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Case Report

Paediatrics Section

Clinical Conundrum: Unveiling a Rare Case of Morquio Syndrome with Rheumatic Heart Disease

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ABSTRACT

A genetic lysosomal storage condition called Mucopolysaccharidosis (MPS) causes a variety of enzyme deficits that result in the build-up of specific glycosaminoglycans in the tissues. These deposits impact several systems, resulting in chronic morbidity, and create a variety of physical abnormalities that give characteristic looks and findings. This is a case study of a male patient who was diagnosed with Rheumatic Heart Disease (RHD) after presenting with cardiac problems. After testing and research, he was found to have Type 4, a very uncommon form of MPS, often known as Morquio syndrome. The child underwent surgical correction for mitral regurgitation, specifically mitral valve replacement This case highlights the need for increased margin of suspicion for RHD in a child with mucopolysaccharidoses and takes timely corrective measures. Morquio syndrome is a type 4 MPS with characteristic features and has multisystemic involvement. Although cardiovascular system inolvement is one of the known involvements in the disease spectrum, the presence of RHD in a child with Morquio is not a frequent occurrence. This case highlights the need to consider and thoroughly examine a child with MPS for cardiac involvement and take necessary corrections in a timely fashion.

Keywords: Aortic valve abnormalities, Echocardiography, Enzyme replacement therapy, Glycosaminoglycan metabolism, Lysosomal storage disorders

CASE REPORT

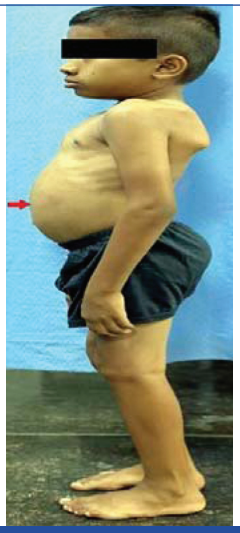
An 11-year-old male child was brought to the outpatient department of Paediatrics with a chief complaint of breathlessness which was intermittent, aggravated on activities or increased physical exertion, relieved on rest. The child was diagnosed with RHD and hepatomegaly of 6-7 cm and was given a course of intramuscular penicillin (6 lac IU) one year back. The patient was later brought in for further surgical management of the heart disorder. Child was administered Growth Hormone (GH) for growth hormone deficiency, treated with benzathine penicillamine G, 6 lakh IU intramuscularly, 4 doses for RHD in an outside institute one year back.

On examination, vitals were within the normal limits; however, the child had atypical head-to-toe findings. The [Table/Fig-1] shows the anthropometric findings of the child which are suggestive of short stature. The child had a broad forehead, chubby cheeks, a short neck, a shielded chest, swelling over the umbilicus, a protuberant abdomen, an enlarged right-sided scrotum and prominent scapulae border and scoliosis,with a short stature [Table/Fig-2-5].

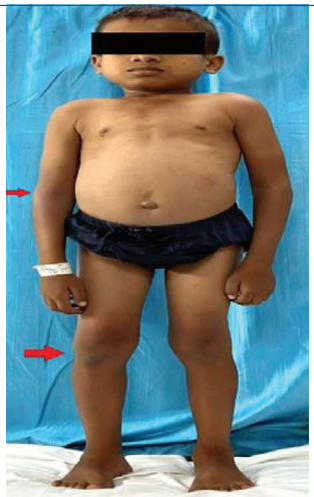
On investigation, GH level was decreased (0.02 ng/mL). The child was administered with GH for three minutes. The child was discharged on Dytor Plus and Metoprolol (1 mg/kg/day), along with Ramipril 2.5 mg once daily. Child was readmitted after 1 month of discharge from the same hospital, and Two-Dimensional (2D) echocardiography was done which was suggestive of severe mitral regurgitation with eccentric jet, moderate mitral stenosis, thickened aortic valve leaflet with no stenosis or regurgitation, mild

Criteria	Observed	Expected	Inference
Weight	22 kg	35 kg	Less than 3rd centile, underweight
Height	118 cm	144 cm	Less than 3rd centile, short stature
Upper segment: Lower segment ratio	1:1.15 (60 cm: 52 cm)	0.9:1	Disproportionate short stature

