ***Case summary:*** A 14-year-old female presented with progressive dyspnoea, fever, and cough. Clinical examination revealed coarse facial features, corneal clouding, skeletal deformities consistent with dysostosis multiplex, hepatosplenomegaly, and hearing impairment. Transthoracic echocardiography demonstrated markedly thickened mitral valve leaflets with severe mitral stenosis, mild mitral regurgitation, thickened aortic valve with mild aortic regurgitation, mild tricuspid regurgitation, and moderate pulmonary hypertension, along with left ventricular dilatation and preserved biventricular systolic function. Chest imaging showed cardiomegaly and characteristic skeletal abnormalities. Laboratory evaluation revealed microcytic hypochromic anaemia, and urinary screening for mucopolysaccharidosis was positive. Based on the constellation of clinical, imaging, and biochemical findings, a diagnosis of mucopolysaccharidosis type I with significant valvular heart disease was established. The patient was managed conservatively and referred for multidisciplinary metabolic and cardiology follow-up. ***Discussion:*** This case illustrates the characteristic pattern of progressive valvular involvement in MPS I and highlights the importance of considering lysosomal storage disorders in young patients presenting with unexplained valvular heart disease and systemic features. Early recognition and regular echocardiographic surveillance are essential to guide management and improve outcomes.

INTRODUCTION

Mucopolysaccharidoses (MPS) are a heterogeneous group of rare inherited lysosomal storage disorders characterized by deficiency of specific enzymes involved in the degradation of glycosaminoglycans (GAGs), leading to their progressive accumulation in multiple tissues and organs [1]. The estimated incidence of MPS collectively ranges from 1 in 25,000 to 1 in 100,000 live births, with considerable phenotypic variability depending on the specific enzyme defect and subtype [2]. Among these, Mucopolysaccharidosis type I (MPS I) results from deficiency of the lysosomal enzyme α-L-iduronidase, causing accumulation of dermatan sulfate and heparan sulfate in connective tissue, cardiovascular structures, and visceral organs [3].

MPS I encompasses a clinical spectrum ranging from the severe Hurler syndrome to the attenuated Hurler–Scheie and Scheie phenotypes, with differences in age of onset, disease progression, and organ involvement [4]. Cardiovascular manifestations are among the most common and clinically significant complications in MPS, contributing substantially to morbidity and mortality [5]. The heart is affected primarily through progressive infiltration of GAGs into the myocardium, cardiac valves, coronary arteries, and conduction system, resulting in structural and functional abnormalities [6].

Valvular heart disease represents the predominant cardiac manifestation in MPS patients, most frequently involving the mitral and aortic valves [7]. Thickening of valve leaflets, chordae tendineae, and subvalvular apparatus leads to varying degrees of stenosis and regurgitation, often progressing insidiously and becoming clinically apparent in adolescence or

early adulthood [8]. Mitral valve involvement is particularly common and may present as isolated mitral stenosis, regurgitation, or a mixed lesion, while aortic valve disease frequently manifests as regurgitation due to leaflet thickening and reduced mobility [9].

Despite advances in enzyme replacement therapy and hematopoietic stem cell transplantation, established valvular disease in MPS often shows limited reversibility, underscoring the importance of early recognition and longitudinal cardiac surveillance [10]. Echocardiography remains the cornerstone for diagnosis and follow-up, allowing detailed assessment of valvular morphology, chamber dimensions, and pulmonary pressures [11]. However, due to the rarity of the disease and variability in presentation, diagnosis may be delayed, particularly when patients present primarily with cardiopulmonary symptoms.

We report a case of Mucopolysaccharidosis type I presenting with significant valvular heart disease, highlighting the characteristic echocardiographic findings, multisystem involvement, and clinical challenges in management. This case emphasizes the importance of considering underlying lysosomal storage disorders in young patients presenting with unexplained valvular pathology and systemic features.

