# Ictiose Arlequim: Caso Clínico

*Patricia A Couto[1], Marcela C Pastore[1], Jessica C N Araujo[1], Cecilya M Mota[1], Caroline A R Chirano[1], Valéria K A Ferreira[1], Sidharta Q Gadelha2 , Elaine D Melo3, Patricia C B de Melo1, Luciana M Santos1*
*[1]Hospital Universitário Getúlio Vargas, Manaus, Brazil.*
*[2]Athoderma Clinic, Manaus, Brazil.*
*[3]Fundação de Dermatologia Tropical e Venereologia Alfredo da Matta, Manaus, Brazil.*

**RESUMO –** Ictiose arlequim é uma doença congênita autossómica recessiva rara, na qual os recém-nascidos apresentam placas de hiperqueratose generalizadas e fissuras profundas, ectrópio, eclábio, malformação do pavilhão auricular e fácies típicas. Embora várias complicações relacionadas à restrição cutânea possam ocorrer, o suporte em terapia intensiva e a introdução precoce de retinóides sistémicos, como a acitretina, têm contribuído significativamente para a melhoria da sobrevida e do prognóstico dos doentes.
O objetivo deste relato é apresentar um raro caso de ictiose arlequim e discutir estratégias para o diagnóstico precoce e o primeiro tratamento de suporte.
**PALAVRAS-CHAVE –** Ictiose Lamelar; Recém-Nascido; Transportadores de Cassetes de Ligação de ATP.

# *Harlequin Ichthyosis: Case Report*

***ABSTRACT –*** *Harlequin ichthyosis is a rare autosomal recessive congenital disease in which neonates present generalized hyperkeratotic plaques and deep fissures, ectropion, eclabium, malformation of the auricular pavilion and typical facies. Although several complications related to the skin restriction may occur, support in intensive care and early introduction of systemic retinoids, such as acitretin, have significantly contributed to patients' survival and improved prognosis.*
*The purpose of this report is to present a rare case of harlequin ichthyosis and to discuss strategies for early diagnosis and first supportive care.*
***KEYWORDS –*** *ATP-Binding Cassette Transporters; Ichthyosis, Lamellar; Infant, Newborn.*

## INTRODUCTION

Harlequin ichthyosis is a rare autosomal recessive congenital disease associated with the mutation of the *ABCA12* gene located at chromosome 2 (2q34) and affects 1 in 300,000 live births,[1] leading to a change in the lipid deposition of the stratum corneum, resulting in skin barrier disruption, compensatory hyperkeratinization, and epidermal desquamation.[2] Clinically, neonates present generalized hyperkeratotic plaques and deep fissures, ectropion, eclabium, malformation of the auricular pavilion and typical facies. There may be several complications such as sepsis (secondary to the deep fissures), respiratory failure due to restriction of chest wall expansion, compartment syndrome, digital ischemia due to vascular compression, hypothermia and fluid and electrolytic imbalance. However, support in intensive care and early introduction of systemic retinoids, such as acitretin, have significantly contributed to improve patients' survival and prognosis.[3] The reported case refers to a neonate who presented partial improvement with emollient dressings derived from petrolatum, but due to the unavailability of the retinoid progressed to death with lung infection and respiratory failure. The purpose of this report is to present a rare case of harlequin ichthyosis and to discuss strategies for early diagnosis and first supportive care.

## CASE REPORT

A preterm newborn, male (34 weeks of gestation), 1815 g, 47 cm, born after normal delivery. APGAR was 8 at 1

**Correspondência:** Patricia A. Couto
Hospital Universitário Getúlio Vargas
Rua Tomás de Villa Nova, nº 4, Praça 14 de Janeiro
CEP: 69020-170, Manaus/AM, Brazil
**E-mail:** pac_86@live.com
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minute and 9 at 5 minutes so no neonatal resuscitation was required. His 19-year-old mother performed adequate prenatal evaluation with all negative serologies and no reports of ultrasound changes. There were no known cases of skin disease in the family.

The neonate was born with ectropion, eclabium, deep fissures, cyanosis of extremities and lamellar scaling at birth. The clinical diagnosis of harlequin icthyosis was assumed. He received neonatal intensive care and showed partial improvement with the use of petrolatum dressings. The Dermatology Department recommended oral acitretin and requested the public health insurance to provide the drug, since the family could not afford its high cost. However, despite the management in intensive care, death due to respiratory infection and sepsis occurred within 15 days of life, even before the medication was available. Interventions by other medical specialties were impaired while the neonate needed clinical stabilization. No genetic study was performed.

## DISCUSSION

The term ichthyosis harlequin refers to the costumes of the popularized italian comic opera servants, arlecchino or harlequin, which have a diamond shapped pattern and resemble the hyperkeratotic plaques in these neonates. It is the most severe form of congenital ichthyoses.[1] As an autosomal recessive disease, the recurrence rate is 25% in subsequent pregnancies. Clinically, neonates present hyperkeratotic plaques and deep fissures with distorted facial features: severely evertid eyelids (ectropion), pulled and fixed lips (eclabium), and malformation of the auricular pavilion with a cartilaginous ear and nasal hypoplasia.[6] Prenatal diagnosis by ultrasound can usually be performed in the second trimester,[5] as some changes may suggest this diagnosis: polydraminia, limb changes such as hypoplasia or fixed flexion, closed hands and crooked feet, eclipse, ectropion, lips changes with the mouth constantly open or micrognathia, ear hypoplasia, short umbilical cord, flat nose and flat facies are characteristic of ichthyosis aarlequin.[1] In addition, it is worth to mention the "snowflake sign" (floating particles in the amniotic fluid).[7] These changes indicate the need for further diagnostic follow-up based on fetal genomic DNA, from the amniotic fluid or chorionic villi.[4,6] Advances in fetal DNA tests and ultrasound techniques have replaced more invasive tests such as fetal skin biopsy.[6] This information is useful for proper prenatal counseling. Harlequin ichthyosis was considered to be a fatal disease because of its typical characteristics and complications. However, support in intensive care, a multidisciplinary approach and the early introduction of retinoids have improved patients' prognosis and survival.[3] Treatment and skin care should include: Cleaning twice daily to moisturize and promote debridement of the stratum corneum. Surgical intervention and fasciotomy to prevent digital necrosis and improve the amplitude of movements.[6] Fluid infusion, protein and electrolyte serum levels, and diet should be well monitored. Treatment with oral retinoids, mainly acitretin, should be initiated within the first 7 days at the dose of 1 mg/