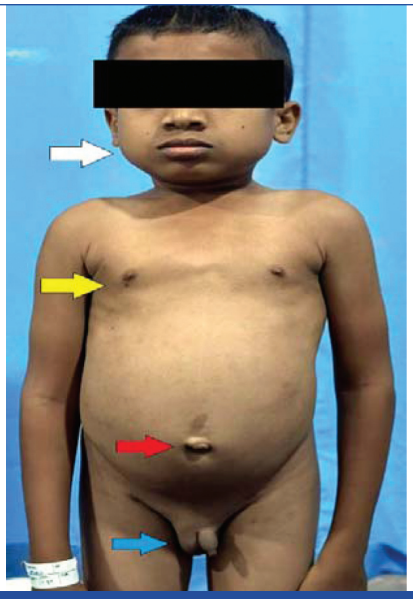
[Table/Fig-1]: Anthropometric findings of the 11-year-old male child reporting to the Dept. of paediatrics.



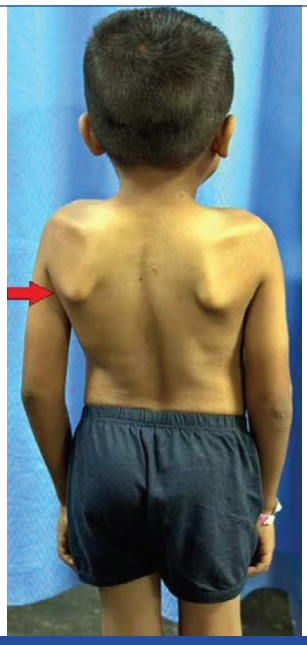
[Table/Fig-2]: Lateral view of the child with a profound protuberant abdomen.



[Table/Fig-3]: The front view of the child shows a disproportionately short stature.



[Table/Fig-4]: Head-to-toe general physical examination: Chubby cheeks (black arrow); Shield chest (yellow arrow); Everted umbilicus (red arrow); enlarged right-sided scrotum (blue arrow).

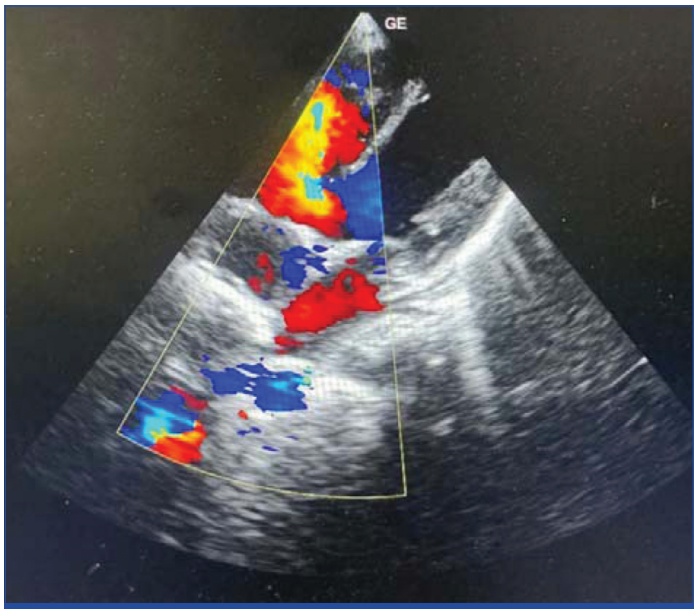


[Table/Fig-5]: Rare back view shows the prominent scapular borders and scoliosis.

