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HARLEQUIN ICHTHYOSIS: A RARE CONGENITAL DERMATOLOGICAL DISORDER

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Abstract: Harlequin ichthyosis is congenital skin disorder which is characterized by thick, scaly keratin skin. The main cause is mutations in the lipid-transporter Adenosine triphosphate-binding cassette A12. It is a skin condition that covers nearly the entire body of a baby and carries a high risk of serious, maybe fatal infection. The incidence of harlequin ichthyosis is about one in every 5,000 individuals. Both sexes are equally susceptible to this illness. The survival rate of affected babies varies from 10 months to 25 years, with the majority not making it past the first week of life. This condition, which causes a thick, dry fish-scale pattern all over the body, has no known cure. HI is still a difficult condition with a high death rate, especially in the neonatal period, despite advancements in medical care. For those with HI, better management and a higher quality of life may result from early discovery, suitable interventions, and a better knowledge of the underlying molecular pathways. The main purpose of this review is to give basic idea of the Harlequin ichthyosis, its symptoms, causes, complications and diagnosis and treatment.

Index Terms **– Harlequin, ABCA12 gene, amniocentesis, hypernatremia**

I.Introduction:

A rare and severe genetic skin illness called Harlequin Ichthyosis (HI) impairs the keratinization process, which takes place between the 20th and 24th week of pregnancy. The ABCA12 gene, which controls lipid-transporting proteins in the epidermis is mutated in the condition. HI has been linked to early-life mortality and prenatal morbidity. With a range of 1/300,000 to 1/1,000,000, the incidence of HI is rather low, and there is no discernible correlation between sex and race. HI is characterized by thick, plaque-like scales that cover the entire body. Other symptoms include thin scalp hair, short limbs, hypoplastic fingers, and an absence of eyebrows and eyelashes. These babies are particularly vulnerable to hypothermia, dehydration, respiratory problems, inadequate nourishment, and low blood sodium, seizures, and skin infection.

Infants with HI have a significant risk of dying from skin infections, fluid loss, or respiratory failure. Infants with HI would pass away in two days after birth, yet in extremely unusual circumstances, some would live for months or even years. Mutations in the ABCA12 gene, which encodes an ATP-binding cassette (ABC) transporter protein, are the cause of the pathophysiology of Harlequin ichthyosis. Defects in ABCA12 function cause glucosylceramides to be transported improperly during terminal differentiation. The hallmark of

Harlequin ichthyosis is the resultant highly thickened plaques of hyperkeratotic scale over the whole skin surface.[1-3]

Fig 1: Harlequin ichthyosis

II. Case report:

This study reports a case of a woman who delivered a foetus with Harlequin Ichthyosis at the age of 24 years. The parents had a distant relationship and had no similar condition of HI in the previous pregnancy or family history. They had a healthy child. In her second pregnancy, she had delivered a stillborn male infant at 38 weeks' gestation due to diminished foetal movement and delay in reaching a hospital. A physical examination showed that the skin was hardened, thicker, and divided unevenly by deep features in a yellowish, leathery white area[3]

II. Symptoms:[6,7,8]

Harlequin ichthyosis symptoms vary with age and are typically more severe in young children.

2.1 In infants

Babies with Harlequin ichthyosis are born before their due date.

Symptoms include:

1) Inward-turning eyelids
2) Eyes that do not close
3) Lips that are pulled taut, causing the mouth to open and making nursing difficult
4) Ears fused to the head
5) Small, swollen hands and feet which leads to restricted movement in arms and legs
6) Breathing difficulties resulting from tight chest skin
7) Infections in deep skin cracks
8) Dehydration
9) Low body temperature and hypernatremia or elevated sodium in the blood.

2.2 In adults and older children:

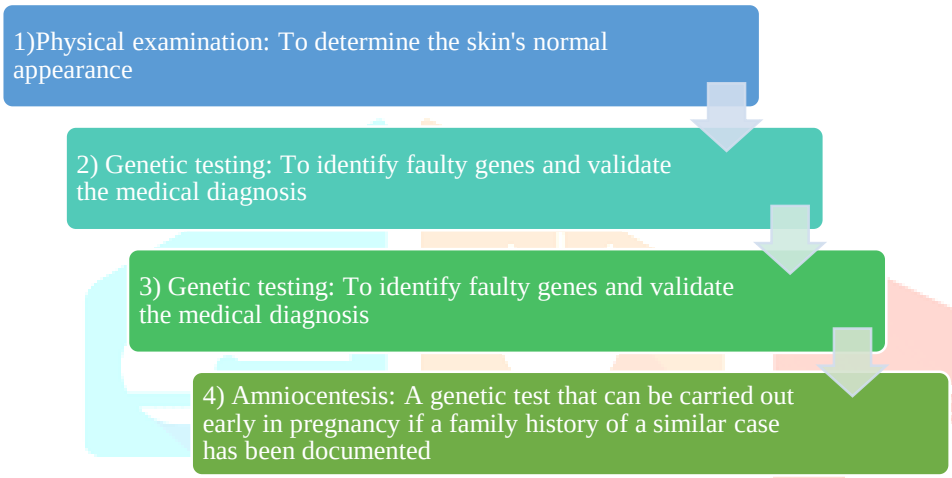
Physical development in children with Harlequin ichthyosis may be delayed. However, they often develop mentally in line with normal kids their age.