Timeline

Time point	Clinical events
2 weeks prior to admission	Progressive shortness of breath associated with fever and cough
Day 0	Presentation to emergency department at Jai Prabha Medanta Super Speciality Hospital, Patna
Day 0	Initial clinical evaluation revealed coarse facial features, macroglossia, corneal clouding, skeletal deformities, and hepatosplenomegaly
Day 1	Chest X-ray showed cardiomegaly, paddle-shaped ribs, thickened clavicles, and vertebral abnormalities
Day 1	Electrocardiogram demonstrated normal sinus rhythm
Day 1	Transthoracic echocardiography revealed thickened mitral valve leaflets with severe mitral stenosis, mild mitral regurgitation, thickened aortic valve with mild aortic regurgitation, mild tricuspid regurgitation, moderate pulmonary hypertension, and left ventricular dilatation with hypertrophy
Day 2	High-resolution computed tomography (HRCT) of the chest showed consolidation with subsegmental collapse and focal atelectasis, along with kyphotic vertebral deformity
Day 2	Laboratory investigations revealed microcytic hypochromic anemia
Day 3	Urinary mucopolysaccharidosis screening (toluidine blue spot test) returned positive
Day 3	Diagnosis of mucopolysaccharidosis type I with significant valvular heart disease was established
Day 3–5	Conservative medical management including intravenous antibiotics, nebulization, and supportive care
Discharge	Clinical stabilization achieved; patient referred for metabolic evaluation and multidisciplinary follow-up

CASE PRESENTATION

A 14-year-old female presented to the emergency department of Jai Prabha Medanta Super Speciality Hospital, Patna, with complaints of progressive shortness of breath, fever, and cough of approximately two weeks' duration. There was no documented history of prior cardiac disease or surgical intervention. Family history was non- contributory, and there was no known history of similar illness among siblings.

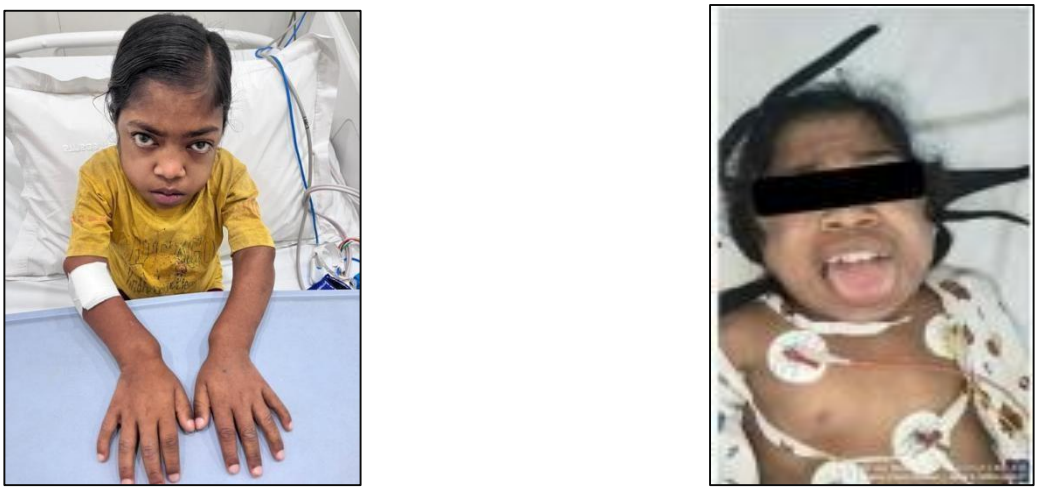

Figure 1. Clinical photograph showing coarse facial features consistent with mucopolysaccharidosis, including broad forehead, depressed nasal bridge, full cheeks, and macroglossia.

On general physical examination, the patient exhibited characteristic dysmorphic features, including coarse facial features, macroglossia, a large forehead, low nasal bridge, full lips and cheeks, and widely spaced eyes. Ophthalmologic examination revealed corneal clouding. Skeletal examination demonstrated features consistent with dysostosis multiplex, including dorsal kyphosis. Abdominal examination revealed hepatosplenomegaly and an associated umbilical hernia. Otolaryngologic evaluation suggested hearing impairment. Vital signs were stable at presentation.

