

Hunter Syndrome - A Case Study

Vijayalakshmi N¹, Blanshie Rajila William²

¹HOD and Professor, Department of Paediatric Nursing, Kg College of Nursing, Coimbatore, India

²Associate Professor, Department of Paediatric Nursing, Kg College of Nursing, Coimbatore, India

Abstract: Hunter syndrome, or mucopolysaccharidosis type II (MPS II), is a lysosomal storage disease caused by a deficiency of the lysosomal enzyme iduronate-2-sulfatase (I2S). The lack of this enzyme causes heparan sulfate and dermatan sulfate to accumulate in all body tissues. This syndrome is found in fewer than 20 cases per million births, making the disease the rarest form of the mucopolysaccharide disorders.

Key Words: Mucopolysaccharidosis Type-II, Iduronate-2-Sulfatase

1. Case History

Master X 5 ½ yrs old child was admitted with the complaints of cough with cold for past three days and history of hurried and difficulty in breathing. On examination the child was evaluated for fever, irritable, tachypneic, respiratory distress, moderate hydration, presence of nasal block, thin built, dull and Disoriented, Enlarged head with frontal bossing, Coarse facies, Symmetrical and heavy eyebrows, Large nose with nasal flaring, Large tongue and thick lips, Intercostal retractions, Distended abdomen, Hepatosplenomegaly, Decreased range of motion, hearing impairment and developmental delay. The child heart rate is 158/min, respiratory rate is 64/min, SPO₂ is 80% in room air 100% with O₂ and CRT is < 3 sec. In early infancy, the child had undergone hernioplasty for umbilical hernia. The history reveals that the child was born by normal delivery with birth weight 1300 kg which was under the classification of high risk newborn. On investigation chest X-ray showed bilateral pneumonia with right middle lobe collapse. Blood counts show low Hb count and thrombocytopenia. CRP was negative. Urinary glycosaminoglycans were positive. Finally the child diagnosed as Hunter syndrome or Mucopolysaccharidosis II with bilateral pneumonia with right middle lobe collapse. In view of respiratory distress, child was kept in high dependency unit. He was treated with Inj.cefotaxime, Inj.Amikacin, Nebulization with steroids, Bronchodilators, Nasal steroids and other supportive measures. In view of anemia packed RBC transfusion was given. Then the child improved clinically, respiratory distress settled.

2. Introduction

Hunter syndrome or Mucopolysaccharidosis type II (MPS II) is a lysosomal storage, which results from the deficiency of the enzyme called iduronate-2-sulfatase (IDS) [1]. This syndrome is genetically inherited, having X-linked recessive inheritance, and it consists in a homozygote mutation of the IDS gene, located on the chromosome Xq28, thus leading to the affliction of the synthesized protein. Hunter syndrome is a rare metabolic

disease that can severely compromise health, well-being and life expectancy [2].

Hunter's syndrome was first described by a Scottish physician Charles A. Hunter in 1917. The disease is inherited in an X-linked recessive manner and usually affects males [3]. There is a deficiency of iduronate-2-sulfatase (I2S), a lysosomal enzyme that cleaves O-linked sulfate moieties from the glycosaminoglycans (GAGs) dermatan sulphate and heparan sulphate, the first step in their degradative pathway. This abnormality leads to accumulation of GAGs within almost all tissues and organs, resulting in the multisystem manifestations of MPS II [4]. Accumulation of the GAG over the time causes the symptoms and complications and gradually worsens and become more noticeable [5]. This results in permanent, progressive cellular damage which affects the appearance, physical abilities, organ and system functioning and in most cases, mental development.

Hunter syndrome appears in children as young as 18 months. It mainly occurs in boys, although very rarely it has been observed in girls. Common risk factors which are noted are two, *Family history*. Hunter syndrome is caused by a defective chromosome and a child must inherit the defective chromosome to develop the disease. Hunter syndrome is what known as an X-linked recessive disease. This means that women carry the defective disease-causing X chromosome and can pass it on, but women aren't affected by the disease themselves. [6]

Sex: Hunter syndrome nearly always occurs in males. Girls are far less at risk of developing this disease because they inherit two X chromosomes. If one of the X chromosomes is defective, their normal X chromosome can provide a functioning gene. If the X chromosome of a male is defective however, there isn't another normal X chromosome to compensate for the problem [6]

Symptoms of the hunters are not present when a child is born, but start to develop after the first year of life. The clinical picture of this syndrome includes cardio-vascular signs and symptoms, as the involvement as myocardium and the valve thickening; neuro-psychiatric disorders: behavioral disorders, cervical myelopathy, hydrocephaly, mental retardation, acquisitions regression, seizures and deglutition difficulties; digestive signs and symptoms like diarrhea, hepatosplenomegaly, Ear involvement like recurrent medium otitis, deafness; eye involvement means retinal dystrophy; muscle and bones disorders: atlanto-axial instability, carpal tunnel syndrome, facial dysmorphism, degenerative hip dysplasia, disostosis multiplex, hernias, joint contractions, kyphosis and macrocephaly; and also respiratory symptoms like obstructive sleep apnea, restrictive pneumopathy, obstruction of the upper airways [7], [8].

