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HARLEQUINN ICTHYOSIS: A CASE BASED ON GENETIC SKIN DISORDER

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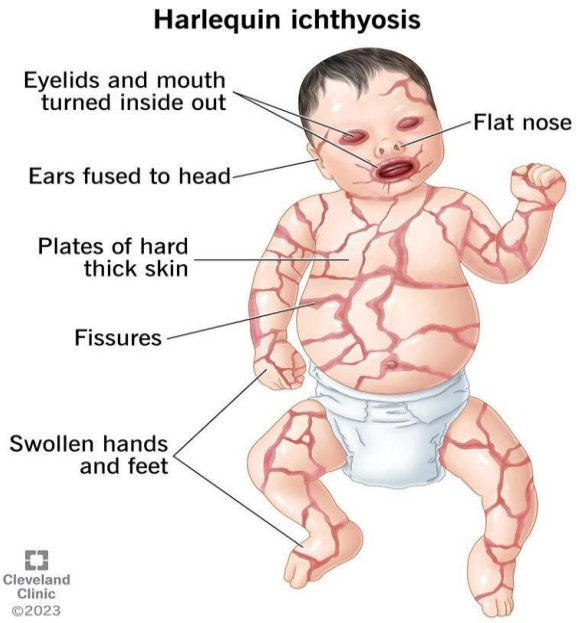
ABSTRACT

Harlequin Ichthyosis (HI) is an exceptionally rare and severe genetic skin disorder that manifests at birth. This condition arises from a mutation in the ABCA12 gene, which is crucial for the formation of the skin's protective barrier. When this gene malfunctions, skin cells fail to shed properly, resulting in the emergence of thick, hard scales that envelop the body. The term "Harlequin" is derived from the diamond-shaped cracks that develop between the thick skin plates, resembling the attire of a harlequin clown. Newborns affected by this condition exhibit extremely tight and thick skin, which can limit movement and lead to deformities such as ectropion (where the eyelids turn outward), eclabium (where the lips protrude), and flattened facial features. Due to the compromised skin barrier, these infants face a heightened risk of dehydration, infections, and respiratory complications. Without prompt medical intervention, the condition can become life-threatening. Diagnosis typically occurs at birth based on physical characteristics and is confirmed through genetic testing. In families with a history of this disorder, prenatal diagnosis via amniotic fluid analysis can detect the gene mutation prior to birth. Treatment primarily focuses on supportive care to maintain skin hydration and prevent infections. Oral retinoids, like isotretinoin, are utilized to reduce skin thickness and enhance survival rates. With the progress in medical treatments, many children diagnosed with Harlequin Ichthyosis can now lead longer lives. In summary, while Harlequin Ichthyosis is a serious genetic disorder, early detection, appropriate treatment, and ongoing care can significantly enhance the quality of life for those affected.

KEYWORDS: Treatment Primarily Focuses on Supportive Care to Maintain Skin Hydration And Prevent Infections

INTRODUCTION

Harlequin Ichthyosis (HI) is one of the rarest and most severe forms of congenital ichthyosis, a group of inherited skin disorders characterized by excessive thickening of the skin due to abnormal keratinization. The term ichthyosis is derived from the Greek word “ichthys”, meaning fish, referring to the scaly appearance of the skin. The prefix “Harlequin” originates from the diamond-shaped patterns that form on the skin surface, resembling the costume of the harlequin clown from Italian theatre. This condition is often fatal in the neonatal period, though advances in medical treatment and neonatal care have significantly improved survival rates in recent years.



HISTORY OF HARLEQUINN ICHTHYOSIS

Early Descriptions

1.1750 – The first known medical description was given by Rev. Oliver Hart in South Carolina.