1) Scaly, red skin for the rest of their life.
2) Thin or sparse hair from scalp scales
3) Strange facial features from stretched skin
4) Decreased hearing from ear scale accumulation
5) Difficulty moving fingers from tight skin
5) Thick fingernails, recurrent skin infections; and overheating from sweating-obstructing scales.

III. Causes:[6]

A hereditary disorder called harlequin ichthyosis is inherited through autosomal recessive genes. It is possible to be a carrier without having the illness itself. For instance, you won't have Harlequin ichthyosis but will be a carrier if the gene is inherited from one parent.
However, you will get the illness if you receive the mutated gene from both parents. There is a 25% probability that a child will have the illness if both parents are carriers. For any pregnancy involving two parent carriers, that percentage is accurate. The National Organization of Rare Disorders estimates that 1 in 500,000 persons have harlequin ichthyosis.
If your child has been diagnosed with Harlequin ichthyosis, it's critical to understand that there was nothing you could have done to stop it. Additionally, there's nothing you did during pregnancy that caused the condition.

IV. Diagnosis :[7-10]



V. Complications :[7-10]

1) External deformities: The child's ears are malformed and their skin is drawn tightly inward, giving them a distorted appearance. swollen eyelids that are difficult to open and shut.

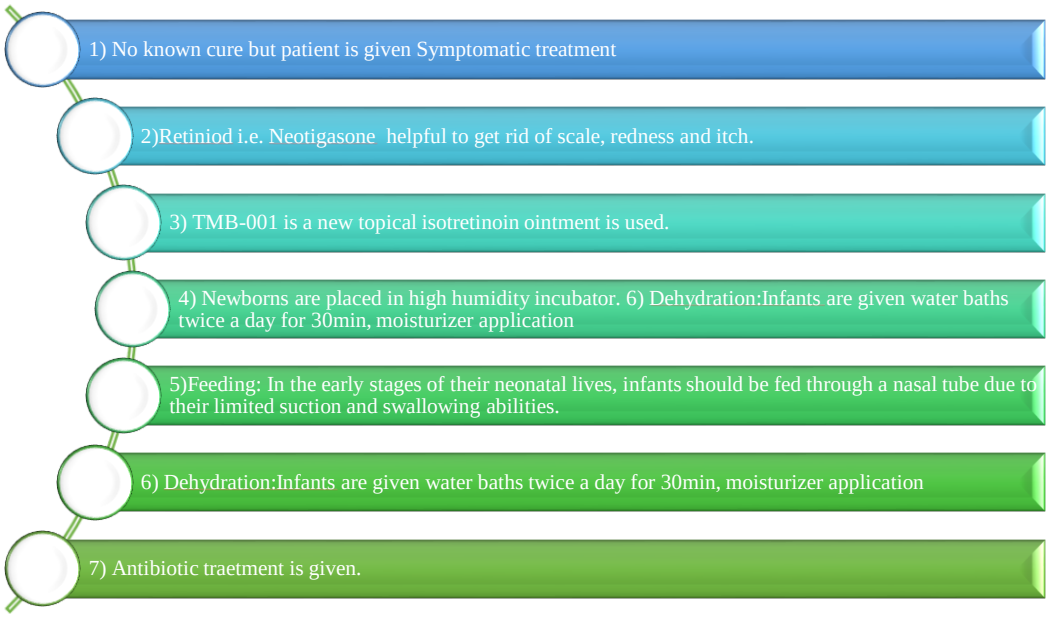
2) Breathing: Tight, thick skin restricts a newborn's ability to move their chest, which causes respiratory issues.

3) Feeding: Due to limited suction and swallowing abilities, infants should be fed via a nasal tube in the early stages of their neonatal lives.

4) Dehydration: Affects how the body regulates its temperature and can lead to hypothermia

5) Infection: When pathogens penetrate the skin barrier during the early stages of life, life-threatening infections can result.

VI. Treatment :[7-10]



Retinoid therapy for treatment of Harlequin Ichthyosis:

Due to a dearth of resources and research, the mortality rate from Harlequin ichthyosis was significant. The likelihood of survival would rise with improved critical care of the patient receiving systemic retinoid therapy initially [6]. A popular treatment for Harlequin ichthyosis is the use of actretin, a second-generation retinoid [9]. Acitretin stimulates intracellular retinoid signaling pathways by acting as a ligand for retinoic acid receptors (RARs) [9]. RARγ, which is mostly expressed in the epidermis, is highly affinitated for it [10, 11]. Genes associated with keratinocyte proliferation, differentiation, and desquamation are expressed differently in response to RARγ signaling [12]. Acitretin can partially compensate for the lipid transport deficit in Harlequin ichthyosis by indirectly restoring a more normal. In particular, despite the underlying ABCA12 mutations, it improves desquamation, promotes lipid transport, and increases keratinocyte differentiation.[5]

VII. Conclusion:

With appropriate prenatal care, the severe inherited skin condition known as harlequin ichthyosis can be avoided. Diagnosing the illness with DNA analysis for the ABC12 mutation can be helpful, although it might be difficult in developing nations. Frequent USG is recommended to detect irregularities. Due to the chronic nature of HI, a multidisciplinary approach and effective communication are necessary. Sonographic methods are essential for prenatal diagnosis. Because of advancements in surgical procedures, oral retinoids, and newborn care, the number of survivors is rising.

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