Evaluation of the disease is confirmed by paraclinical investigations (blood tests, X-rays, CT, MRI, DEXA, EKG, and so on...), and not ultimately, the molecular analysis of the IDS gene, with major importance. The specific treatment of mucopolysaccharidosis type II is just a substitutive one, without being curative, and it consists in the administration of the enzyme iduronate2-sulphatas [9].

Traditionally, treatment for MPS II has targeted the symptoms, with the aim of providing palliative benefit. However, in recent years, clinical trials have demonstrated improvements in selected laboratory markers, certain somatic features and measures of clinical function with the use of enzyme replacement therapy (ERT) comprising regular intravenous administration of idursulfase, a recombinant form of human I2S. Enzyme replacement therapy (ERT) can help slow the disease for boys with milder Hunter syndrome. It replaces the protein their body doesn't make. ERT can help to improve the breathing, walking and growth. Still it is unclear to what extent they are mirrored by improvements in health-related quality of life (HRQL) [10].

3. Discussion

Mucopolysaccharidosis is a group of inherited diseases characterized by defective lysosomal enzymes responsible for the degradation of mucopolysaccharides, which are major components of intercellular connective tissue. This leads to an accumulation of incompletely degraded mucopolysaccharides in the lysosomes which affect various body systems through enzymatic activity [11]. The accumulation of GAG within the lysosomes is responsible for the clinical manifestations of this disorder. Patients typically appear normal at birth in both forms of the disease, in severe form the clinical features appears between two and four years of age, while in the mild form the clinical feature appears in the second decade of the life of the child. [12]. Severe form poses with severe mental retardation and loss of skills. Death usually occurs in the first or second decade of life, may be due to airway obstruction or cardiac failure. Milder form there is possibility of mental retardation with normal intelligence, the clinical features are less obvious and progress very slowly [13]. This case is with mild form of disease. Enzyme replacement therapy has emerged as a new treatment for mucopolysaccharidosis disorders.

4. Conclusion

MPS II is a severe progressive multi systemic disorder that has the potential to cause disease in most body systems and is usually fatal in the second and third decade of life. Based on the clinical representation, it is possible to diagnose a case of MPS. Early detection of the disease and appropriate management through a multidisciplinary approach is recommended to improve the quality of life. A careful and systemic approach is needed to accurately diagnose the exact type as enzymatic studies are not available in most centers.

References

- [1] Lorena Elena Melit, Oana Marginean, Carmen Duicu, Cristina Campean, Maria Oana Marginean, A Rare Case Of Hunter Syndrome – Case Report. *Revista Română de Pediatrie*; 2015. Volumul LXIV, NR. 1, 38-40.
- [2] Wraith JE, Scarpa M, Beck M, Bodamer OA, Meirleir LD, Guffon N, 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.
- [3] Mandal A, What is Hunter Syndrome? 2014 (9). <https://www.news-medical.net/health/What-is-Hunter-Syndrome.aspx>.
- [4] Nelson J: Incidence of the mucopolysaccharidoses in Northern Ireland. *Hum Genet* 1997, 101:355–358.
- [5] Young ID, Harper PS: Mild form of Hunter's syndrome: clinical delineation based on 31 cases. *Arch Dis Child* 1982, 57:828–836
- [6] <https://www.mayoclinic.org/diseases-conditions/hunter-syndrome>
- [7] Wraith J.E., 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.
- [8] Martin R., Beck M., Eng C., Giugliani R. et al. Recognition and diagnosis of mucopolysaccharidosis II (Hunter syndrome). *Pediatrics* 2008; 121:377-86.
- [9] Burton B.K., Giugliani R. Diagnosing Hunter syndrome in pediatric practice: practical considerations and common pitfalls. *Eur J Pediatr* 2012; 171:631-639.
- [10] Muenzer J, Wraith JE, Beck M, Giugliani R, Harmatz P, Eng CM, Vellodi A, Martin R, Ramaswami U, Guzsav-Calikoglu M, et al: A phase II/III clinical study of enzyme replacement therapy with idursulfase in mucopolysaccharidosis II (Hunter syndrome). *Genet Med* 2006, 8:465–473.
- [11] Kliegman RM, Behrman RE, Jenson HB, Stanton FB. 18th ed. Vol. 1. Philadelphia: Saunders; 2007. *Nelson Textbook of Pediatrics*; pp. 620–6.
- [12] Tuschl K, Gal A, Paschke E, Kircher S, Bodamer OA. Mucopolysaccharidosis Type II in females: Case report and review of literature. *Pediatr Neurol*. 2005; 32:270–2.
- [13] Shah GS, Mahal T, Sharma S. Atypical clinical presentation of mucopolysaccharidosis type II (Hunter syndrome): A case report. *J Med Case Reports*. 2010; 4:154.