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Unveiling harlequin ichthyosis beyond the neonatal period: A case from North Sumatra, Indonesia

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Case Report

ABSTRACT

Harlequin ichthyosis (HI) is a rare and life-threatening form of autosomal recessive congenital ichthyosis, typically diagnosed in the neonatal period due to its distinctive clinical features. We report a 7-year-old boy from North Sumatra, Indonesia, who survived well beyond infancy despite limited resources. He was born preterm at 35 weeks to consanguineous parents, with a history of a sibling who died in early infancy from a similar condition. The patient presented with ectropion, eclabium, underdeveloped ears, severe contractures, and generalized hyperkeratotic plaques with deep fissures. Clinical management focused on supportive dermatologic care, including twice-daily bathing, emollient application, topical antibiotics for erosions, and multidisciplinary referrals. Notably, the patient did not receive systemic retinoids or neonatal intensive care, yet the survival was achieved with minimal but consistent supportive measures. This case underscores the importance of early recognition of HI, the role of family history and consanguinity in clinical suspicion, and the potential for survival in resource-limited settings. It also highlights the profound psychosocial burden on affected families and emphasizes the need for genetic counselling to reduce recurrence in high-risk populations.

INTRODUCTION

Harlequin ichthyosis (HI) is the most severe and rare form of autosomal recessive congenital ichthyosis, with an estimated global incidence of 1 in 300,000 live births.[1] It is caused by mutations in the ABCA12 gene, which encodes a lipid transporter essential for the formation and maintenance of the skin barrier.[2] Disruption of this gene results in defective lipid transport, leading to thickened, hyperkeratotic skin plates, fissures, and classical craniofacial deformities such as ectropion, eclabium, and hypoplastic ears.[3] Infants with HI often experience severe complications shortly after birth, including respiratory failure, dehydration, and sepsis, making survival beyond the neonatal period exceedingly rare.[4]

The majority of HI cases are diagnosed immediately after birth, and many infants do not survive past the first few weeks.[5] Advances in neonatal care and early use of systemic retinoids have slightly improved the prognosis in recent years.[6] Rare reports have documented long-term survival of HI patients beyond infancy in low-resource settings, achieved through consistent supportive care alone.[7] In Indonesia, where access to genetic testing, systemic retinoids, and neonatal intensive care units (NICUs) is limited, such outcomes remain exceptionally rare.[8] Several studies and clinical guidelines have outlined structured approaches to HI management and emphasized the need for multidisciplinary involvement even when advanced resources are unavailable.[9,10] Prenatal diagnosis through ultrasonography and molecular testing are important in early detection, especially in high-risk pregnancies.[10,11] In rural or remote areas, the situation

is more difficult with inadequate access to train dermatologists, limited diagnostic facilities, and a lack of prenatal counselling or early screening programs.[11] This gap in healthcare accessibility contributes to delayed diagnosis and poorer outcomes for patients with rare genetic disorders, including HI.[12,13]

In contrast to most reported survivors who received intensive neonatal management and systemic retinoid therapy, we report a patient who was born in a rural hospital without such facilities and survived up to seven years with only minimal yet consistent supportive care, making this an exceptionally rare case. This case highlights the importance of recognizing HI beyond the neonatal period, the value of family history in guiding clinical suspicion, and the potential for survival with basic yet consistent supportive care. This report aims to raise awareness about HI, support early recognition in resource-limited areas, and emphasize the significance of genetic counselling in populations with consanguinity.

CASE DESCRIPTION

A 7-year-old Batak boy from Samosir, North Sumatra, presented with generalized erythematous, thickened, and scaly skin that had been present since birth. He is the third child of consanguineous parents (first cousins). His eldest sibling is healthy, while the second sibling was born with similar skin abnormalities and died at 14 weeks of age. The patient was born preterm at 35 weeks of gestation via spontaneous vaginal delivery at a local hospital, with a birth weight of 2300 grams. At birth, his skin appeared shiny and was encased in a thick yellowish membrane, which gradually peeled off within the first few weeks of life. Since then, his skin has remained persistently thick, dry, and scaly all over his body. There was no history of systemic illness, prior hospitalizations, or medication use. The pedigree suggests a possible genetic inheritance pattern, as illustrated in Figure 1.

