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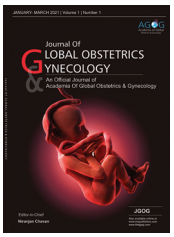
Case Report



Harlequin ichthyosis – A Rare Disorder

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ABSTRACT

Harlequin-type ichthyosis is a genetic disorder that results in thickened skin over nearly the entire body at birth. Although relatively uncommon, with an incidence of one in 200,000 births, effective treatments for the condition are currently lacking. The skin forms large, diamond/trapezoid/rectangle-shaped plates that are separated by deep cracks. These affect the shape of the eyelids, nose, mouth, and ears and limit movement of the arms and legs. Restricted movement of the chest can lead to breathing difficulties. These plates fall off over several weeks. Other complications can include premature birth, infection, problems with body temperature, and dehydration. HI is a rare autosomal recessive disorder with a notably high mortality rate. The condition is the most severe form of ichthyosis (except for syndromes that include ichthyosis, for example, Neu–Laxova syndrome), a group of genetic disorders characterised by scaly skin.

Key words: Harlequin-type ichthyosis, Genetic disorder, Premature birth, Neu–Laxova syndrome

INTRODUCTION

Harlequin ichthyosis (HI) is a rare and severe genetic skin disorder that affects developing fetus, with underlying mechanisms not yet fully understood. Although relatively uncommon, with an incidence of one in 200,000 births,[1] effective treatments for the condition are currently lacking. HI is categorized by genetic defects leading to generalized dry skin, scaling, and hyperkeratosis.[2] It represents the most severe form of ichthyosis, a rare dermatological disease caused by gene mutations.

Recent research by Akiyama *et al.*[3] shed light on the pathogenesis of HI, revealing it to be a lipid metabolism disorder caused by mutations in the adenosine triphosphate-b cassette transporter, ABCA12.

ABCA12 protein typically facilitates lipid transport from the cytosol into lamellar granules in healthy skin.

These lamellar granules then merge with the cell membrane, releasing their contents into the intercellular lamellae.

Dysfunction of ABCA12 in HI patients disrupts lipid transfer, leading to the formation of abnormal lipid-containing vacuoles in corneocyte cytoplasm.

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Consequently, the skin exhibits defective lipid layer formation, resulting in a notably thickened stratum corneum (Hovnanian, 2005).

Previous studies have shown that homozygous mutations in ABCA12, causing truncation of the protein, result in severe HI phenotypes, while heterozygous mutations lead to milder forms of the condition.

CASE REPORT

The present case is of 29 year, primigravida, non-consanguineous marriage 3 years ago. She came to our hospital at 3 weeks of gestation with complaints premature rupture of membranes for 6 h.

The pregnancy was uneventful and the mother had received regular antenatal care.

There are no signs of hyperglycemia and hypertension during the pregnancy.

Her ANC profile and thyroid profile were normal.

Sonography for anomaly done at 20 weeks of gestation found no abnormalities in fetal development. A growth sonography at 27 weeks of gestation also did not show any abnormalities in fetal growth.

On examination, she was vitally stable with no evidence of pallor, icterus, lymphadenopathy, or edema.

Obstetric examination showed uterus 28 week, cephalic presentation with good fetal heart rate with 1–2 contractions in every 10 min lasting for 10–15 s.

On P/V examination, patient was 5 cm dilated with good cervical effacement of around 60-70% with ruptured membranes, liquor was clear, station at -1 with vertex as a presenting part pelvis was adequate.

A single dose of corticosteroid was administered immediately and neonatologist informed. The pat progressed spontaneously and delivered vaginally within 3–4 h giving birth to a female child of weight around 980 g.

At birth, the baby exhibited a striking presentation characterized by armour-lik, thick yellowish scales, accompanied by extensive deep fissures that extended into the dermis. These scales and fissures formed a diamond-like pattern covering most of the body, with pronounced severity around the facial features. The limbs appeared rigid, held in a semi-flexe position. Additional features included clarion, marked by a fixed, open mouth, a flattened nose with keratin blocking the nostrils, small and underdeveloped external ears, severe ectropion (outward turning of eyelids), absent eyebrows, eyelashes, and scalp hair. Edema of the limbs was present, along with inflexible digits due to taut skin, and nails exhibited dystrophy and ischemia.

Figure 1 shows other systems were unremarkable.

Soon after delivery, the b handed over to pediatrician and was kept on ventilatory support. However, due to poor prognosis, baby died within 2 h of delivery.

DISCUSSION

HI, also known as keratosis diffuse fatal, represents a distinct form of congenital ichthyosis resulting from a mutation in the ABC transporter ABCA12, which plays a crucial role in lipid transportation across cell membranes.[3-5]

HI is a rare autosomal recessive disorder with a notably high mortality rate.[1]

In the majority of instances, fetuses carrying the mutation do not survive pregnancy, precluding the possibility of a live birth.[6,7]

Infants born with HI face a significant probability of mortality, primarily due to complications such as respiratory failure, dehydration, or skin infections.[8,9]

Figure 1: Armour-lik, thick yellowish scales, with extensive deep fissures extended into the dermis

Sonography serves as a valuable diagnostic tool for identifying HI, although it may not definitively distinguish fetal HI from other conditions such as fetal macroglossia or congenital tumors such as fetal angioma.[10]

Genetic testing is essential for accurately differentiating HI from other genetic conditions associated with macroglossia.[11,12]

Management

In the past, HI was almost always fatal, primarily due to complications such as dehydration, sepsis, respiratory difficulties caused by the thickened skin, or related factors.[13] Systemic infection was the leading cause of death, with very few individuals surviving beyond a few days. However, advancements in neonatal intensive care and the early initiation of treatment with oral retinoids like isotretinoin have shown promise in improving survival rates.[14,15]

Typically, mortality within the first 3 months was attributed to sepsis and/or respiratory failure in about 75% of cases.[5] Early intervention with retinoid therapy and the timely administration of antibiotics has been associated with a more favorable prognosis for HI.[11]

As of 2019, the mortality rate for HI remains high, with approximately 50% of cases resulting in death globally. However, a review of 45 cases by Rajpopat *et al.* reported a survival rate of 56%, with individuals ranging in age from 10 months to 25 years. Notably, Nusrit "Nelly" Shaheen, born in 1984, stands as the oldest known survivor, still in relatively good health as of June 2021.[16]

Skin management strategies typically involve daily baths, gentle debridement using emulsifying ointments, and the application of urea cream three times daily. Regular use of moisturizers helps soften the skin gradually, leading to the shedding of thickened skin plaques, revealing a red surface covered with thinner, whitish skin. Improvement in skin condition enables normal feeding and sucking behaviors. Bacterial conjunctivitis, if present, is managed with gentamicin ointment.

None of the reviewed studies addressed the potential for recurrence or preventive measures for HI in future pregnancies.

CONCLUSION

Understanding this disorder and promptly diagnosing it immediately after birth is crucial. Susceptible parents should be counseled on genetic factors, and prenatal screening and diagnosis should be recommended. The present case report underscores the necessity of a multidisciplinary approach, involving obstetricians, pediatric surgeons, pediatricians, ophthalmologists, dermatologists, dietitians, and psychologists, to enhance future treatment strategies.

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