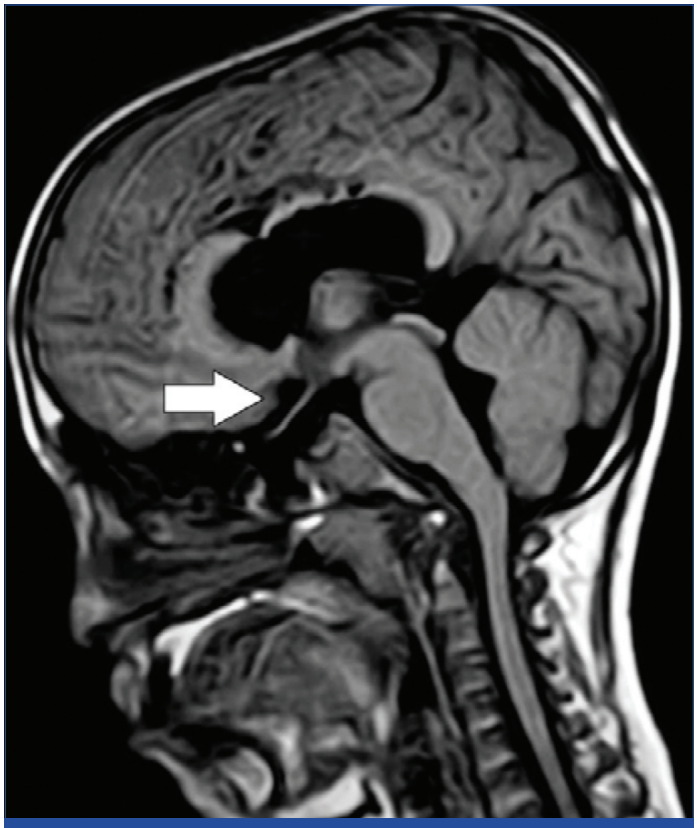
tricuspid regurgitation, no evidence of pulmonary hypertension was noted. The child was transferred to the Department of Paediatrics i/v/o genetic workup. The child was advised to undergo high-risk surgery for Mitral Valve (MV) replacement. However, the parents declined further intervention; therefore, no additional treatment was administered subsequently.

is serum vitamin D3 level was 33.8 ng/mL, and the Cardiothoracic (CT) ratio was 0.46. Cardiovascular examination revealed a precordial bulge, a grade 4/6 pansystolic murmur best heard at the 4th-5th intercostal space, along with a palpable thrill and parasternal heave. Abdominal examination demonstrated hepatomegaly, with a liver span of approximately 14.9 cm. Positive cough impulse was evident along with swelling above the umbilicus. Examinations of the respiratory system and central nervous system revealed no developmental delays. USG abdomen pelvis revealed Umbilical hernia with 7 mm opening along with omental fat herniation on coughing was noted. Liver 14.9 cm hepatomegaly with enlarged right-sided scrotum was noted; no phimosis or hypospadiasis was appreciated. USG inguinoscrotal region revealed encysted hydrocoele of right spermatic cord. On 2D echocardiography severe mitral regurgitation with eccentric jet, moderate mitral stenosis, thickened aortic valve-trileaflet with mild tricuspid regurgitation, no aortic stenosis or regurgitation, no pulmonary artery hypertension or coarctation of aorta. Findings were suggestive of RHD [Table/Fig-6].

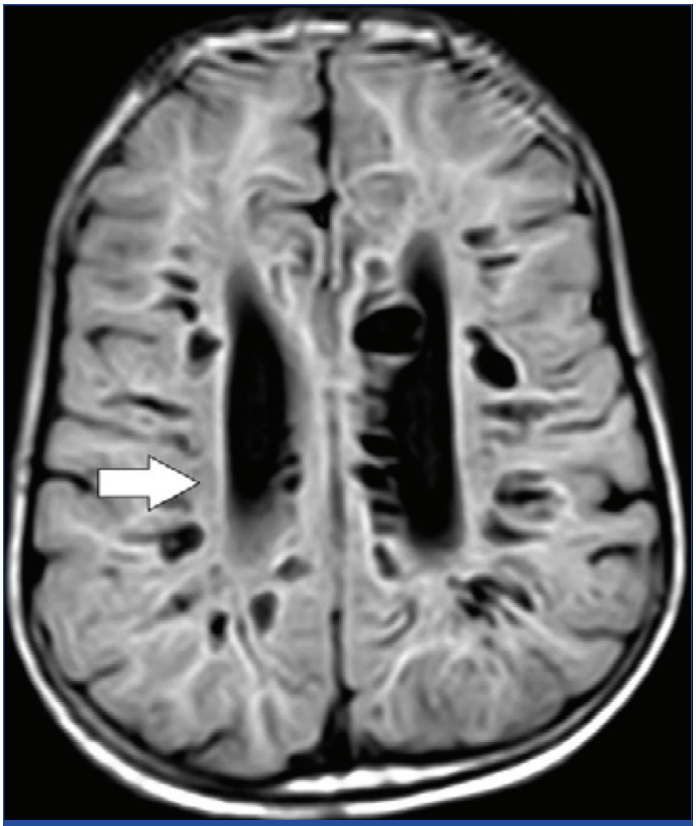
MRI of the brain revealed multiple predominantly cystic altered signal intensity areas diffusely involving the subcortical and deep periventricular white matter as well as the corpus callosum. These lesions appeared hyperintense on T2-weighted/FLAIR sequences and hypointense on T1-weighted images, with no diffusion restriction on Diffusion-Weighted Imaging (DWI) and corresponding high signal on ADC maps. Dilatation of all horns of the bilateral lateral ventricles and the fourth ventricle was noted, suggestive of hydrocephalus (Evans index: 0.41). Diffuse cerebral atrophy was also observed. A J-shaped sella turcica was identified. Overall, the imaging findings were suggestive of mucopolysaccharidosis. [Table/Fig-7] shows a J-shaped sella turcica in MRI brain. [Table/Fig-8] shows MRI scan with altered signal intensity in multiple areas.