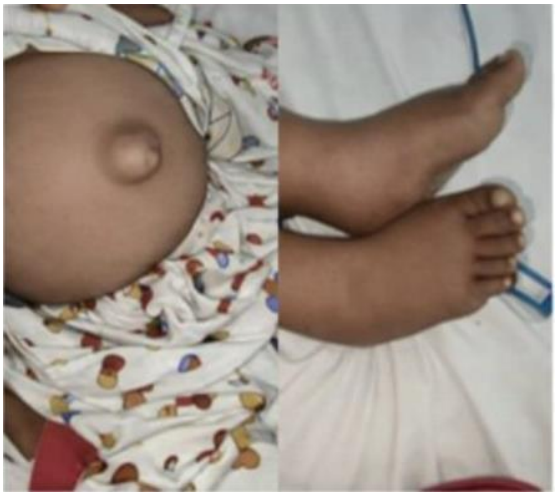

Figure 2. Clinical photograph showing umbilical hernia and lower limb involvement with short, broad feet and soft-tissue thickening consistent with dysostosis multiplex in mucopolysaccharidosis.

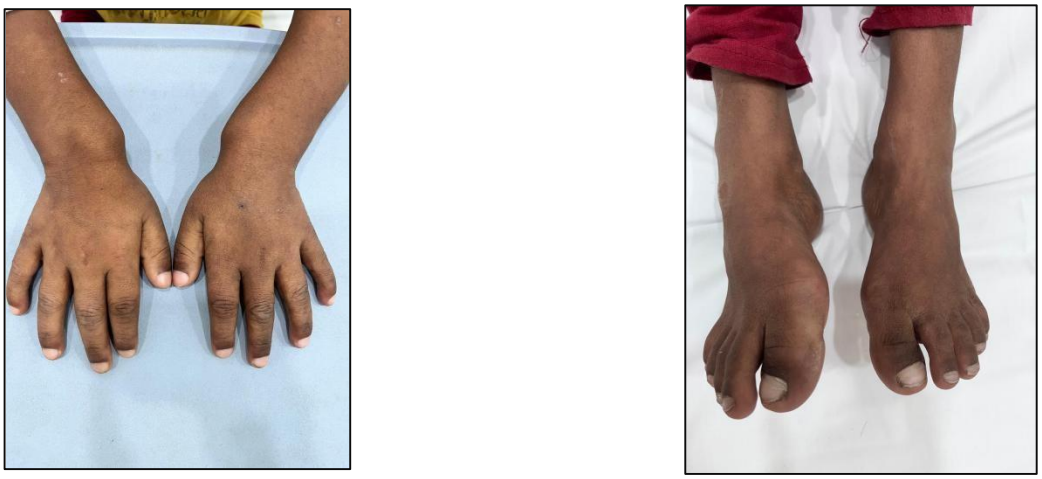

Figure 3. Photograph of both hands and feets showing short, broad fingers and soft tissue thickening, characteristic of dysostosis multiplex in MPS I.

Cardiovascular examination revealed cardiomegaly on clinical assessment, with no audible rhythm abnormalities. Electrocardiography demonstrated normal sinus rhythm. Transthoracic echocardiography showed marked thickening of the mitral valve leaflets and subvalvular apparatus, with reduced leaflet mobility, resulting in severe mitral stenosis with a mitral valve orifice area of 1.7 cm^2 and a maximum/mean transmitral gradient of 17/11 mmHg. Mild mitral regurgitation was also noted. The aortic valve appeared thickened with reduced cusp mobility, associated with mild aortic regurgitation without significant stenosis.

