

## CASE REPORT

## A NEWBORN IN WESTERN NEPAL WITH HARLEQUIN ICHTHYOSIS: A CASE REPORT

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**ABSTRACT****Introduction:** Harlequin ichthyosis (HI) is a rare autosomal recessive congenital ichthyosis with an incidence of 1 in 300,000 live births. It is lethal in 44% of cases and baby is usually prematurely born. These babies have thick, highly keratinized armor-like skin, forming large diamond, trapezoid or rectangular plates separated by fissures. These affect the shapes of eyelids, nose, mouth and ears, and limit movement of the arms, legs and chest.

This condition is linked with a nonsense or frameshift mutation in the ABCA12 gene, which is responsible for lipid transport in keratinocytes. This gene synthesizes a protein that transports a lipid, epidermoside, a glucosylceramide, out of stratum corneum cells in the epidermis.

To our knowledge, this is the first case report on Harlequin ichthyosis from western Nepal, which makes this case unique.

Take away lesson is that couples with consanguineous marriages should undergo screening of ABCA12 gene if they plan to conceive.

**Keywords:** ABCA12 gene mutation; Autosomal recessive congenital ichthyosis; Harlequin ichthyosis.**INTRODUCTION**

Harlequin ichthyosis (HI) is an autosomal recessive, non-syndromic, congenital ichthyosis linked to a deletion and truncation mutation of the keratinocyte lipid transporter gene ABCA12 (ATP binding cassette A12) located on chromosome 2.<sup>1,2</sup>

Its rarity and severity can be imagined from the fact that its incidence is 1 out of 300,000 live births and fatality can be as high as 44%.<sup>2</sup> Approximately 50% of babies die within their first month of life; even if they survive longer, they tend to be severely affected by delayed growth, joint contractures and red skin.

These babies are born with armor-like skin with truncal plates and plenty of fissures. Severe keratinization

also impairs with movement even during drinking or breathing.<sup>3</sup>

These babies are at high risk of hypothermia, hyperthermia, dehydration and respiratory distress. These may further predispose to malnutrition, electrolyte imbalance, seizure, infection and even death.<sup>4</sup> In a few cases, patients have been reported to have survived up to adulthood.

**CASE REPORT**

A 24-year-old primigravida presented to our hospital at the 32<sup>nd</sup> week period of gestation in labor. She had never been to a doctor in the past. All health check-ups she had in the past were done by a paramedic near her house.

She gave birth to a live female baby by normal vaginal delivery. There was a history of consanguinity as she was married to her first cousin. There was no skin disorder in the family members of the couples and she had an uncomplicated antenatal course. At the time of birth, the child's APGAR scores<sup>5,6</sup>(appearance, pulse, grimace, activity and respiration) were 5/10 and 8/10 at one and five minutes, respectively. The child weighed 3 kg at birth.

The mother's ultrasonographic scans of the first and second trimester had shown no signs of any abnormality.

The baby was born with thick, hard and hyperkeratotic skin with wide fissures that had a red base (figure 1).



**Figure 1: Baby with armor-like thick scales all over body.**

Ectropion was present in both the eyes in both upper and lower eyelids. The ear auricles were immature and attached to the scalp causing loss of retro-auricular space. The nostrils and external auditory canal were full of keratinous material (figure 3). Both the lips were widely separated and turned outwards (figure 3). The hands and feet of the baby were clubbed (figure 2). The diagnosis of Harlequin ichthyosis was made solely on the basis of physical examination. Genetic testing for mutation in ABCA12 gene could not be done because the case was discovered in a rural and hilly setting from where transport of samples was not possible at that time. Prognosis regarding survival was explained to parents. Because the child was born prematurely, was cyanosed at time of birth and the hard skin was causing difficulty in breathing, it was given supportive care with oxygen and

transported in incubator from labor room to newborn intensive care unit (NICU) for further management. Liberal frequent application of petroleum jelly and paraffin was done and the keratinous materials in the ear and nostrils were removed. However, the parents self-discharged the baby on the same day and information regarding survival couldn't be obtained.



**Figure 2: Hands and feet appear clubbed.**



**Figure 3: Eclabium and nostrils filled with keratinous material.**

## DISCUSSION

HI is a disorder of keratinization that is inherited in an autosomal recessive pattern and presents with hyperkeratosis and visible scaling throughout the body.<sup>7</sup> "Ichthys" is a Greek word meaning "fish". Ichthyosis results in abnormal differentiation or abnormal desquamation causing impaired corneocyte shedding or

accelerated keratinocyte production. Hyperkeratosis in these diseases is simply a homeostatic repair response to an abnormal epidermal barrier.<sup>2</sup>

HI is a non-syndromic autosomal recessive congenital ichthyosis (ARCI) involving the ABCA12 gene.<sup>8</sup> ARCI includes harlequin ichthyosis, bathing suit ichthyosis, lamellar ichthyosis, congenital ichthyosiform erythroderma, collodion baby and self-improving congenital ichthyosis.<sup>2</sup>

