Case Report

Harlequin Ichthyosis in a Term Neonate with Consanguineous Parents: A Fatal Case Report

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ABSTRACT

Background: Harlequin Ichthyosis (HI) is a rare, severe autosomal recessive keratinization disorder caused by mutations in the lipid-transporter gene ABCA12. The mutation leads to defective lipid transport, impaired ceramide formation, and failure of epidermal barrier development, predisposing neonates to infection, dehydration, and respiratory compromise. **Case Presentation:** A 38–39-week gestational age male neonate, born via lower-segment cesarean section to second-degree consanguineous parents, presented at birth with generalized rigid hyperkeratotic yellow skin plates separated by deep erythematous fissures, bilateral ectropion, eclabium, malformed ears, and limb contractures. Supportive care, including emollients, sterile non-adherent dressings with topical antibiotic over fissures, and graded enteral feeding, was provided. On day 3, the neonate developed progressive respiratory insufficiency with oxygen desaturation, requiring endotracheal intubation; however, he succumbed to death within hours due to respiratory failure. Postmortem genetic sequencing could not be performed. **Conclusion:** This case highlights the fulminant clinical course of severe HI phenotype, persistent mortality risk in resource-limited settings, and the importance of early clinical suspicion, multidisciplinary supportive care, informed consent-based photo documentation, and parental genetic counseling.

Key words: Harlequin ichthyosis, ABCA12 protein, newborn, consanguinity, respiratory insufficiency.

Harlequin ichthyosis (HI) is the most severe form of autosomal recessive congenital ichthyosis. Neonates characteristically present at birth with rigid, armor-like hyperkeratotic skin plates separated by deep fissures, facial distortion including eclabium, and restricted limb mobility. The pathogenesis involves loss of ABCA12 lipid-transporter function, impairing the formation and secretion of long-chain ceramides essential for a functional epidermal barrier [1].

The hyperkeratotic plates restrict the chest wall, upper and lower limbs from moving, leading to respiratory distress, hypoventilation, and respiratory failure. Infants are at higher risk of infection due to the compromised skin's protective barrier [2, 3]. The incidence of HI has been reported to be 1 in 300,000 births [4]. ICU management is mainly supportive. Loss of the skin barrier leads to trans epidermal water loss and the resulting electrolyte imbalance [1].

The worldwide mortality rate for HI is high, approximately 50%. With neonatal intensive care and oral retinoid therapy (acitretin 0.5-1 mg/kg/day orally), the survival rate can be increased compared to the past. Topical retinoids like tazarotene can be used to treat local and mechanical circulatory problems due to hyperkeratosis [5].

A severe case of HI in a neonate is presented here, with the neonatal death by day 3.

CASE REPORT

A full-term male neonate was referred from a private hospital at 4th hours of life for abnormal facial appearance and generalized skin thickening present since birth. He was delivered by lower-segment cesarean section due to the maternal history of previous cesarean delivery. Birth weight was 2.5 kg.

The mother was 26 years old, second gravida, with one previously unaffected child. Antenatal complications included pregnancy-induced hypertension, for which she was receiving oral Nifedipine, oligohydramnios, and urinary tract infection. The parents had a second-degree consanguineous marriage. There was no family history of similar dermatological or genetic disorders.

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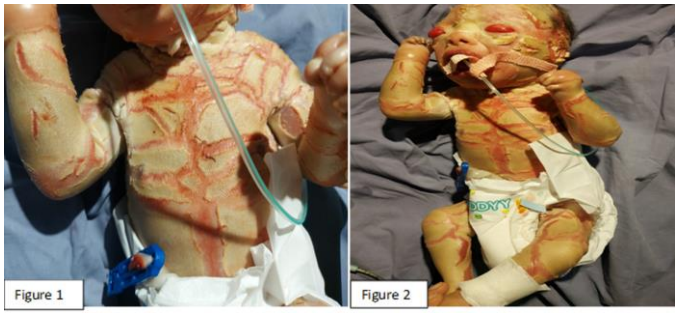
The neonate was vitally stable. Systemic examination was normal. Cutaneous and craniofacial evaluation revealed: generalized thick, rigid yellow hyperkeratotic plaques separated by deep erythematous fissures across the body; semi-clenched fists; hypoplastic hands and feet; and flexion contractures of both upper and lower limbs (figures 1 and 2), bilateral ectropion; eclabium; malformed ears with absent retroauricular folds (figure 3). Clinical features were consistent with HI.



