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JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Case Report

Open Access, Volume 5

A case report of harlequin ichthyosis in newborn

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Received: Aug 01, 2024
Accepted: Aug 16, 2024
Published: Aug 23, 2024
Archived: www.jcimcr.org

DOI: www.doi.org/10.52768/2766-7820/3220

Abstract

A rare and serious genetic skin disorder called harlequin ichthyosis can affect a developing fetus. The most severe and debilitating type of autosomal recessive ichthyosis is harlequin ichthyosis. This disease is caused by mutation in the lipid transporter's A12 adensine triphosphate binding cassette. In this case, we describe a patient with harlequin ichthyosis who had no family history. No abnormality was observed in the ultrasound examinations performed during pregnancy. A 23-year-old pregnant woman was referred to our hospital, who was experiencing premature rupture of membranes and labor pain. A baby boy with harlequin ichthyosis was born to his mother. The baby died on the fourth day.

Keywords: Ichthyosis; Genetic skin; A12 mutations; Sonography; Autosomal.

Introduction

A rare and serious genetic skin condition called Harlequin Ichthyosis (HI) can develop in the growing fetus. Harlequin ichthyosis is an autosomal recessive genetic disorder [1], linked to chromosomes 5P & 9P, and is primarily attributed to a mutation occurring in the adenosine triphosphate binding cassette A12(ABCA12) gene. Research has revealed that a substantial proportion of individual affected by harlequin ichthyosis carry a mutation within the ABCA12 gene on their chromosomes. The most severe form of non-syndromic ichthyosis [2,3]. HI is linked to prenatal morbidity and potential early-life mortality. The incidence rate for HI ranges from 1/300,000 to 1/1,000,000, which is quite low [4,5]. Race and ethnicity have no clear association with the prevalence of HI [6]. In subsequent pregnancies, there is a 25% chance that the condition may recur [7]. Harlequin Ichthyosis ia a rare genetic disorder characterized by the presence of thick, plaque-like scales that cover the entire body [8]. Additionally, this condition is known to manifest with various facial abnormalities, including ectropion (outward turning of the eyelids), eclabium (eversion of the lips), and ear deformities. Moreover, individuals with Harlequin Ichthyosis typically exhibit short limbs hypolastic (underdeveloped) digits, and a complete of eyelashes & eyebrows. Additionally, low body temperature, dehydration, respiratory problem, inadequate nutrition, low blood salt, convulsion & skin infections are all serious risks for infants [12,13].

Infants with HI have a higher chance of death from skin infection, fluid loss, or respiratory failure. In very rare circumstances,

some infant with HI may survive for several months or years. However, most infants with HI die within 2 days of birth. The successful management of Harlequin ichthyosis necessitates a comprehensive, multidisciplinary approach right from the beginning. In industrialized countries, advanced therapies such as retinoids and new technologies have increased survival rates [14]. However, this is not the case in underdeveloped countries [15-17]. A case of a mother giving birth to a child with HI at age 24 is described in this study.

Case presentation

On July 26, 2023, at approximately 2:10 p.m., a 23-year-old pregnant woman, expecting her first child, was admitted to the maternity ward at NEST Hospital in Haryana. She presented with premature rupture of membranes and signs of distress during labor. Based on her last menstrual period, her gestational age was estimated to be 35 weeks and 1 day. However, ultrasound measurements indicated a slightly different gestational age of 35 weeks and 4 days. Throughout the course of her pregnancy, ultrasound examinations conducted during both the ninth and twenty-fifth weeks did not reveal any developmental abnormalities in the fetus.

Genotypic identification and genetic analysis were not performed before the birth of the infants. At 10:55 a.m. on July 27, 2023, a live baby boy was delivered by cesarean section due to a slow fetal heart rate and persistent labor pains. The baby was diagnosed with HI. Apgar score was 8.20 and birth weight, height & head circumference were 2800 kg, 43 cm, and 35.5 cm, respectively.

Figure 1: A baby boy with flattened ears and a nose, open wide mouth & cracked skin.

In the fifth minute, Apgar measured 9 points. Babies have pressure on the ears, ichthyosis on the scalp, face, and neck, bulging outwards, and fishy mouths and eyes that are enlarged due to the rotation of the eyelids from the eyeballs. The scalp showed slight hair loss (Figure 1). Infants were not tested for inflammatory markers, electrolytes, or other parameters at birth. After birth, the infant was transferred to the Neonatal Intensive Care Unit (NICU). The nursing team made several efforts to administer an Intravenous (IV) line to the baby, but they were unable to do so successfully. Consequently, the decision was made to transfer the baby to the NICU two days later. Antibiotics were not given according to the doctor's advice. Eye emollients, saline compresses, and mild emollients were part of the skin care regimen. But he died on the fourth day.

Discussion

The ABC transporter ABCA12 plays a crucial role in the transfer of lipids across the cell membrane. Mutations in this transporter are associated with some of the most severe autosomal recessive genetic conditions. These mutations lead to a significant reduction in lipid production by fetal epidermal keratinocytes, which in turn results in the breakdown of the skin's lipid barrier. As a consequence, this condition, known as Harlequin Ichthyosis (HI), occurs at a rate of approximately 1 in 300,000 live births [18,19].

