Letter

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Early screening for respiratory and cardiac complications in pediatric mucopolysaccharidosis IVA: Insights from a case

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SUMMARY: Mucopolysaccharidosis type IVA (MPS IVA) is a rare genetic disorder characterized by the deficiency of N-acetylgalactosamine-6-sulfate sulfatase, leading to significant growth and developmental challenges, increased morbidity, and reduced life expectancy. We report the clinical characteristics and genetic basis of MPS IVA in an 11-year-old male patient, emphasizing the critical role of early diagnosis and intervention. The combination of enzyme activity testing and genetic testing screening for suspected clinical cases may shorten the diagnosis time and reduce the difficulty of diagnosis. Early screening for respiratory and cardiac complications in confirmed cases is beneficial for reducing patient mortality.

Keywords: mucopolysaccharidosis type IVA, pulmonary hypertension, mitral regurgitation, delay diagnosis, optimize the diagnostic process

Mucopolysaccharide IVA (MPS IVA) is an autosomal recessive lysosomal storage disorder caused by a deficiency of N-acetylglucosamine 6-sulfate esterase. The estimated incidence rate of MPS IVA in China is 1.57–4.95 per 100,000 people (*1*). The clinical manifestations of MPS IVA patients are diverse and involve multiple systems, so the diagnosis of this disease cannot be based solely on symptoms without other more direct evidence. The occurrence of cardiac complications may be insidious and lead to early death in MPS IVA patients (*2*).

Here, we report a male adolescent patient with a history of growth delay for over ten years. Due to early reliance on clinical symptoms and enzyme activity testing for screening, the diagnosis was delayed but ultimately diagnosed as MPS IVA through exome sequencing. And due to the lack of early screening for cardiac complications and ineffective treatment, he ultimately died. This study was performed in accordance with the ethical standards laid down in the Declaration of Helsinki, and the Medical Ethics Committee of Shandong Provincial Hospital affiliated to Shandong First Medical University approved all procedures in this report (LCYJ:NO.2019-147). Informed consent was obtained from the patient's guardian.

The patient was an 11 year and 6-month-old boy who presented to the Pediatric Endocrinology Department of Shandong Provincial Hospital for treatment on January 22, 2025. He had a history of growth retardation for up to ten years, and in the past 2–3 years, his motor ability had gradually deteriorated, resulting in his inability to walk. He developed acute upper limb weakness 10 days before admission. The patient's parents and sister are both in good health.

On physical examination, the patient exhibited coarse facial features, macrocephaly (head circumference 58 cm), severe pectus carinatum, and generalized short stature (height 90 cm, Standard Deviation Score (SDS)-8.34; Body Mass Index (BMI) 24.69 kg/m^2). Neuromuscular assessment revealed hypotonia, hyperextensible joints, shortened metacarpals, and complete loss of ambulatory function. A grade 2/6 systolic murmur was auscultated at the cardiac apex, and a 1 × 2 cm benign anal polyp was noted. Vital signs included tachycardia (Heart rate 120 bpm) and tachypnea (Respiratory rate 23/min), with stable blood pressure (Blood pressure 111/70 mmHg) (Supplementary Figure S1, *https://www.irdrjournal.com/action/getSupplementalData.php?ID=276*).

Echocardiography displayed left atrial and ventricular dilation, moderate-severe mitral regurgitation, patent foramen ovale (0.3 cm left-to-right shunt), and pulmonary hypertension (pulmonary arterial systolic pressure PASP 36 mmHg). Hand radiography displayed that the patient had shortened metacarpals, osteopenia, dysplastic epiphyses, and delayed bone age (equivalent to 6–7 years) (Supplementary Figure S2, *https://*

www.irdrjournal.com/action/getSupplementalData.php?ID=276).

Two heterozygous variations of the Galactosamine (N-acetyl)-6-sulfatase (*GALNS*) gene were detected in blood samples, which are associated with mucopolysaccharidosis type IVA. The gene is *GALNS* NM_000512.5, including one pathogenic variant located at chromosome chr16:88907448 at c.374C>T p.Pro125Leu. Currently, a total of 573 GALNS variants have been reported in all publications (Supplementary Figure S3, *https://www.irdrjournal.com/action/getSupplementalData.php?ID=276*).