**Figure 1 -** Neonate at birth presenting typical characteristics of harlequin's ichthyosis.

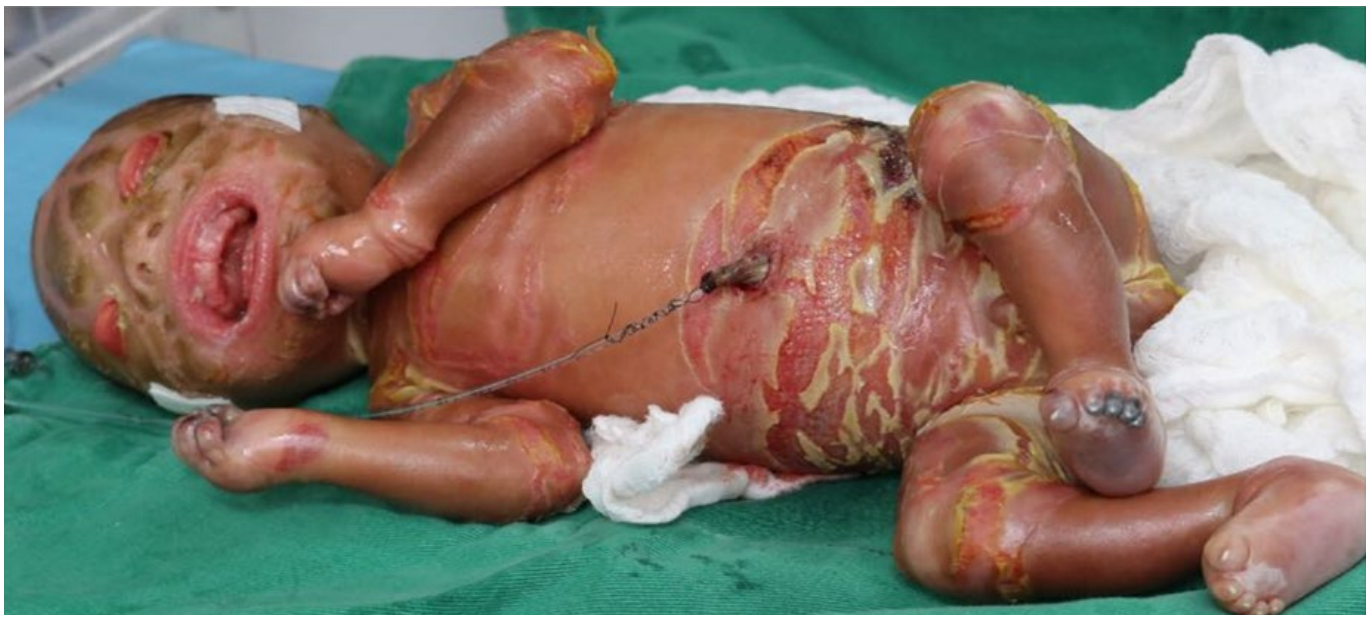

**Figure 2 -** Clinical aspect after daily cleansing and use of petrolatum dressings.

kg/day. It reduces the thoracic and digital constriction from cutaneous hyperkeratinization and prevents further complications.[7] However, accessing the medication is still difficult by some populations.

Newborns who survive progress to a life-long skin disease similar to congenital ichthyosiform erythroderma, that needs to be managed on a daily basis with the frequent use of topical emollients and sometimes intermittent use of oral retinoids. Vitamin D supplements are also necessary to compensate sunshine restriction. Clinical outcomes of older children may include poor hair growth, thickened nails, digital contractures, autoamputated fingertips and fissured plantar skin. These features contribute to a delay in motor development. Joint pain secondary to inflammatory arthritis was also described. Ectropion frequently recurs after surgical correction and periocular topical retinoid treatment can be an alternative approach. As skin debris may cause recurrent blockage of the external auditory canal, regular microsuctioning is indicated. Although breastfeeding should be encouraged, due to difficulty in sucking some neonates may need nasogastric tube feeding until they eat a high-calorie diet. Moreover, those who feel self-conscious about their appearance must receive careful psychological support.[7]

## CONCLUSION

As this is a disease with a high fatality rate, prompt diagnosis and a multidisciplinary management of the complications inherent to harlequin's ichthyosis are essential to increase the survival of these patients.[2,3] In the presented case, a restriction in the thoracic cavity expansion, due to the small elasticity of the skin, and associated deep skin fissures, led to a respiratory infection and failure, and death before acitretin was available. It is important to consider genetic counseling through mutational screening of the *ABCA12* gene, since parents who have had a child with congenital ichthyosis have a 25% risk of presenting a new case of ichthyosis in each pregnancy.[1,3] Although the survivors may present some delay in achieving developmental milestones, adequate multiprofessional support can give patients a chance to conquer an independent adult life.

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