Babies born with Harlequin Ichthyosis face an extremely high risk of mortality and have a grim prognosis. Sadly, most infants affected by this condition do not survive beyond the first day of birth due to a combination of factors including respiratory difficulties, susceptibility to infections, heat exhaustion, and severe dehydration [10]. It's important to note that the chances of survival are influenced by the specific type of mutation present in the ABCA12 gene. Compared to babies with homozygous mutations, children with compound heterozygous mutations have a higher survival rate. According to previous studies [21], the median survival rate of HI patients who survive the early neonatal period is estimated to be around 55% [20]. The age range of these patients is 10 months to 25 years. The babies in this experiment died on the fourth day. Many affected newborns survive to adulthood thanks to recent improvements in neonatal care in industrialized countries. Greater chance to survive. Pregnancy ultrasound and genetic testing are very important because there is a 25% chance of getting pregnant again [10-22]. Ultrasonography is the most common clinical method for diagnosing HI. can be used to diagnose rare genetic diseases such as congenital ichthyosis. Essentially, the goal of this approach is to identify causal mutations in gene families associated with one or more genetic diseases. Compared to conventional sequencing methods, NGS has significantly improved clinical diagnosis and changed the face of genetic testing, especially in rare hereditary diseases [23]. Fetal DNA testing is available for parents of children with HI [24,25]. ABCA12 mutations are detected more quickly and reliably using reporter RNA analysis using hair samples, according to the study [26]. A pregnancy ultrasound can sometimes detect signs of HI, including ectropin, primordial, contractures, and thick floating particles in the amniotic fluid [27]. Early use of antibiotics and retinoid therapy may increase the incidence of HI [28]. In neonates with HI, early systemic retinoid administration has been shown to induce faster shedding of hyperkeratotic plaques, and continuous administration has been shown to reduce the risk of ectopia and eclabium [29]. According to a 2021 study, regular use of retinoids may have additional therapeutic effects that benefit corneal repair in newborns with HI [30]. HI neonates were treated at 4 months of age after receiving neonatal treatment with acitretin at a dose of 0.5 mg/kg per day [31]. Dogabitdi is a promising alternative to acitretin for the treatment of ichthyosis. Although topical retinoids habe been suggested as an alternative to surgery, Tsivilika et al. admitting that in most cases there are no good results. It is also noted that vitamin D supplementation should be considered to prevent the adverse effects of retinoids. HI treatment strategies may include surgical procedures [9]. Tsivilika et al. evaluated the effect of surgical procedures in the management of HI in a narrative review. Surgical procedures for necrosis of

the fingers and eyes are mentioned in the evaluation. Previous studies have found that early surgery has a beneficial therapeutic effect in the case of HI [32,33]. There is no evidence that surgery between 6 and 12 months results in less ectopy. Surgical procedures involve risks, and surgical wounds increase the risk of infection [34-36]. HI can be very difficult to treat medically and surgically. More research is needed on this topic. Hospitalization for HI patients should be performed in a tertiary care facility, level III NICU [9]. A multidisciplinary team including nurses, physical therapists, orthopedics, plastic surgeons, ophthalmologists, otolaryngologists, geneticists, dermatologists, and neonatologists are involved in the management of resuscitation [4-38].

The nursing team, especially nurses, is responsible for maintaining skin integrity, preventing hospital-acquired infections and emergency hospital care, and providing necessary guidance and assistance to family members and caregivers. According to Moraes et al. the multidisciplinary effectiveness of the therapy depends on the nursing procedure, especially on the care plan [39]. To reduce the risk of infection during a patient's hospitalization, nursing staff must take aggressive measures [39].

Postnatal circulation, airway formation, and breathing are the main treatments for infants with HI. Use adequate emollients and salt packs to keep the skin supple and speed up the desquamation process. According to research, affected infants should be kept in an incubator with higher humidity [40]. Continuous monitoring of liver & kidneys is essential [39-41]. Monitoring of serum electrolytes, daily weight and urine output is recommended. In addition, infection prevention is essential to improve survival during neonatal treatment [9].

Conclusion

Harlequin Ichthyosis (HI) is an exceedingly rare genetic skin condition that demands continuous, comprehensive management. While HI does not typically lead to death, it remains a serious, chronic ailment that poses significant challenges in terms of care. Thus, the long-term well-being of HI patients necessitates a multidisciplinary approach, with open lines of communication between the medical team, healthcare providers, and family members.

Due to the severity of HI, striking a delicate balance between pain management and minimizing potential side effects can prove to be quite challenging for caregivers. Early utilization of sonographic techniques for prenatal diagnosis is crucial for timely intervention and treatment planning.

Furthermore, as most infants born with HI do not survive past infancy, it is imperative that medical professionals and psychologists offer unwavering support to parents facing this devastating diagnosis. Thankfully, advances in neonatal care, early administration of oral retinoids, and surgical procedures have led to improved survival rates for those afflicted with HI.

Declarations

Acknowledgments: Thanks to Dr. Renu Rathi (HOD) for providing the case report, patient image, and consent.

Contributions from the writers: The final text was actively written, edited, and approved by all authors.

Availability of data and material: This article does not fall under the category of data sharing because no data sets were created or examined for this investigation.

Conflicts of interest: No potential conflicts of interest were disclosed by the authors with regard to the publication of this paper.

Funding: The publication of this paper was all done without any financial assistance from the author.

Informed consent: The child's legally appointed representatives gave their written approval for the publication of their child's anonymised information in this article.

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