[Table/Fig-6]: A 2D Echocardiography of 4-chamber view shows the severe mitral regurgitation with eccentric jet.



[Table/Fig-7]: J shaped sella turcica noted during the MRI scan of the brain.



[Table/Fig-8]: T2/FLAIR imaging showing multiple altered signal intensity areas mostly cystic, noted diffusely in subcorticular and deep periventricular white matter and corpus callosum appearing hyperintense.

Subsequent investigations revealed no corneal haziness during the fundus examination but rather suggested hypertrophied adenoids and a modest amount of chorioretinitis atrophy. The child's physical characteristics pointed towards the Mucopolysaccharidosis (MPS), most likely Type 4 MPS, or Morquio syndrome. In order to corroborate the clinical suspicion of mucopolysaccharides, whole genome sequencing was sent. The clinical suspicion of the same was validated by the investigation reports. As the clinical features of the child were strongly in favour of Morquio syndrome, other differential diagnosis was ruled out. Genetic testing was also sent as a confirmatory test for the same.

As 2D echocardiography was suggestive of severe mitral regurgitation, child underwent MV replacement. Child was also started on physiotherapy with rehabilitative care. Physiotherapy was administered in two sessions. The first session, lasting 30 minutes, was conducted for assessment of the patient's needs and formulation of an individualised treatment plan. Child underwent three more sessions, each of half an hour, focusing on increasing joint mobility, improving breathing techniques and educating on postoperative care for the child. Child was later scheduled for postoperative, rehabilitative, and orthopaedic follow-up. He was brought for follow-up one month after discharge and then did not return.

DISCUSSION

This case highlights the complexity of diagnosing an underlying metabolic disorder in a paediatric patient initially presenting with RHD. While the child was initially managed for valvular dysfunction, the presence of disproportionate stature, craniofacial anomalies, skeletal abnormalities, and hepatomegaly led to further evaluation, ultimately revealing MPS type IV (Morquio syndrome). The absence of corneal clouding and the presence of J-shaped sella turcica, hydrocephalus, and cerebral atrophy on imaging further supported this diagnosis.

Given the progressive nature of both MPS IV and RHD, surgical intervention was necessary to address the severe mitral regurgitation and mitral stenosis. The patient underwent MV replacement, followed by postoperative rehabilitative care, including physical therapy and orthopaedic follow-up to manage systemic manifestations of Morquio syndrome.

This case underscores the importance of multisystem evaluation in paediatric patients with complex presentations. While valvular heart disease prompted initial medical attention, the presence of atypical physical features led to the diagnosis of MPS IV. Early recognition of such conditions is crucial for optimising management strategies, preventing complications, and improving long-term functional outcomes.