Initial management included supplemental oxygen and coenzyme Q10 supplementation, which was discontinued due to possible adverse effects (blurred vision and hearing decline). The patient rapidly progressed to acute respiratory failure, characterized by refractory hypoxemia (SpO_2 < 70%), hypercapnia, and oliguria. Despite aggressive intervention — diuretics, sodium bicarbonate, corticosteroids, and repeated cardiopulmonary resuscitation — the patient developed cardiopulmonary arrest and expired on January 26, 2025.

The patient's growth retardation was first observed in infancy. The patient had clinical features of mucopolysaccharidosis such as delayed growth and development, bone and joint deformities, and rough facial features. Therefore, in 2017, the activity tests of alpha glucosidase, beta glucuronidase, and iduronidase were performed at the first visit without any abnormalities. But no further screening was conducted on other types of mucopolysaccharide diseases, and no genetic testing was performed. When readmitted in 2025, both physical and laboratory examination results indicated the presence of cardiac complications in the patient, and a significant increase in Pro-B-type natriuretic peptide (proBNP) levels suggested the possibility of long-term cardiac overload (*3*). The results of echocardiography also confirm this point. So heart failure has become the main cause of deterioration and even death in patients.

Delayed diagnosis and early misdiagnosis are common in mucopolysaccharide diseases, including MPS IVA, with an average delay of 9.42 months and an average misdiagnosis of 4.56 times (*4*). There are two main reasons for delayed diagnosis. One reason is that pediatricians or orthopedic doctors lack experience with this disease, and the clinical symptoms of multiple subtypes of mucopolysaccharidosis overlap (*5*). The second reason may be limited by testing capabilities of different medical institutions. However, early diagnosis during the initial or asymptomatic period may have a significant impact