Figures 1 and 2: Generalized thick, rigid, hyperkeratotic yellow skin plates separated by deep erythematous fissures over the trunk and extremities, consistent with the classical phenotype of HI.

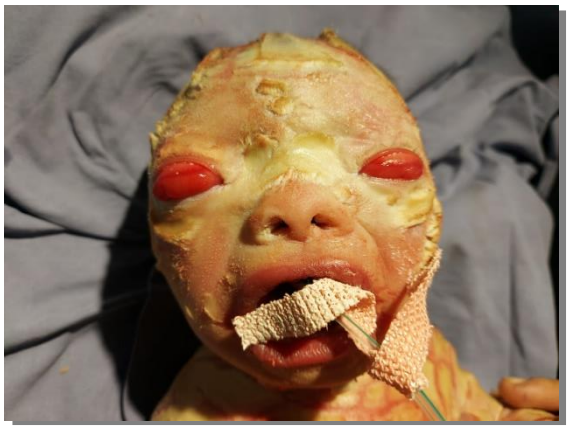


Figure 3: Craniofacial abnormalities showing bilateral ectropion, eclabium, depressed nasal bridge, malformed auricles with absent retroauricular folds.

Enteral feeds were initiated and incrementally graded while monitoring tolerance. Skin care included liberal use of emollients along with sterile, non-adherent liquid-paraffin-based dressings, and topical Mupirocin applied over fissures for infection prevention. Ophthalmic care included lubrication and aminoglycoside-based antibiotic eye drops.

On day 3 of life, the neonate developed progressive respiratory distress with persistent oxygen desaturation. He required endotracheal intubation and mechanical ventilation but expired within a few hours due to respiratory failure. Genetic analysis could not be performed postmortem.

Parents were counseled regarding the 25% recurrence risk due to autosomal recessive inheritance and informed about options for targeted prenatal molecular diagnostic testing in future pregnancies.

DISCUSSION

More than 100 cases of HI have been reported, but only a few have been reported from India [6]. In most reported cases, there is either stillbirth or preterm delivery. Live-born infants usually die within the first few days of life from respiratory infections, hypoglycaemia, or dehydration-related disorders. The present case also expired due to respiratory failure on day 3. Evidence suggests improved survival when early systemic retinoids are initiated in the immediate neonatal period [5]. In the present case, the infant expired early due to rapid respiratory deterioration, limiting the window for systemic retinoid therapy.

A review of 45 HI cases by Rajpopat et al. showed that there were 20 deaths with a 44% mortality rate. The ages of survivors ranged from 10 months to 25 years. The most common cause of death was fulminant sepsis in 75% cases, respiratory failure in 25%, and a combination of both. Early oral retinoids may improve survivability in 83% cases when compared to 76% who died without receiving retinoid intervention [7].

Consanguinity remains a significant contributor to disease risk for HI in the Indian subcontinent. The inbred individual may carry two gene copies that were present in a single copy in the common ancestor of their consanguineous parents. This recessive gene may express for the first time in an inbred descendant after remaining hidden for generations. Thus, consanguinity influences the incidence of HI. In our case also, the couple was consanguineous, supporting the evidence [6].

While survival rates have improved in selected neonatal care centers, mortality remains substantial in fulminant presentations in resource-limited settings. Hence, reinforcing the need for early suspicion of such genetic disorders, fluid-infection-nutrition protocols, genetic counseling, and prenatal diagnostic planning, to prevent the incidence of HI.

CONCLUSION

The present case shows a severe HI phenotype in a term male neonate resulting in early neonatal death from rapidly progressive respiratory failure. The case reinforces the critical role of early diagnosis, standardized multidisciplinary supportive care, informed parental consent for image documentation, and future prenatal molecular diagnostic and genetic counseling planning.

Informed Consent: Parental written informed consent was obtained specifically for publication of all clinical photographs included above.

Authors' Contribution: All authors contributed to patient care, manuscript writing, critical review, and final approval of the manuscript.

Ethical Clearance: Institutional Ethics Committee waiver was obtained for publication of this case report.

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