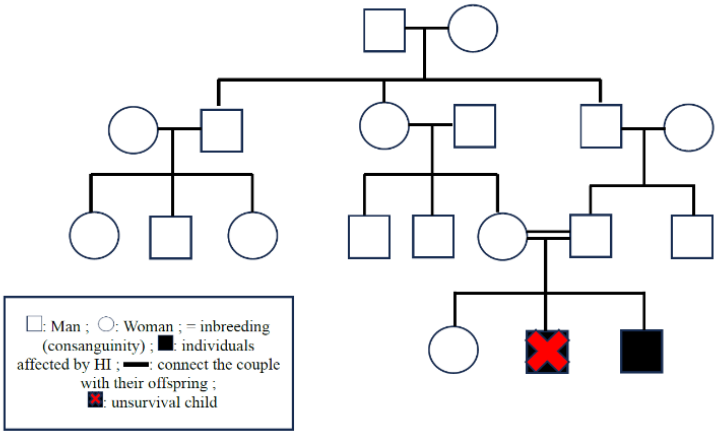

Figure 1. Patient's family pedigree

On physical examination, the patient was conscious, cooperative, and undernourished (body weight 14.2 kg; height 100 cm). Vital signs were stable. Facial features included marked ectropion, eclabium, a flattened nasal bridge, and underdeveloped ears. He was unable to fully close his eyes or mouth. His digits were hypoplastic with tapering tips, and he had contractures of both upper and lower extremities. Dermatological examination revealed generalized erythematous macules with thick whitish-yellow scales, hyperkeratosis, erosion, and fissures involving the scalp, face with ectropion, eclabium, the trunk, and on the extremities with deformities (Figure 2).