2. He described a newborn with thick, hard, plate-like skin with deep cracks, resembling a harlequin costume.

3. At that time, the condition was poorly understood and always fatal within days.

19th–Early 20th Century

1. Doctors recognized it as a congenital skin disorder, but the cause was unknown.
2. It was Often confused with other ichthyosis types.
3. Most infants died shortly after birth due to:

- Severe dehydration
- Infections
- Breathing difficulty

Mid–Late 20th Century

1. Advances in neonatal intensive care (NICU) slightly improved survival.
2. The term "Harlequin Ichthyosis" became standard.
3. Researchers suspected a genetic cause, inherited in an autosomal recessive pattern.

2005 – Major Breakthrough

1. Scientists identified mutations in the ABCA12 gene as the cause.
2. ABCA12 is essential for lipid transport in the epidermis, required for a normal skin barrier.
3. This discovery allowed
4. Genetic testing.
5. Prenatal diagnosis (amniocentesis, chorionic villus sampling).

Modern Era (2000s–Present)

1. Early use of oral retinoids (e.g., isotretinoin, acitretin) helps shed thick skin.
2. Improved NICU care (temperature control, infection prevention, hydration).
3. Many children now survive into adolescence and adulthood.
4. HI is still extremely rare (~1 in 300,000 births).

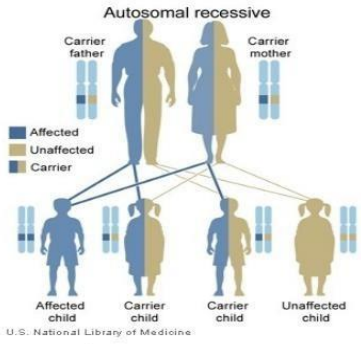
FAMILY AND ITS HISTORY

AUTOSOMAL RECESSIVE

Both Sexes

Homogenous for Abn Allele is 'AFFECTED'

25% Transmission



No Family History (Carriers)

Some of the most notable modern cases include

1. **Ryan Gonzalez (USA, born 1984)** – Ryan was one of the first documented long-term survivors of Harlequin Ichthyosis. Treated with isotretinoin as a newborn, he grew into adulthood and became an advocate for rare skin disorders, raising awareness through interviews and public appearances.

2. **Hunter Steinitz (USA, born 1994)** – Another widely recognized survivor, Hunter has lived with HI since birth. She continues to manage her condition through strict skincare routines and oral medication, and she actively participates in awareness campaigns and rare disease advocacy. Her story has been featured on medical documentaries and social media platforms, highlighting both the medical and social aspects of the disorder.

3. **Nusrit "Nelly" Shaheen (United Kingdom, born 1984)** – Nelly was the first known British person with Harlequin Ichthyosis to survive into adulthood. Her survival was considered remarkable at the time, given that the condition was thought to be fatal. Nelly's case was featured on several UK health programs, inspiring global recognition of the advances in care.

4. **Devan Mahadeo (June 11, 1985 – January 23, 2023)** was born in Trinidad and Tobago and lived to be 37 years old. He was involved in the Special Olympics for over 17 years and participated in both the Winter and Summer Games. He earned silver medals in football at Dublin, Ireland, in 2003 and Shanghai, China, in 2007, bronze in floor hockey at the 2013 Winter Games in Pyeongchang, South Korea, and gold at the 2015 Special Olympics World Games in Los Angeles, California.

5. **Stephanie Turner (1993 – 2017)** third oldest in the US with the same condition, and the first ever to give birth. Turner's two children do not have the disease. She died on March 3, 2017, at age 23.

6. **Mui Thomas (born in 1992 in Hong Kong)** is 33 years old, making her one of the oldest individuals living with the condition. In 2016, she qualified as the first rugby referee with harlequin ichthyosis.

7. **Mason van Dyk (born 2013)-** despite being given a life expectancy of one to five days, survived to at least July 2018. Doctors told his mother, Lisa van Dyk, that he was the first case of harlequin ichthyosis in South Africa, and that she has a one-in-four chance of having another

child with the disease.

8. A female baby born in Nagpur, India in June 2016 died after two days. She was the first case of harlequin ichthyosis reported in India. Nagpur: India's first case of Harlequin Ichthyosis baby was reported in Nagpur on Saturday. A Harlequin baby was born to a young couple in Lata Mangeshkar Hospital: Suffering from this rare genetic disorder known as Harlequin Ichthyosis in medical term, the baby girl was born with hard thick skin that covered her entire body with cracks in between.

