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Harlequin ichthyosis – management from birth to 3 years of age

Ictiose arlequim – manejo do nascimento aos 3 anos de idade

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RESUMO: A ictiose arlequim possui uma prevalência de 1/100.000 nascimentos e é frequente o óbito ocorrer no período neonatal. Objetivo: descrever um caso em que o tratamento adequado permitiu a sobrevida da paciente. Descrição do caso: Recém-nascido (RN) do sexo feminino com 2665g, nasceu com placas hiperceratósicas e fissuras difusas pelo corpo, ectrópio bilateral com oclusão palpebral, eclábio e pés e mãos fletidos características de Ictiose congênita do tipo arlequim. O acitretin foi iniciado aos 7 dias de vida associado ao tratamento suportivo, evitando o óbito neonatal. Comentários: Atribui-se a sobrevida da paciente à intervenção com acitretin oral precoce e os cuidados intensivos neonatais.

Keywords: Ictiose lamelar; Anormalidades congênitas; Dermatologia; Pediatria.

ABSTRACT: Harlequin ichthyosis has a prevalence of 1/100.000 births and is frequent that the death occurs in neonatal period. Objective: to describe a case in which the adequate treatment allowed the patient's survival. Case description: Newborn, female, with 2665g, was born with hyperkeratotic plaques and diffuse fissures in the body, bilateral ectropion with palpebral occlusion, foot and hands flexed, characteristics of congenital harlequin Ichthyosis. Acitretin was started in the first 7 days associated with supportive treatment, preventing that the newborn evolved to neonatal death. Comments: The survival of the patient is attributed to the precocious intervention with acitretin and the intense care in the neonatal period.

Keywords: Ichthyosis, Lamellar; Congenital abnormalities; Dermatology; Pediatrics.

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INTRODUCTION

Ichthyoses are characterized by alterations in skin keratinization with varying severity. The condition is hereditary, but some forms are acquired and associated with malignancy, infectious and autoimmune diseases or nutritional deficiencies.[1] Hereditary forms are determined by mutations in genes that encode structural proteins or enzymes involved in cellular functions, such as DNA repair and homeostasis of skin barrier.[1] Abnormalities in these components result in epidermal hyperplasia and excess of stratum corneum, accompanied by abnormal desquamation.[2]

Harlequin ichtyosis has an incidence of 1/100.00 births and is associated with mutations in the ABCA12 gene.[3] The neonatal mortality rate is approximately 50%.[4] It is characterized by thick armour-like scales that involve the entire skin and lead to changes in temperature regulation, fluid balance and protection against infection, as well as respiratory difficulties, as they restrict the expansion of the rib cage. After birth, the child develops deep cracks and fissures associated with ectropion, eclabion and malformation of ear.[5]

The objective of this case report of harlequin ichthyosis was to describe the treatment in the neonatal period and the evolution in three years of life.

CASE REPORT

A 25-year-old primigravid woman at 36 weeks and 6 days gestation was admitted for delivery and referred for caesarean section due to dystocia. An ultrasound at 28 weeks showed anomalies including hypoplasia of the face, short nose, flat nasal bridge, maxillary hypoplasia and protrusion of the tongue. Gestational diabetes was controlled in prenatal care.

Female baby was born with 2665g and Apgar score of 8/9 in the 1st and 5th minute of life, respectively. The hyperkeratotic plaques and fissures spread over the body (Figure 1) were compatible with congenital harlequin ichthyosis, and the newborn was admitted to a neonatal ICU.

The clinical features of the patient included bilateral upper eyelid ectropion with eyelid occlusion – corrected at two years of age –, eclabium, contractures of hands and feet, bilateral hypoplasia of the external ear, and moderate bilateral conductive hearing loss.

Since the second day of life, the patient was treated with multiple antimicrobials selected according to blood cultures. Acitretin treatment was started at 7 days of life and led to a reduction in cracks and flaking and later to an appearance of congenital ichthyosiform erythroderma. The treatment also included continuous use of dexpanthenol ophthalmic gel, lubricating eye drops, body moisturizers with petrolatum in the neonatal period and, after 60 days, N-acetylcysteine 5% and urea 5%. The patient showed a significant improvement in skin desquamation, which became less intense on the face and more accentuated on the limbs. She is now three years old and has good control of the disease. (Figure 2).

