WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 11, 1888-1891. Case Study ISSN 2277– 7105

CASE REPORT ON HUNTER SYNDROME: A REVIEW

Vaishnavi L. R.[1]*, Anju Deepak Unnithan[2] and Supriya S.[3]

[1]Pharm D Intern, PRS Hospital, Killipalam, Trivandrum.

[2]Pediatrician, Department of Pediatrics, PRS Hospital, Trivandrum.

[3]Supriya S, Clinical Pharmacologist, PRS Hospital Killipalam, Trivandrum.

Article Received on
10 July 2021,

Revised on 30 July 2021,
Accepted on 20 August 2021

DOI: 10.20959/wjpr202111-21518

***Corresponding Author**
Vaishnavi L. R.
Pharm D Intern, PRS Hospital, Killipalam, Trivandrum.

ABSTRACT

Hunter syndrome is an X linked recessive mucopolysaccharidosis (type II) caused by the deficiency of iduronate 2-sulfatase. This in turn leads to the accumulation of glycosaminoglycans, dermatan and heparan sulfate. The intracellular and extracellular accumulation of these substances lead to multisystemic organ abnormality. It is a rare syndrome with a very low prevalence of 1.3:100 000 male live births. Hunter syndrome is one of a group of diseases called mucopolysaccharidoses.

INTRODUCTION

Hunter syndrome is a rare, inherited disorder in which the body does not properly digest (break down) sugar molecules in the body. When these molecules build up in organs and tissues over time, they can cause damage that affects physical and mental development and abilities. The disorder almost always occurs in boys. Hunter syndrome is almost always diagnosed in males. Doctors diagnose it in roughly 1 out of 100,000 to 170,000 males. Females can be carriers of the genetic mutation that causes MPS II.People are at a higher risk for Hunter syndrome if they have a family member with the disease. Boys have a higher risk of inheriting the disease than girls do. This difference exists because the disease is linked to the X chromosome. Girls inherit 2 X chromosomes, while boys have only 1. If a girl inherits the faulty gene, her other X chromosome can provide the necessary enzyme. Hunter syndrome results from a gene mutation (abnormality) passed down from a mother to her child. The affected gene is responsible for regulating the production of a specific enzyme (substance that sparks chemical reactions in the body). This enzyme breaks down complex sugars the body produces. In people with the disease, the body does not produce any or enough of this enzyme. The missing enzyme causes molecules of the sugars to build up in

organs and tissues throughout the body. These buildups can damage organs and tissues throughout the body. Hunter syndrome symptoms vary in severity and include:

- Stiff joints
- Thickening of facial features including nostrils, lips and tongue
- Delayed appearance of teeth or wide spaces between teeth
- Larger than normal head, wide chest and short neck
- Hearing loss that gets worse with time
- Delayed growth, especially starting around age 5
- Enlarged spleen and liver
- White growths on the skin

A doctor uses several tests to diagnose Hunter syndrome

- **Urine test:** Checks for unusually high levels of sugar molecules
- **Blood tests:** Can show low or absent levels of enzyme activity, which is also a sign of the disease
- **Genetic testing:** Identifies mutations (changes) in the gene to confirm diagnosis

Treatment for Hunter syndrome depends on the symptoms. A team approach, with specialists in different areas of expertise, could help manage the potential problems associated with the condition and give patients the best possible care. The goal of treatment is to slow the progression of the disease and improve quality of life. The treatment shown to do this best is enzyme replacement therapy. Doctors replace the missing enzyme with a human-made version of the enzyme, called Elaprase®. Doctors usually deliver this treatment intravenously (through a needle inserted into the vein) once a week.

CASE REPORT

This was a five-year-old male patient, first pregnancy of healthy non-consanguineous parents, with a healthy two-year-old brother. Generalised hypertonia was observed at 3months and psychomotor retardation was evident from 16 months; the consultation was for the patient's behavioural disorder characterised mainly by aggression. At the age of 3, he was diagnosed with bilateral conductive hearing loss. He had a history of repeated upper respiratory tract infections, on several occasions requiring hospital admission. He had an uncomplicated tonsillectomy at the age of 4.Physical examination showed the patient's general condition to be poor, with psychomotor disabilities and severemal nutrition, normocephalic, coarse facial features, prominent frontal bone, depressed nasal bridge, broad base of nose with anteverted

nostrils, thick lips, prominent ears, short neck with low hairline, lung fields well-ventilated, heart sounds regular with good intensity, abdomen obese with liver 2 cm below the costal margin, umbilical hernia, male genitalia, limbs with restricted extension, mainly in elbows and knees, claw hand and generalised hypertrichosis.