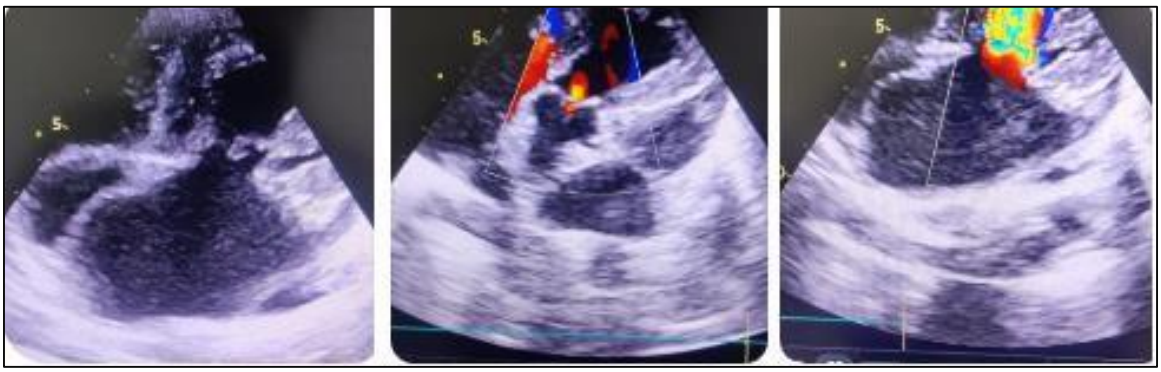

Figure 4A-4C. A -Two-dimensional echocardiography showing thickened mitral valve leaflets with restricted motion. B-Color Doppler demonstrating turbulent. transmitral flow consistent with severe mitral stenosis. C-High-velocity Doppler jet across the mitral valve indicating significant obstruction.

Mild tricuspid regurgitation was present with estimated moderate pulmonary hypertension. The left ventricle was dilated with concentric hypertrophy, while biventricular systolic function remained preserved. Increased echogenicity of the myocardium and subvalvular structures was observed, suggestive of glycosaminoglycan deposition.

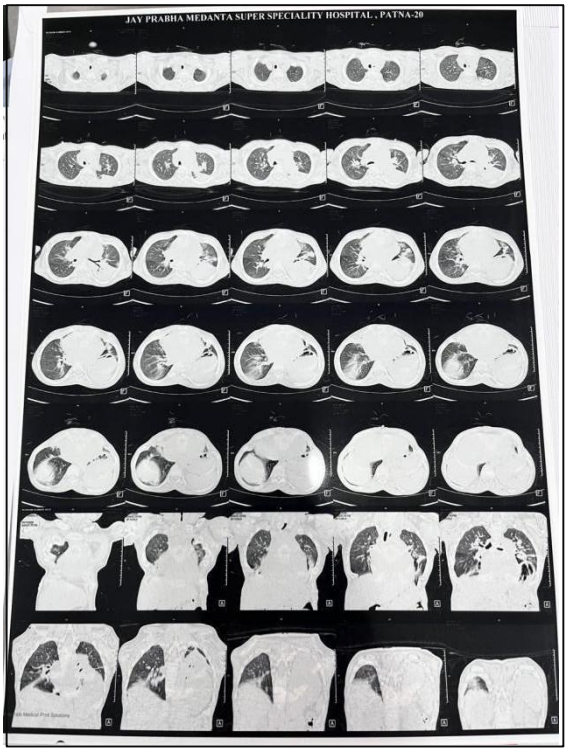

Figure 5. HRCT chest showing pulmonary consolidation with subsegmental collapse and associated kyphotic vertebral deformity.

Chest radiography demonstrated cardiomegaly, thickened clavicles, paddle-shaped ribs, wedge-shaped vertebral bodies with widened intervertebral disc spaces, and dorsal kyphosis. High-resolution computed tomography of the chest revealed areas of consolidation with subsegmental collapse in the left upper and lower lobes, focal atelectasis in the right lung, and a focal kyphotic deformity at the L1 vertebral level.