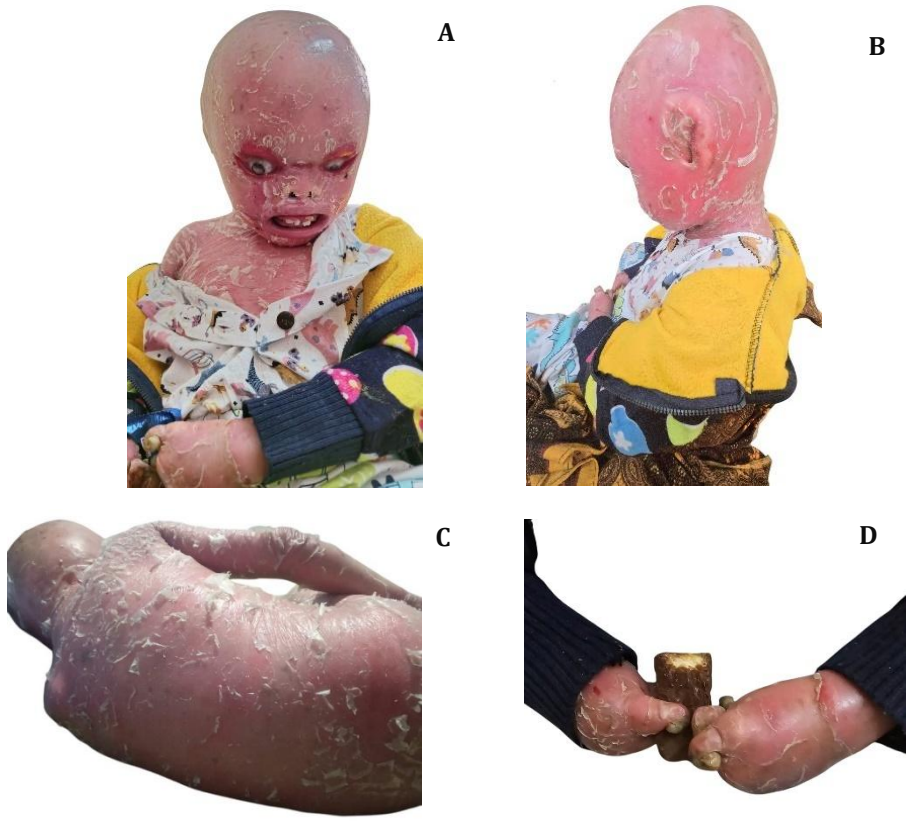

Figure 2. Erythematous macules covered with thick, whitish-yellow scales, accompanied by marked hyperkeratosis, erosions, and deep fissures involving (A) the scalp, face with ectropion, eclabium, (B) auricular area with underdeveloped auricles, (C) the trunk, (D) the upper extremities with deformities.

Diagnosis was based on clinical features typical of harlequin ichthyosis, supported by family history and consanguinity. The patient was managed with supportive therapy. Daily treatment included bathing twice daily with lukewarm water and hypoallergenic soap, application of moisturizers containing petrolatum to the entire body, and gentamicin cream applied twice daily to erosive lesions. Dietary counselling was provided to address nutritional needs and support wound healing, and the patient was referred to pediatrics for growth and developmental monitoring and to ophthalmology for ectropion evaluation.

On follow-up visits, the patient showed mild improvements in skin hydration and reduced erosions, although hyperkeratosis persisted. Nutritional intake improved modestly. Adherence to the regimen was reported to be good by the caregiver.

DISCUSSION

Harlequin ichthyosis (HI) is a rare and severe form of autosomal recessive congenital ichthyosis, caused by mutations in the ABCA12 gene that impair lipid transport across the epidermis, resulting in a defective skin barrier. Clinically, it is characterized by thick hyperkeratotic plaques with deep fissures, ectropion, eclabium, flattened nasal bridge, and limb contractures.[1,2] These infants are often born preterm and exhibit high mortality rates in the neonatal period due to complications such as dehydration, respiratory failure, infections, and feeding difficulties.[3] Historically, the prognosis was extremely poor, with most infants not surviving beyond the first few days or weeks of life.[4]

In recent decades, survival has improved in high-resource countries due to early recognition, neonatal intensive care unit (NICU) availability, multidisciplinary care, and the use

of systemic retinoids such as acitretin or isotretinoin, which improve skin barrier function by modulating keratinization and reducing hyperkeratosis.[5,6] These agents, combined with aggressive infection control, nutritional support, and skin barrier maintenance, have made longer survival possible, though still uncommon.[13] Patients in such settings typically benefit from coordinated care involving dermatologists, neonatologists, geneticists, ophthalmologists, and nutritionists. Moreover, access to prenatal and preimplantation genetic screening allows for early diagnosis and informed reproductive decisions.[8,14,15] With these resources, survival rates of up to 83% have been reported in recent cohorts.[16,17] In addition, consistent application of emollients and supportive topical care has been recognized as a key component in enhancing survival by maintaining skin barrier integrity, preventing fissures, and reducing infection risk in the absence of systemic therapy.[6,10]

This case is particularly remarkable as it documents the long-term survival of a 7-year-old boy with clinical features consistent with HI in a remote, low-resource region of North Sumatra, Indonesia. Unlike most reported cases, the patient did not receive systemic retinoids or neonatal intensive care, as such facilities were not available in the local hospital where he was born. Initial management consisted of empiric antibiotics and emollient application, followed by long-term home care with routine use of moisturizers. Despite the absence of advanced interventions, he survived up to seven years, underscoring the potential of consistent yet minimal supportive therapy. A multidisciplinary approach was initiated after presentation to our center. Pediatric consultation emphasized undernutrition and severe developmental delay, as the child had not achieved speech and showed markedly impaired growth compared to age norms.