Investigations and Laboratory tests

Chest X-ray and echocardiogram within normal parameters. Abdominal ultrasound with moderate hepatomegaly, bileducts show no structural changes. Electroencephalogram normal with no epileptic activity. Extraction of genomic DNA from peripheral blood was carried out using conventional methods. The IDS gene was analysed by polymerase chain reaction (PCR) and direct DNA sequencing. The PCR products obtained were sequenced on an ABI 3730 Automated Sequencer. Qualitative analysis of glycosaminoglycans (GAGs) in urine with toluidine blue positive. Iduronate sulfatase enzyme activity in plasma diminished at 1.2 L mol/l/h (ref-erence value: >2 L mol/l/h), confirming the diagnosis of MPSII. Molecular analysis of the IDS gene, which codes for the enzyme iduronate sulfatase, detected that the patient was hemizygous for the mutation (c.1403G>A, p.R468Q). The patient died of respiratory complications 6 months after being diagnosed with MPS II.

DISCUSSION

Hunter syndrome is a rare inherited disease in which, because of its progressive nature and the irreversible damage it causes, early diagnosis and therapeutic intervention are of utmost importance. In our patient, given his clinical manifestations, this syndrome could have been suspected, but over the course of his medical visits and admissions to hospital, no diagnosis was made. Recombinant human synthetic enzymes (Enzyme Replacement Therapy or ERT) are currently used as treatment for some lysosomal storage diseases, including Hunter syndrome.

The main benefits of ERT include a significant reduction in urinary GAG excretion, with improved joint mobility, ability to walk, lung function, cardiac parameters and hearing, and reduced liver and spleen volume. However, ERT administered intravenously does not cross the blood-brain barrier, so nervous system damage cannot be repaired. Also, despite ERT, no improvement has been reported in ophthalmological or skeletal problems or respiratory function, again emphasising the importance of early diagnosis. ERT has been shown to be safe in patients under a year old. Clinical evidence shows that early interventions with ERT produce a better response to treatment with a clear improvement in patients'quality of life.

The mutation found in the patient was first described by Whitley et al. in 1993; an adenine replaces a guanine in exon 9 of the IDS gene, which produces a sub-stitution of glutamine for arginine at position 468 on the protein. Sukegawa et al., in a study of expression, demonstrated decreased enzyme activity in fibroblasts of patient with this mutation. This mutation has been reported in several ethnic groups and is associated with severe phenotypes. Other mutations, R468Wand R468L, have been reported in the same codon, suggesting that this site is a mutational‘‘hot spot’’ for the IDS gene. Over 350 mutations have been described in the IDS gene to date. In conclusion, we must emphasise the need to keep up to date and create expert teams of doctors and scientists specialised in inborn errors of metabolism. It would be reasonable to think that the vast amount of resources that social security systems and government programmes assign to this type of disease would not only be used for medical care but also be dedicated to research and the production of new medical knowledge.

REFERENCES

1. Baehner F, Schmiedeskamp C, Krummenauer F et al. Cumulative incidence rates of the mucopolysaccharidoses in Germany. *J Inherit Metab Dis*, 2005; 28: 1011–17. 10.1007/s10545-005-0112-z
2. Hunter C. A rare disease in two brothers. *Proc R Soc Med*, 1917; 10: 104–6.
3. Wang RY, Bodamer OA, Watson MS et al. Lysosomal storage diseases: diagnostic confirmation and management of presymptomatic individuals. *Genet Med*, 2011; 13: 457–84. 10.1097/GIM.0b013e318211a7e1
4. Wraith JE, Scarpa M, Beck M et al. Mucopolysaccharidosis type II (Hunter syndrome): a clinical review and recommendations for treatment in the era of enzyme replacement therapy. *Eur J Pediatr*, 2008; 167: 267–77. 10.1007/s00431-007-0635-4
5. Gajula P, Ramalingam K, Bhadrashetty D. A rare case of mucopolysaccharidosis: Hunter syndrome. *J Nat Sci Biol Med*, 2012; 3: 97–100. 10.4103/0976-9668.95984
6. Shah GS, Mahal T, Sharma S. Atypical clinical presentation of mucopolysaccharidosis type II (Hunter syndrome); a case report. *J Med Case Rep*, 2010; 4: 154 10.1186/1752-1947-4-154.
7. Ben Simon-Schiff E, Bach G, Zlotogora J et al. Combined enzymatic and linkage analysis for heterozygote detection in Hunter syndrome: identification of an apparent case of germinal mosaicism. *Am J Med Genet*, 1993; 47: 837–42. 10.1002/ajmg.1320470608
8. Froissart R, Da Silva IM, Maire I. Mucopolysaccharidosis type II: an update on mutation spectrum. *Acta Paediatr Suppl*, 2007; 96: 71–7. 10.1111/j.1651-2227.2007.00213.x