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Case Report

Mucopolysaccharidosis Type I: Clinical Outcomes of Late Treatment

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Abstract

Mucopolysaccharidosis type I (MPS1) is a lysosomal storage disease caused by α-L-iduronidase deficiency. The therapeutic approach of the disease with recombinant human α-L-iduronidase (laronidase), with a significant improvement in patient's quality of life in various studies.

This review evaluates clinical, paraclinical outcomes, and patients quality of life, after an average of 13.5 months of laronidase treatment in two patients, diagnosed after the age of 9 with Hurler syndrome. The outcome was satisfactory. The treatment improved the patient's quality of life, but not curative.

Keywords: *Mucopolysaccharidosis Type I; Enzyme Replacement Therapy; Laronidase; Storage Diseases; Quality of Life*

Introduction

Mucopolysaccharidosis type I (MPS1) is an autosomal recessive disease caused by α-L-iduronidase deficiency, that affects an average of 1 in 100,000 live births in the United States and 0.82 in 100,000 live births in Europe.

α-L-iduronidase deficiency leads to the accumulation of glycosaminoglycans (GAGs) in lysosomes, resulting in multisystemic involvement that develop during the first year of life. It manifests as a vague of clinical symptoms extending from severe form (Hurler syndrome) to milder form (Scheie syndrome).

The best therapeutic approach for MPS1 is a combination of hematopoietic stem cell transplantation (HPSCT) and enzyme replacement therapy. However, HPSCT has limited applications due to its advantages such mortality and morbidity rates and the need for compatible bone marrow donors. Since 2003, the enzyme replacement therapy (Aldurazyme) is available, is reduces GAG's accumulations in various tissues and decreasing its urinary excretion. Early diagnosis and treatment are crucial to improve patients' quality of life.

This study was conducted on two patients being followed in the pediatric unit 2 at Harouchi Hospital for MPS1 disease to evaluate the therapeutic benefits of enzyme replacement therapy, regardless of the late diagnosis.

Case Report

Observation 1

The first patient, a 14-year-old not from a consanguineous marriage, she presented with advanced clinical dysmorphic features, such coarse facial features, frontal bossing, brood nose, floral nose, anteverted nares, macrocephaly, macroglossia, and a short neck, associated

with stature retardation (-3 SD) and sleep apnea. Abdominal examination revealed a femoral hernia accompanied by hepatomegaly and splenomegaly. The musculoskeletal examination indicates limited range of joint mobility, genu varum, and scoliosis. The patient walking range was severely limited. Ear nose throat examination reveals tonsillar hypertrophy and adenoids associated hypoacusis. The ophthalmological examination identified severe corneal cloudy with reduced visual acuity bilaterally and increase of intraocular pression at 29 mmHg.

Echocardiography shows moderate mitral disease with aortic insufficiency grade II, complicated by moderate dilated cardiomyopathy with global left ventricular ejection fraction and mild pulmonary arterial hypertension.

Spinal and pelvic X-rays shows a double convex dorsal and lumbar scoliosis, along with femoral dysplastic. The enzyme activity demonstrate α-L-iduronidase activity levels is diminished at level 0 (normal range is more 1.5), genetic testing confirm a double mutation, c.1598>G (p. (Pro534Arg)), confirming the diagnosis of mucopolysaccharidosis type I.

Enzyme replacement therapy was started immediately. After 14 months of efficiently delivered treatment (one infusion per week), a significant clinical improvements were observed such weight gain of 7 kg, regression of nocturnal snoring, sleep apnea frequency, and reduction in the size of the femoral hernia and resolution of hepatomegaly and splenomegaly. The six-minute walk test improved to 700 meters. However, the persistence of cardiac manifestation, corneal clouding, and skeletal deformities despite the treatment (Figure 1). The patient reported an improved quality of life, with significant amelioration in energy levels and endurance.