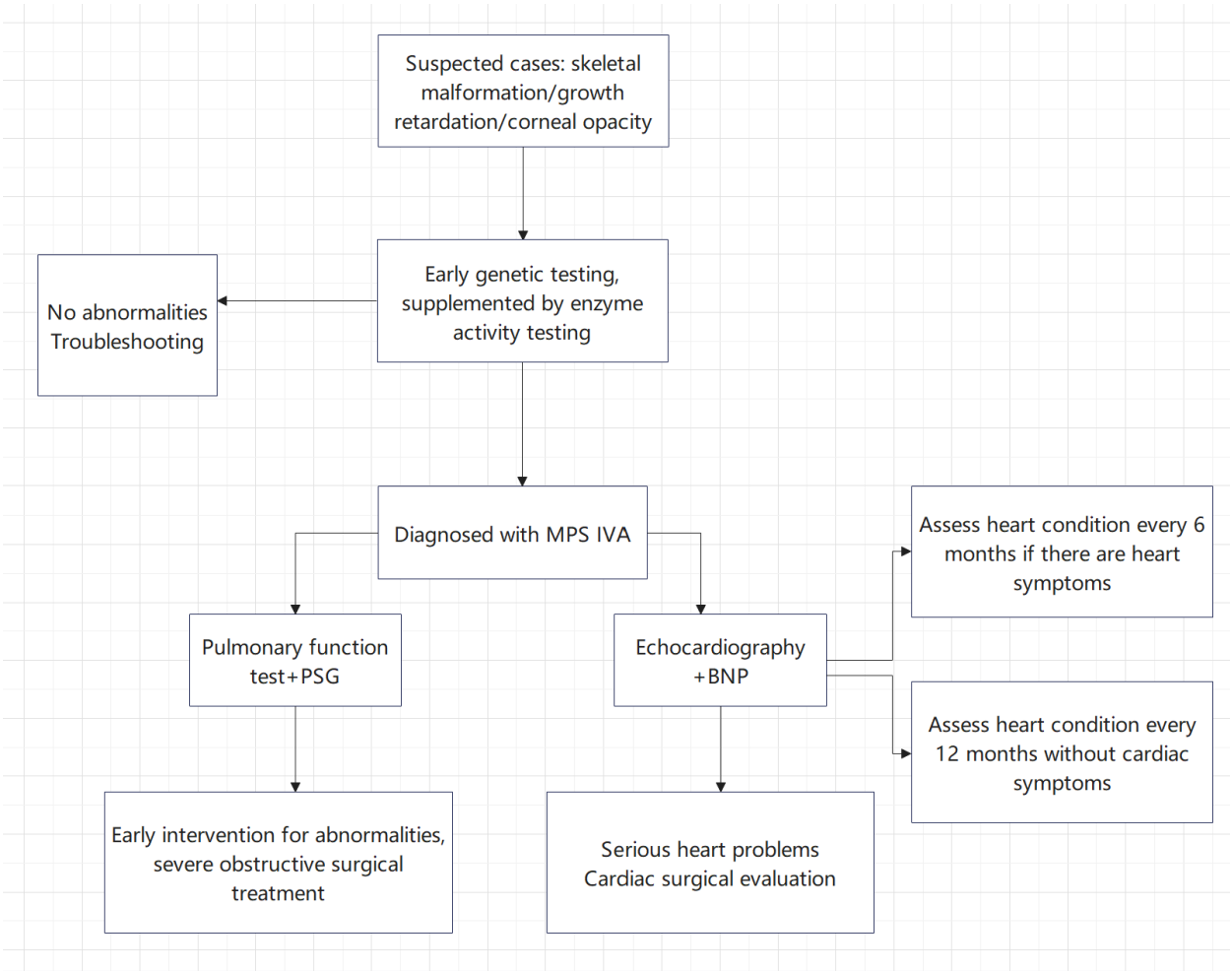

Figure 1. Mucopolysaccharidosis type IVA (MPS IVA) improved diagnostic process diagram.

on the final treatment outcome. So early diagnosis and intervention may have different outcomes.

Simultaneously conducting genetic testing while detecting enzyme activity can compensate for the subjective experience of doctors and the shortcomings of enzyme activity testing, while also benefiting genotype phenotype databases for better diagnosis, treatment, and evaluation of prognosis. Early gene detection may not only improve the identification of MPS, but also accurately calculate the incidence rate of MPS (*6*).

From the situation of this case, we believe that early screening for cardiac and respiratory complications after diagnosis is also very necessary. Respiratory failure and cardiac complications are the two leading causes of death in this disease, and studies have shown that early enzyme replacement therapy has a better improvement effect on the heart (*7*). Early respiratory intervention can significantly reduce mortality (*8*). When pediatricians or orthopedic surgeons encounter children with bone and joint deformities or growth retardation, it is recommended to undergo early genetic testing supplemented by enzyme activity testing for early diagnosis. Early screening for respiratory and cardiac complications after diagnosis and early intervention treatment are needed to maximize treatment effectiveness (Figure 1).

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Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Borges P, Pasqualim G, Giugliani R, Vairo F, Matte U. Estimated prevalence of mucopolysaccharidoses from population-based exomes and genomes. Orphanet J Rare Dis. 2020; 15:324.
2. Lavery C, Hendriksz C. Mortality in patients with morquio syndrome a. JIMD Rep. 2015; 15:59-66.
3. Ruskoaho H. Cardiac hormones as diagnostic tools in heart failure. Endocr Rev. 2003; 24:341-356.
4. Kang Q, Fang Y, Yang Y, Li D, Zheng L, Chen X, Tu X, Jin C. Health service utilization, economic burden and quality of life of patients with mucopolysaccharidosis in China. Orphanet J Rare Dis. 2024; 19:324.
5. Zhou J, Lin J, Leung WT, Wang L. A basic understanding of mucopolysaccharidosis: Incidence, clinical features, diagnosis, and management. Intractable Rare Dis Res. 2020; 9:1-9.
6. Çelik B, Tomatsu SC, Tomatsu S, Khan SA. Epidemiology of mucopolysaccharidoses update. Diagnostics (Basel). 2021; 11:273.
7. Andrade MFA, Guimarães ICB, Acosta AX, Leão EKEA, Moreira MIG, Mendes CMC. Left ventricular assessment in patients with mucopolysaccharidosis using conventional echocardiography and myocardial deformation by two-dimensional speckle-tracking method. J Pediatr (Rio J). 2019; 95:475-481.
8. Kenth JJ, Thompson G, Fullwood C, Wilkinson S, Jones S, Bruce IA. The characterisation of pulmonary function in patients with mucopolysaccharidoses IVA: A longitudinal analysis. Mol Genet Metab Rep. 2019; 20:100487.

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