PERSISTENT CLINICAL COMPLICATIONS DESPITE ENZYME REPLACEMENT THERAPY IN TWO SIBLINGS WITH MUCOPOLYSACCHARIDOSIS VI: A CASE-BASED REFLECTION OF 17 YEARS OF FOLLOW-UP

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INTRODUCTION

Mucopolysaccharidosis type VI (MPS VI, Maroteaux-Lamy syndrome) is a rare autosomal recessive lysosomal storage disorder caused by arylsulfatase B (ARSB) deficiency, leading to dermatan sulfate accumulation and progressive multisystem involvement. Enzyme replacement therapy (ERT) with galsulfase improves survival and slows disease progression, but its ability to prevent complications remains uncertain. This report highlights that early diagnosis and long-term ERT do not fully prevent disease progression and expands the longitudinal follow-up of two affected siblings.

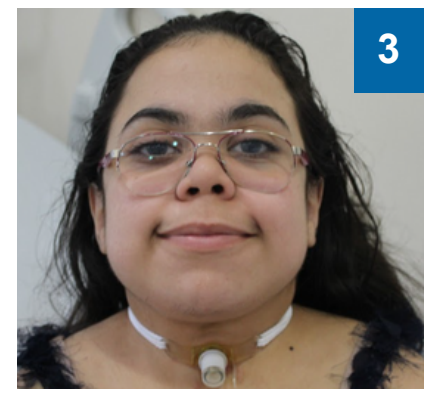
CASE REPORT

Sibling 1

The older sister was referred for genetic evaluation at age 8 due to short stature and dysmorphic features. At diagnosis, she had already undergone cardiac surgery for mitral and aortic valve involvement and had a dilated, hypertrophic left ventricle. Retrospectively, signs like recurrent respiratory infections and a heart murmur had been present since infancy. At age 5, worsening cardiac function and impaired growth prompted suspicion of a lysosomal storage disorder. Biochemical testing in both siblings-at 8 years and 8 months-revealed markedly elevated urinary glycosaminoglycans (GAGs) and reduced ARSB enzyme activity in leukocytes. Molecular analysis identified the intronic variant IVS5-8T>G (c.1143-8T>G) in homozygosity, along with IVS3-22T>C and P397P polymorphisms, also in homozygosity. The IVS5-8T>G variant, though underreported in the literature, has been recurrently observed in Brazilian, Portuguese, and Spanish individuals and is associated with classical or severe MPS VI phenotypes. ERT was initiated in both siblings at 8 years and 10 months and 1 year and 5 months of age, respectively.

Sibling 2

The younger sister demonstrated milder facial coarseness, slower progression of valvular disease, and notably surpassed her sister in height after 6 years of ERT. Both siblings experienced fewer upper respiratory infections and lower apnea indices after ERT. Nevertheless, they developed progressive manifestations including corneal clouding, claw hands, and skeletal dysplasia. The younger sibling later developed cervical spinal canal stenosis secondary to craniovertebral junction dysplasia, leading to compression of the bulbomedullary junction. She lost ambulation at age 12 and underwent elective laminectomy (C1-C2), laminoplasty (C3-C6), and posterior fossa craniectomy at 14. The procedure was complicated by difficult intubation and failed extubation, requiring permanent tracheostomy. She remains tracheostomized at age 18.



Pictures: (1) Older sister. Facial dysmorphisms. (2) Siblings: younger (right) and older (left). (3) Younger sister. Facial dysmorphisms.

DISCUSSION

These sibling cases emphasize the importance of early diagnosis and timely ERT initiation. However, they demonstrate that early treatment may not prevent progression of cardiac, skeletal, and especially spinal canal complications. They also highlight challenges in airway management during surgery, underscoring the need for multidisciplinary care and perioperative planning.

REFERENCES