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Short Communication

Hurler Syndrome

Abdulelah Awaji Madkhali*

Medical Technologist II at King Abdul Aziz Medical City-NGHA-Saudi Arabia, Medical Genetics Masters student at UQU, Saudi Arabia

***Corresponding Author:** Abdulelah Awaji Madkhali, Medical Technologist II at King Abdul Aziz Medical City-NGHA-Saudi Arabia, Medical Genetics Masters Student at UQU, Saudi Arabia.

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Hurler syndrome is an autosomal recessive condition induced by a deficiency of the enzyme α-L-iduronidase1 of the mucopolysaccharide metabolism. Hurler syndrome is the classic prototype of a mucopolysaccharide disorder, where 1:100,000 births are very limited, and no predilection is observed for sex or race. In 1919, German pediatrician Gertrud Hurler identified Hurler syndrome for the first time. This is one of 11 mucopolysaccharidosis (MPS) diseases. Hurler's syndrome is known to be type I mucopolysaccharidosis (MPH I) and commonly referred to as gargoylism [1]. MPS -IH showed clinical criteria with mental retardation, large head with bulging frontal bones, depressed nasal bridge with broad nasal tip and anteverted nostrils, full cheeks and enlarged lips (Figure 1).

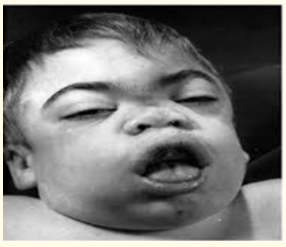

Figure 1: It shows the clinical features of a patient with MPS-IH.

Biochemistry of IDUA metabolism

Those who have Hurler syndrome cannot break down the mucopolysaccharides or glycosaminoglycans-glycosaminoglycans-of long sugar molecules by alphas-l-iduronidase, a glycosaminoglycans degradation lysosomal enzyme. GAGs may accumulate in the brain, heart, liver, bones, and other body organs lysosome. The build-up of GAGs in the human body causes organ damage [2] (Figure 2).

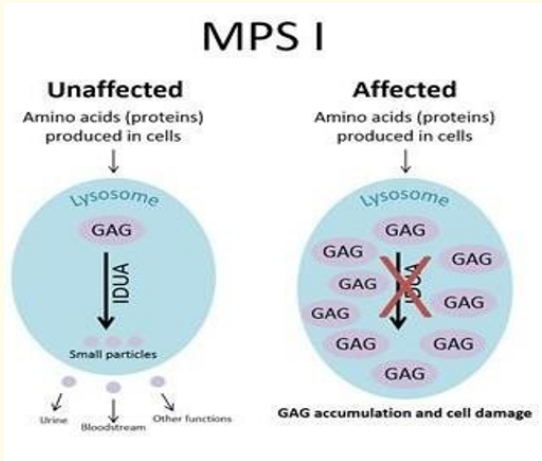

Figure 2: The metabolic pathway of alpha -L-idurnidase.

The Gene responsible for the disease

The α-L-iduronidase gene (IDUA) (Phenotype MIM #607014 and Gene /Locus MIM #252800) is located on chromosome 4p16.3 spanning 19 kb comprising 16 exons that generate two alternatively spliced mRNAs that encode two distinct protein isoforms; isoform a is a 653 amino acid precursor protein and isoform b is a 521 amino acid protein. Removal of the 26 amino acid signal peptides from the isoform a preprotein generates the enzymatically functional glycoprotein that is active as a monomer.

Molecular genetics of the disease

Two abnormal copies of the IDUA gene are passed to children with the Hurler Syndrome. This is the gene that encodes the iduronidase enzyme. More than 201 mutations were found to cause MPS I in the IDUA gene in 2018 [3]. Since Hurler syndrome is an autosomal recessive condition, the people afflicted have two versions of the gene without functioning. The born person is considered a carrier with a regular copy and a faulty copy. It is less α- L-iduronidase than a human with two natural gene copies. However, decreased enzyme output in carriers is still adequate for normal operating conditions; no signs of the disease should be present.

Management of the disease

Multidisciplinary management. For patients under 2,5 years of age (and chosen patients above this age limit), hematopoietic stem cell transplantation (HSCT) is the option therapy since it can extend longevity and maintain neurocogne and enhance some of the somatic characteristics. Until developmental degradation occurs, HSCT should be done early in disorder. Laronidase enzyme replacement therapy (ERT), which is a permanent procedure that alleviates non-neurological effects is indicated for all Hurler patients. The early use of ERT indicates that certain clinical characteristics of this disease are deferred or even stopped. Additional Hurlers syndrome treatment is generally positive, requiring surgery (e.g., adenotonsillectomy, reconstruction of adenosillitomy, hernia, ventrikopritoneal shunting, coronary valve reversal, the release of carpal tunnel, spinal decompression) [4]. Recent therapies: research in animal model gene therapy involving the supply of iduronidase enzymes genes using viral vectors has been undertaken [5]. Correction of liver, spleen and brain diseases have been shown to some degree. A potential alternative medical cure for MPS disease could be offered by gene therapy.

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