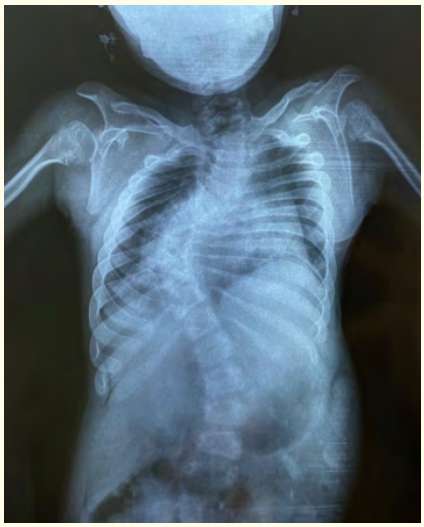

Figure 1: *Stationary appearance of scoliosis in a patient with MPS I.*

Observation 2

A 9-year-old patient, with clinical onset at the age of 3, she was born from a third-degree relatives marriage, she had a brother diagnosed with MPS type I. The clinical examination revealed facial dysmorphic features, macroglossia, statural retardation (-2.5 SD), a distended abdomen with hepatosplenomegaly, and an umbilical hernia present since birth, which progressively increased in size, it was surgically repaired at the age of 7, but it replaced. Musculoskeletal examination reveals a limited range of joint mobility with a claw reappearance of 3rd, 4th, and 5th fingers on both hands. The ophthalmologic examination revealed the cloudy corneal.

On further paraclinical evaluation, spinal pelvic X-rays reveals lumbar intervertebral forum widening, mild pelvic asymmetry, and flared iliac wings. Echocardiography show mild mitral stenosis with mild to moderate aortic insufficiency. Enzyme testing of α-L-iduronidase activity in leukocytes reveals severe reduced of α-L-iduronidase activity at 0.3 µmol/l/h (normal > 1.5). Genetic analysis identified a double mutation, c.1598C>G (p. (Pro533Arg)), confirming the diagnosis of MPS type I.

The patient received enzyme replacement therapy for 15 months. Showing a clinical evolution including stabilization of weight and height, regression of hepatosplenomegaly, and significant improvement in the six-minute walk test, which increased to 900 meters. However, the umbilical hernia persisted, and no improvement of skeletal deformities, limited range of joint mobility, or corneal clouding. Paraclinically, echocardiography demonstrated stability of mitral valve involvement.

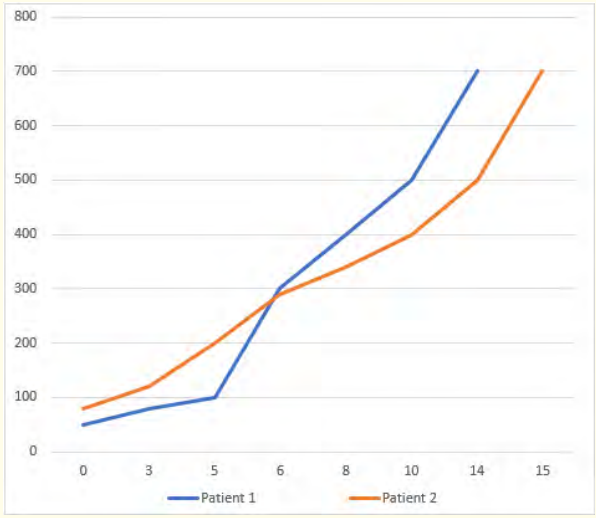

Figure 2: *Evolution of the 6-minute walk test in the 2 patients.*

Discussion

Mucopolysaccharidosis type I is a systemic lysosomal storage disease characterized by α-L-iduronidase leading to the accumulation of glycosaminoglycans (GAGs) in various tissues of the body [1].

The deposition of glycosaminoglycans in various cell types indecency significant hepatosplenomegaly, airway obstruction, and excessive urinary elimination of GAGs by the kidneys. The accumulation of GAG's in connective tissues manifests as short stature, joint stiffness and limited range of mobility, and severe skeletal abnormalities.

Substrate deposition in the corneal stroma of the eye may progressively lead to corneal clouding [1,2].

Cardiac manifestation mainly affects the heart valves and coronary vessels, leading to heart failure and pulmonary hypertension. Which can contribute to progressive disability and an increase risk of premature death, particularly in patients with the severe Hurler form of MPS I, with a limited life expectancy 10 years [3].