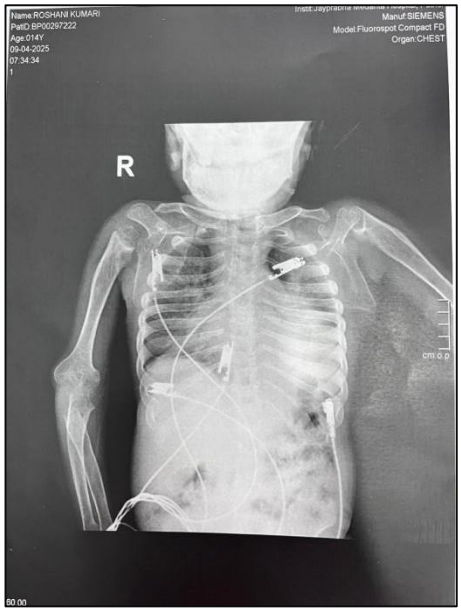

Figure 6. Chest radiograph showing cardiomegaly with paddle-shaped ribs, thickened clavicles, and vertebral abnormalities consistent with dysostosis multiplex.

Laboratory investigations showed microcytic hypochromic anemia. Screening for mucopolysaccharidosis using the urinary toluidine blue spot test was positive. Based on the constellation of clinical, radiological, echocardiographic, and biochemical findings, a diagnosis of mucopolysaccharidosis type I with significant valvular heart disease was established. The patient was managed conservatively with intravenous antibiotics, nebulization, and supportive care, resulting in clinical stabilization, and was subsequently referred for metabolic evaluation and multidisciplinary follow-up.

DISCUSSION

Mucopolysaccharidosis type I (MPS I) is a progressive lysosomal storage disorder in which cardiovascular involvement develops early and worsens over time, often determining overall prognosis. Cardiac manifestations are frequently underrecognized, particularly in resource-limited settings, leading to delayed diagnosis and advanced disease at presentation [12]. Valvular heart disease remains the most consistent and clinically relevant cardiac abnormality in MPS I. Histopathological studies have demonstrated extensive glycosaminoglycan deposition within valve leaflets, annulus, chordae tendineae, and papillary muscles, resulting in thickened, stiff valves with impaired excursion [13]. These infiltrative changes explain the predominance of stenotic lesions in MPS compared with degenerative or rheumatic valve disease. In the present case, severe mitral stenosis with associated subvalvular involvement and mild regurgitant lesions reflects this characteristic infiltrative process.

Mitral valve disease is reported as the earliest and most severely affected valve in MPS I, followed by aortic valve involvement [14]. The development of severe mitral stenosis in adolescence, as observed in this patient, highlights the relentless progression of valvular pathology when diagnosis and disease-specific therapy are delayed. Unlike rheumatic disease, commissural fusion is typically absent, and surgical repair may be technically challenging due to diffuse tissue infiltration [15].

Myocardial involvement in MPS, though less frequently emphasized, contributes significantly to cardiac morbidity. Increased myocardial echogenicity and ventricular hypertrophy, as seen in this case, have been correlated with myocardial storage of GAGs and interstitial fibrosis, leading to impaired diastolic function and reduced ventricular compliance [16].

These changes may predispose patients to heart failure even in the presence of preserved systolic function.
Pulmonary hypertension is a multifactorial complication in MPS and is associated with increased mortality. Contributing mechanisms include chronic left-sided valvular disease, restrictive lung disease, recurrent respiratory infections, and upper airway obstruction [17]. Its presence in this patient underscores the importance of comprehensive cardiopulmonary evaluation in suspected storage disorders.

Although enzyme replacement therapy and hematopoietic stem cell transplantation have shown benefits in reducing systemic GAG burden, their impact on established valvular disease is limited, particularly when initiated later in the disease course [18]. Consequently, early diagnosis and routine echocardiographic surveillance are essential to detect subclinical cardiac involvement and guide timely intervention [19].

This case emphasizes the need for heightened clinical awareness of metabolic disorders in young patients presenting with unexplained valvular heart disease accompanied by systemic features. Early cardiology involvement and a multidisciplinary approach are crucial to improving long-term outcomes in patients with MPS I.

CONCLUSION

Mucopolysaccharidosis type I can present with progressive and clinically significant valvular heart disease in adolescence, with mitral valve involvement being particularly prominent. This case highlights the importance of considering underlying metabolic disorders in young patients with unexplained valvular pathology and systemic features. Early diagnosis, regular echocardiographic surveillance, and a multidisciplinary approach are essential to optimize clinical outcomes.

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