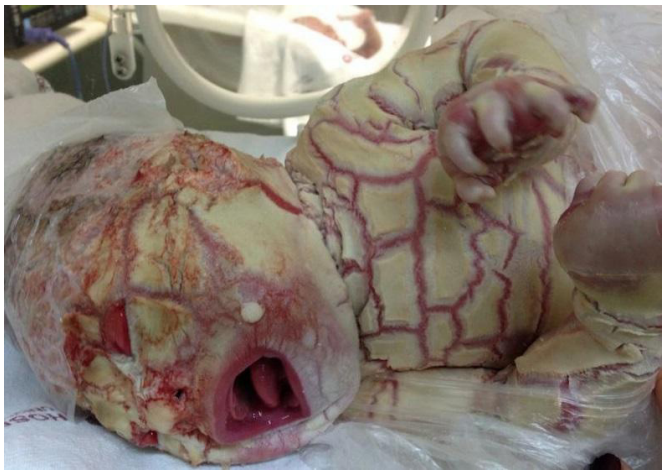

Figure 1: Thick scales, deep fissures and ectropion with 2 hours of life

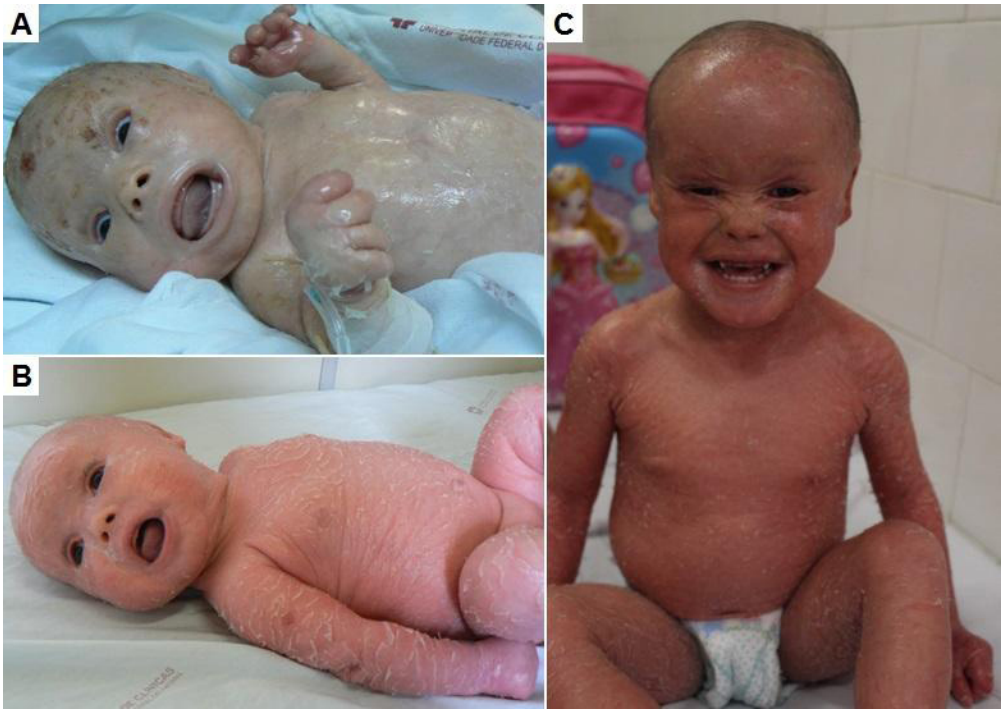

Figure 2: (A) After 30 days on acitretin with significant improvement, still with ectropion and eclabium, (B) erythema and abnormal desquamation at 3 months and (C) at 3 years old.

DISCUSSION

Harlequin ichthyosis has been associated with high mortality and morbidity rates. However, the early introduction of oral retinoids and the admission in the Neonatal Intensive Care Unit have dropped the mortality rate to less than 50%[6,7]. The use of retinoids prevent hyperkeratosis and reduce the scaling that is characteristic of ichthyosis[8]. Acitretin is a synthetic analog of retinoic acid that helps controlling epithelial proliferation[9].

Another factor that influences the prognosis of the disease is the prenatal diagnosis, performed by ultrasound in the third trimester. Features suggestive of the condition include rudimentary ears, flexion contractures in the knees, dense particles in amniotic fluid, protruding tongue and everted lips[6,7]. The 28-week ultrasound showed facial abnormalities such as oral malformations and protruding tongue. However, these findings were not associated with ichthyosis, but with malformation of the oral cavity. In pregnant women with a previous history of children with harlequin ichthyosis, it is possible to analyze amniotic fluid DNA or chorionic villi to search for mutations in the ABCA12 gene[10,11].

Harlequin ichtyosis has no cure. Its treatment is supportive and aimed at preventing or treating complications[12]. Nutritional support is necessary as eclabium makes breastfeeding difficult[12], but the patient in this case report could be fed orally on the second day of life. The use of petrolatum, such as petroleum jelly, and other topical moisturizers is indicated to reduce water and electrolytic losses through the skin, but it is common for patients to receive intravenous fluid[13,14]. Blood cultures are drawn daily for the first week of life and once weekly for the remainder of the hospital stay, with the objective of managing infection, detecting bacterial proliferation and treating sepsis early[15]. In this study, the patient developed episodes of bacterial and fungal sepsis. It is necessary to use ocular lubricants, as the ectropion affects eye lubrication.6

The survival of the patient in this study is probably related to the treatment with acitretin initiated at the end of the first week of life. This measure is associated with an increased survival of 80% and a proper management of infections[6]. Thus, minimizing transepidermal water loss is one of the keys to survival in this dermatosis, as it prevents electrolyte imbalance, temperature dysregulation, respiratory distress, malnutrition and infections[15].

The phenotypes of ichthyosis can change in response to treatment with retinoids. Children with harlequin ichthyosis who survive after the neonatal period may have a similar evolution to another type of ichthyosis, congenital ichthyosiform erythroderma, a milder form of the disease[1]. This evolution seems to be associated with heterozygous mutation of the ABCA12 gene, the nature of its mutation and its location within the protein[6,17,18]. This

form of the disease has characteristics such as generalized erythema, scalp abnormalities, and alopecia,1 which were present in the patient in this study.

Despite of the severity of the disease, harlequin ichthyosis can have a favorable evolution if there is an early diagnosis and treatment. Retinoids should be used for the rest of the patients' lives depending on the therapeutic response, and multidisciplinary follow-up should be provided to reduce disease-related morbidity.

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