There are two kinds of Morquio syndrome, A (galactose 6-sulphatase) and B (β-galactosidase), an autosomal recessive condition. Accumulation of materials such as glycosaminoglycans, keratin sulphate, and chondroitin-6-sulphate sulphatase is caused by a deficiency of N-galactosamine-6-sulfatase (GALNS). This eventually affects the tendons, bone, and cartilage and by the time they reach their second decade, the majority of patients are wheelchair-bound, and the morbidity rate is found to be substantial [1]. In contrast to other MPS, MPS type 4 has a very normal mental state as long as hydrocephalus has not occurred. Chromosome 16q24 contains the GALNS gene, which is involved in Morquio syndrome 3. The vast range of clinical characteristics observed in individuals with Morquio syndromes has been linked to the discovery of 185 GLANS mutations [2,3]. While the other MPS syndromes have a severe impact on mentation, MPS type 4 typically exhibits preserved intelligence regardless of the severity of the disease [4]. Different MPS exhibit multiple phenotypical similarities, such as corneal clouding, hydrops foetalis and behavioural abnormalities. Types 1, 2, and 7 show extensive somatic involvement, whereas type 3 presents with little to no somatic involvement but severe neurological impairment. Type 1 and 2 display dystosis multiplex, while type 4 has cervical spine involvement—instability that results in hydrocephalus. Type 6 also lacks cognitive involvement, but its somatic manifestations are similar to those of MPS types 1, 2, and 7. Skeletal involvement often presents similar to juvenile idiopathic arthritis but no improvement on non-steroidal anti-inflammatory drugs helps differentiate the diagnosis [5].

In a study conducted by Morrone A et al., it was seen that there are many different types of GALNS mutations linked to Morquio A, and new modifications are always being discovered. The results showed that 48% of patients had one GALNS change classified as homozygous, 39% have two GALNS alterations recognised as heterozygous, and 13% have just one GALNS alteration found [6]. In a different study conducted by Hendriksz CJ et al., the GALNS gene has been shown to include more than 180 distinct mutations, which most likely accounts for the disorder's clinical variability. Short stature and skeletal dysplasia (dysostosis multiplex), which includes atlantoaxial instability and cervical cord compression, are the main symptoms of accumulation of C6S and KS. Nonetheless, MPS IVA patients may also experience anomalies in their respiratory, cardiovascular, optical, or auditory systems. The clinical examination, skeletal radiography, urine Glycosoaminoglycans (GAG), and the enzymatic activity of GALNS in fibroblasts or blood cells are usually used to make the diagnosis. Although a typical evaluation for the laboratory diagnosis of MPS IVA is a deficiency of GALNS activity, gene sequencing for MPS IVA is now more widely available and is frequently used to validate enzyme results [7].

In investigation done by Leong HY et al., clinical deficits were present in all MPS IVA patients. Gaining more knowledge about the clinical and genetic spectrum, as well as the natural history of MPS IVA in this group, might help with early diagnosis, improved management, and enable earlier genetic counselling and prenatal diagnosis [8]. A case series conducted by Kılavuz S et al., of Morquio A patients supports findings from clinical trials that demonstrate endurance stabilises over time after treatment starts, regardless of age, and suggests that very

early (ERT) starting maximises growth results [9]. In a different setting, it was seen that although all patients developed in vitro Neutralising antibodies (NAb) and Total Antidrug antibodies (TAb), there was no correlation found between the immunogenicity of elosulfase alfa and clinical outcomes or safety. During a 5-year period, no tendencies towards declining endurance, respiratory function, or capacity to conduct daily activities were noted in this cohort, which is in contrast to the documented natural history of Morquio A [10].

Studies have shown that patients with MPS IVA have access to ERT as a treatment option, and there are hints that haematopoietic stem cell transplantation could be a different approach. Nevertheless, as neither treatment appears to be curative, at least for MPS IVA patients' skeletal dysplasia, novel strategies are being researched to improve efficacy and lower costs for MPS IVA patients [11,12]. In a different setting investigated by Harmatz PR et al., and Schrover R et al., the Six-Minute Walk Test (6MWT) was used to measures a gradual deterioration in endurance, which is characteristic of the natural history of Morquio A syndrome. Growth likely influences the longitudinal trends in Forced Vital Capacity (FVC) and Maximum Voluntary Ventilation (MVV), with increases observed in younger individuals and declines noted in older patients. Modifications in 6MWT might accurately indicate the advancement of the illness in individuals with ambulatory Morquio A [13,14].

CONCLUSION(S)

Mucopolysaccharidosis can be quickly diagnosed based on clinical suspicion and physical investigation. Children with MPS have better lifestyles thanks to early corrective actions and rehabilitation therapies. Involving a multidisciplinary team in treating these situations lowers morbidity and facilitates the prompt reversal of emerging illnesses.

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