Harlequin baby dies two days after birth in Nagpur: After fighting for her life for two days, a baby girl in Nagpur who was born with a rare congenital condition with almost no exterior skin passed away on Monday. The 1.8kilogram girl had thick slabs of broken, hardened skin covering her body, revealing her internal organs. She was diagnosed with Harlequin Ichthyosis, a disease that affects one in 300,000 births. She passed away at the privately run Lata Mangeshkar Medical College and Hospital on Monday morning after being put on oxygen. She was born on Saturday to a 23-year-old Amravati, Maharashtra's Vidarbha region resident. Her grandma and the infant's impoverished Amravati farmer father were taken aback upon seeing her. They have acknowledged the circumstances, though," Dr. Kajal Mitra remarked. The baby was placed on a ventilator because of respiratory issues that started in the morning. According to the experts, the illness wasn't identified sooner since the mother wasn't a frequent patient at the hospital. "Conventional ultrasonography is not able to detect skin disorders, particularly Harlequin Ichthyosis," noted Dr. Mitra.

What is ABCA12?

ABCA12 belongs to a group of genes called the ATP-binding cassette family, which makes proteins that transport molecules across cell membranes. The ABCA12 gene is active in some

types of skin cells and in several other tissues, such as testis, placenta, lung, stomach, and fetal brain and liver.

Advances in Research and Future Directions

Since the discovery of the ABCA12 gene, research has expanded into gene therapy, molecular correction, and stem-cell approaches. Scientists are studying how to restore normal ABCA12 function through CRISPR-based gene editing or lipid-replacement therapy. While these are still in experimental stages, they represent hope for a more permanent solution in the future. Recent studies also explore the psychosocial aspects of living with HI. Survivors often face emotional challenges such as social stigma, bullying, or psychological distress due to their visible differences. Support groups, counselling, and awareness organizations have become an essential part of long-term care.

Genetic Cause

The root cause of Harlequin Ichthyosis lies in mutations in the ABCA12 gene located on chromosome 2q34. This gene encodes the ATP-binding cassette sub-family A member 12 (ABCA12) protein, which is responsible for transporting lipids (fats) within skin cells, especially keratinocytes. Lipids play a crucial role in forming the protective skin barrier that prevents water loss and shields the body from infections. When the ABCA12 gene is defective, lipid transport is disrupted, leading to improper formation of the lipid barrier. This results in the accumulation of thick keratinized skin layers and severely impaired barrier function.

Pathophysiology

Under normal circumstances, keratinocytes in the epidermis mature and move from the deeper layers of the skin to the surface, where they form the stratum corneum and are eventually shed off. In Harlequin Ichthyosis, this natural process of shedding (desquamation) is defective. Instead of shedding, skin cells pile up, forming thick, plate-like scales. The fissures between these plates can become deep and painful, often leading to bleeding and a high risk of bacterial infection.

Furthermore, the absence of a proper skin barrier leads to excessive water loss, making infants highly susceptible to dehydration, electrolyte imbalance, and temperature instability. The rigidity of the skin can also compress the chest wall, leading to breathing difficulties. These complications make early medical intervention critical for survival.

Clinical Features

At birth, infants with Harlequin Ichthyosis exhibit a striking and distinct appearance. The thick, shiny, and rigid skin plates form diamond-shaped cracks all over the body. The eyelids are turned outward, exposing the inner surfaces, and the lips are stretched open in a fixed position, giving the mouth a characteristic "fish-like" shape. The ears and nose are often small, flattened, or poorly developed. Movement of the arms, legs, and fingers may be restricted, sometimes leading to swelling and joint contractures.