ARCI are associated with mutations in genes that encode proteins involved in lipid transport such as ABCA12 and in lipid biosynthesis such as CERS3, in fatty acid metabolism or have a role in assembling in structures such as cornified envelope.<sup>9</sup>

The ABCA12 gene codes for proteins that transfer lipids such as glucosylceramides into lamellar bodies which are necessary for formation of the epidermal barrier. Nonsense or frameshift mutations in this gene leads to HI.<sup>2,9</sup>

Affected neonates are born with armor-like skin and have truncal plates with fissuring which considerably impairs movement and interferes with ability to even drink or breathe. They have bilateral ectropion, eclabium and lack retro-auricular folds.<sup>10</sup> 10% of these children have autoamputation of digits.<sup>2</sup>

HI is not only a skin disease but also involves the lungs and causes alveolar collapse. Death is usually because of respiratory problems.<sup>2</sup>

If the child survives, it may develop congenital ichthyosiform erythroderma, low body weight, rickets or osteomalacia later in the life.<sup>2,4</sup>

Histopathologic examination reveals orthokeratotic stratum corneum with variable acanthosis and the granular layer is variably decreased.<sup>7</sup> Electron microscopy can also be used for diagnosis.

Treatment involves starting oral retinoids especially Acetretin, topical therapy to facilitate desquamation along with newborn intensive care unit (NICU) support.<sup>4</sup>

HI has the most severe phenotype among all the

autosomal recessive congenital ichthyoses. Though survival rates are expected to rise following early topical and oral retinoid therapy, unfortunately side effects like bone toxicities, ligament calcification and concerns of teratogenicity are raised following long term retinoid therapy. Hence only option for family is prevention in subsequent pregnancies via prenatal diagnosis.<sup>8</sup>

## CONCLUSION

Children with Harlequin ichthyosis are born prematurely and have breathing difficulty so proper medical management with or without NICU care should be maintained. Counseling of the parents about the baby needing special medical care and regarding the prognosis of the disease should be clearly done.

We suggest mutation screening of the ABCA12 gene and genetic counseling of couples that have consanguineous marriages.

## DATA AVAILABILITY

All data underlying the results are available as part of the article and no additional source data are required.

## CONSENT

Written and well-informed consent was obtained from the mother of the child for publication of clinical details and clinical images of the baby.

## REFERENCES

1. Couto PA, Pastore MC, Araujo JCN, et al. Caso Clínico Ictiose Arlequim : Caso Clínico Harlequin Ichthyosis : Case Report Caso Clínico. 2019;77(January):55-58. [DOI]
2. Oji V, Metze D, Traupe H. Inherited Disorders Of Cornification. In: Griffiths C, Barker J, Beliker T, Creamer D, eds. Rook's Textbook of Dermatology. 9th ed. John Wiley & Sons Limited; 2016:65.6-65.7.
3. Liang Q, Xiong FU, Liang X, et al. Two successive cases of fetal harlequin ichthyosis: A case report. *Exp Ther Med*. 2019;17(1):449-452. [DOI]
4. Harvey HB, Shaw MG, Morrell DS. Perinatal management of harlequin ichthyosis: A case report

- and literature review. *J Perinatol.* 2010;30(1):66-72. [DOI]
5. Hegyi T, Carbone T, Anwar M, et al. The Apgar score and its components in the preterm infant. *Pediatrics.* 1998;101(1 I):77-81. [DOI]
  6. Li F, Wu T, Lei X, Zhang H, Mao M, Zhang J. The Apgar Score and Infant Mortality. *PLoS One.* 2013;8(7):1-8. [DOI]
  7. Fleckman P, Digiovanna john j. The Ichthyosis. In: Goldsmith lowell A, Katz stephen I, Gilchrist barbara A, Paller amy S, Leffel david J, Wolff K, eds. *Fitzpatrick's dermatology in general medicine.* 8th ed. the McGraw Hill companies, Inc.; 2012:507-537.
  8. Sheth JJ, Bhavsar R, Patel D, Joshi A, Sheth FJ. Harlequin ichthyosis due to novel splice site mutation in the ABCA12 gene: postnatal to prenatal diagnosis. *Int J Dermatol.* 2018;57(4):428-433. [DOI]
  9. Akiyama M. Corneocyte lipid envelope (CLE), the key structure for skin barrier function and ichthyosis pathogenesis. *J Dermatol Sci.* 2017;88(1):3-9. [DOI]
  10. Kün-Darbois JD, Molin A, Jeanne-Pasquier C, Paré A, Bénateau H, Veyssière A. Facial features in Harlequin ichthyosis: Clinical findings about 4 cases. *Rev Stomatol Chir Maxillofac Chir Orale.* 2016;117(1):51-53. [DOI]