Hematopoietic stem cell transplantation, used since 1981 to treat MPS I, it prevents the onset of neurological manifestation in moderate or severe forms. However, it has not affected the existing neurological manifestations, musculoskeletal, ocular, or valvular cardiac

manifestations. HPSCT use is limited?? significant morbidity and necessity of compatible bone marrow. It's not indicated in moderate forms due to a negative benefit-risk ratio [4].

The first study on enzyme replacement therapy using α-L-iduronidase human recombinant was in 1997. The results obtained after one year of treatment showed reduced levels of lysosomal storage and significant clinical improvements [5]. Later, after a study involving 45 patients with MPS I, laronidase (Aldurazyme®) was approved in the United States and the European Union in 2003 [6].

The first evidence of the effectiveness of enzyme replacement therapy is the reduction of GAG levels urinary. Indeed, significant reductions of up to 73% were recorded after three months of treatment [9,10].

Various studies have shown that average values for weight and height are improved after the enzyme therapy. According to Tylki-Szymanska., *et al*. the effectiveness the effect of the enzyme replacement therapy is evident is evident in the height and weight [7] which corresponds our study outcomes.

After administration of enzyme replacement therapy, a significant improvement in physical activity was observed, expressed by an increase tolerance to exercise, although the distance remains below the normal range for children of the same age [8]. This is corresponds to the results of our study.

Many studies, including ours, have found that enzyme replacement therapy leads to improvement in spleen and liver size as early as the third week of treatment, as well as stabilization of cardiac manifestations. However, this studies didn't show any improvement regarding skeletal deformities or corneal clouding. This is explained by the enzyme replacement therapy using α-L-iduronidase??? delivery to organs such bone cartilage and eye remains minimal [7,8].

A clear improvement in the patient's vital capacity was observed. This corresponds with previous published studies showing that the vast majority of patients experience improvement of life quality few months after receiving of treatment [7].

Conclusion

Despite the delayed diagnosis and the late administration of enzyme replacement therapy in MPS I, which has proven it's effective in inducing significant changes. These changes are particularly evident in the improvement of certain clinical symptoms, offering a better quality of life for the patient and their family. These results highlight the crucial importance of early screening and therapeutic intervention in the management of mucopolysaccharidosis type 1.

Bibliography

1. M Sifuentes., *et al*. "A follow-up study of MPS I patients treated with laronidase enzyme replacement therapy for 6 years". *Molecular Genetics and Metabolism* 90.2 (2007): 171-180.

2. BT Poll-The., *et al* "The eye as a window to inborn errors of metabolism". *Journal of Inherited Metabolic Disease* 26.2-3 (2003): 229-244.

3. JE Wraith. "The first 5 years of clinical experience with laronidase enzyme replacement therapy for mucopolysaccharidosis I". *Expert Opinion on Pharmacotherapy* 6.3 (2005): 489-506.

4. J Muenzer and A Fisher. "Advances in the treatment of mucopolysaccharidosis type I". *New England Journal of Medicine* 350.19 (2004): 1932-1934.

5. ED Kakkis., *et al*. "Enzyme-replacement therapy in mucopolysaccharidosis I". *New England Journal of Medicine* 344.3 (2001): 182-188.

6. JE Wraith., *et al*. "Enzyme replacement therapy for mucopolysaccharidosis I: a randomized, double-blinded, placebo-controlled, multinational study of recombinant human alpha-L-iduronidase (laronidase)". *Journal of Pediatrics* 144.5 (2004): 581-588.

7. A Tylki-Szymanska., *et al*. "Efficacy of recombinant human alpha-L-iduronidase (laronidase) on restricted range of motion of upper extremities in mucopolysaccharidosis type I patients". *Journal of Inherited Metabolic Disease* 33.2 (2010): 151-157.

8. V Valayannopoulos and FA Wijburg. "Therapy for the mucopolysaccharidoses". *Rheumatology (Oxford)* 50.5 (2011): 49-59.

9. ED Kakkis., *et al*. "Long-term and high-dose trials of enzyme replacement therapy in the canine model of mucopolysaccharidosis I". *Biochemistry and Molecular Medicine* 58.2 (1996): 156-167.

10. JM Resnick., *et al*. "Pathology of the liver in mucopolysaccharidosis: light and electron microscopic assessment before and after bone marrow transplantation". *Bone Marrow Transplant* 10.3 (1992): 273-280.

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