The skin's inability to function as a normal barrier leads to secondary problems such as infection, hypothermia, and difficulty feeding. In severe cases, the rigid skin can even restrict chest expansion, causing respiratory distress. Despite these challenges, with proper medical care and hydration, many of the thick scales begin to peel off within the first few weeks of life, revealing red and delicate skin underneath.

Sign, Symptoms and Causes

What are the symptoms of Harlequin ichthyosis?

Babies with harlequin ichthyosis are typically born prematurely. When they're born, their bodies are covered in thick, platelike scales of skin. Skin tightness causes the scales to form deep cracks (fissures). The tightness also pulls the skin around your baby's eyes and mouth, causing their eyelids and lips to turn inside out. It also pulls on the skin of your baby's chest and abdomen, making it difficult to breathe and eat. Other symptoms may include

- Flat nose.
- Ears fused to their head.
- Small, swollen hands and feet.
- Abnormal hearing.
- Frequent respiratory infections.
- Decreased joint mobility.
- Low body temperature.

Diagnosis

Diagnosis is usually made immediately after birth based on physical appearance. However, prenatal diagnosis is possible in families with a history of the disorder. Techniques such as amniocentesis or chorionic villus sampling (CVS) can be used to test fatal DNA for ABCA12 mutations. Additionally, advanced ultrasound imaging may show features like fixed fatal limbs or abnormal facial structures that suggest the disorder before delivery. Early diagnosis is crucial

for preparing specialized neonatal care immediately after birth.

Management and Treatment

Managing Harlequin Ichthyosis is complicated and lasts a lifetime. Right after birth, care for the baby focuses on keeping them hydrated, controlling their body temperature, and stopping infections from happening. The skin of the baby needs to be kept moist all the time using emollients like petroleum jelly or lanolin. The best medical treatments are systemic retinoids, like isotretinoin or acitretin. These drugs help speed up the process of shedding thick skin and help normal skin layers grow. Often, antibiotics are needed to stop or treat infections, and in the first few days, the baby might need help with feeding and breathing. Parents and caregivers learn how to keep the skin clean and watch for any signs of infection. As the child gets older, dermatological care continues for their whole life, focusing on keeping the skin hydrated, gently exfoliating, and protecting it from environmental factors.

Psychological and Social Impact:

Beyond physical symptoms, Harlequin Ichthyosis can have a significant emotional and social impact. Patients often deal with social stigma, low self-esteem, and psychological stress due to their physical appearance. Family counselling and support groups play an essential role in helping families cope with the emotional aspects of the condition. Increased awareness and education about rare genetic disorders can promote understanding and inclusion.

PREVENTION

Living With How do I take care of my child?

Some ways to help take care of your child include

- **Learning about your child's condition.** Become an expert on your child's condition by reading reputable sources of information.
- **Keeping your child as healthy as possible.** Provide nutritious food, make sure they get enough exercise and keep up with their regular checkups.
- **Finding what works for your child.** Every child is unique, and what works for one person may not work for another. Find a daily skin care routine that fits your child's needs.
- **Think about your child's environment.** Forced air heat and/or cold and dry temperatures can make your child's skin more brittle and can affect how they feel overall.
- **Have a personal skin care kit.** Put together and carry a bag containing all of your child's necessary skin care items, such as sunscreen, ointment or pain relievers.
- **Let your child take charge.** Eventually, your child will need to learn how to care for

themselves. Give your child some responsibility over their skin care needs.

- **Infant care.** Skin-to-skin care with your baby and breastfeeding is encouraged.

CONCLUSION

In summary, Harlequin Ichthyosis is a rare, severe, and genetically inherited skin disorder that affects the normal development of the skin barrier. It is caused by mutations in the ABCA12 gene, leading to defective lipid transport and abnormal keratinization. Although once considered fatal, modern medical advances—especially the use of systemic retinoids and improved neonatal care—have transformed the outlook for affected individuals. Ongoing research into gene therapy and molecular medicine may one day offer a permanent cure. Early diagnosis, genetic counselling, and continuous multidisciplinary care remain vital in improving both survival and quality of life for patients with Harlequin Ichthyosis.

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