Nutritional counselling was provided to the parents to improve caloric intake and promote wound healing, which aligns with recent evidence showing that children with ichthyosis are at high risk of malnutrition and benefit from dietary interventions to support growth and skin repair.[18,19] Ophthalmological evaluation confirmed bilateral ectropion, with recommendations for regular use of ocular lubricants to reduce exposure keratitis and protect the cornea. Preservative-free ocular lubricants are first-line therapy for ocular surface disease in ichthyosis, and with preferred practice guidelines recommending artificial tear ointments as the most effective preventive measure against exposure keratopathy.[20-22] These simple measures highlight the importance of involving pediatric and ophthalmology specialists even in settings where advanced therapeutics are unavailable.

Beyond the clinical aspects, the psychosocial consequences in this patient were profound. The child had never attended school and remained non-verbal, limiting communication and social interaction. Parents reported significant stigma in their community and feelings of shame, which contributed to social isolation and hindered access to education and peer support. Similar findings have been described in families of children with ichthyosis, where social discrimination and psychological stress exacerbate the disease burden.[3,23] These observations underline the necessity of counselling and community support systems for affected families, not only to improve medical adherence but also to promote integration and reduce stigma.

Compared to previously published reports, survival in HI has generally been associated with intensive neonatal management, early systemic retinoid therapy, and advanced supportive care.[24] Recent literature over the past five years confirms that while survival beyond infancy is being increasingly reported, most long-term survivors still require these interventions, and survival beyond five years without them remains exceptionally rare.[24] In contrast, our case demonstrates surviving child in the absence of both neonatal intensive care and systemic retinoids, relying solely on consistent basic measures such as emollient application, wound care, topical antibiotics, nutritional advice, and family support. This highlights the potential of minimal but diligent care to prolong survival, even though quality of life remains severely compromised.

The presence of a previously affected sibling and parental consanguinity in this case strongly supports autosomal recessive inheritance.[14] This underlines the importance of genetic counselling, particularly in communities with a high prevalence of consanguineous marriage, where public health strategies are essential to reduce recurrence of such disorders.[25]

Strengthening awareness among healthcare workers in resource-limited areas can facilitate earlier recognition, timely referral, and holistic support for affected families. These recommendations align with Sustainable Development Goal (SDG) 3, which emphasizes equitable access to quality healthcare, including for individuals with rare and neglected genetic conditions.

CONCLUSION

This case demonstrates that survival beyond infancy in harlequin ichthyosis can be achieved even in the absence of advanced neonatal care, provided that consistent basic supportive measures are maintained within the family. It reinforces the importance of early clinical recognition, meticulous daily management, and multidisciplinary involvement. Equally critical are genetic counselling and community-based public health interventions aimed at reducing recurrence and alleviating the psychosocial burden borne by affected families. Collectively, these measures highlight strategies to improve both survival and quality of life for patients with harlequin ichthyosis in resource-limited settings.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest regarding the publication of this case report. The authors have no financial relationships with any organizations that might have an interest in the submitted work.

Written informed consent was obtained from the patient's legal guardian for the publication of this case report and accompanying clinical images.

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DATA AVAILABILITY STATEMENT

All data supporting the findings of this study are included in the article. No additional datasets are available.

SUPPLEMENTARY MATERIAL(S)

No supplementary materials are available for this case report.

AUTHORS CONTRIBUTIONS

WGM was responsible for the conception and design of the case report, acquisition and interpretation of clinical data, and drafting of the manuscript. DAP supervised the clinical management, literature review, provided critical revisions for intellectual content, and approved the final version of the manuscript. KAN contributed to the clinical evaluation of the patient and critical discussion of the case in relation to current dermatological evidence. All authors read and approved the final version of the manuscript.

DECLARATION OF USING AI IN THE WRITING PROCESS

No generative artificial intelligence (AI) tools were used in the writing or editing of this manuscript. The authors are fully responsible for the content of this publication.

LIST OF ABBREVIATIONS

HI: Harlequin Ichthyosis; GA: Gestational Age; ABCA12: ATP-binding cassette sub-family A member 12; H&E: Hematoxylin and Eosin.

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