Multidisciplinary team approach in Harlequin baby: A case report

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ABSTRACT • Harlequin ichthyosis (HI) is an autosomal recessive disorder with a mortality rate of 44%. HI is caused by a homozygous mutation in a protein adenosine triphosphate binding cassette subfamily A member 12. We present a case of HI in one of two dizygotic twins successfully managed using a multidisciplinary approach and discharged from the hospital at day 65 of life. Keywords: harlequin, ichthyosis, congenital diseases

INTRODUCTION

Ichthyosis fetalis, otherwise known as harlequin ichthyosis (HI) is a devastating, extremely rare form of congenital ichthyosis with an autosomal recessive inheritance pattern. It is a severe keratinizing disorder that carries a mortality rate of 44% [1].

The affected babies are frequently born prematurely and small for gestational age [2]. They harbor a characteristic armor-like skin consisting of thick white scaling plates separated by deep red grooves that resemble a harlequin costume. Clinical findings include bilateral ectropion, eclabium, constricting bands that could disrupt vascular flow to the extremities and deformed nose and ears. The defective skin barrier puts the baby at risk for severe dehydration, electrolyte disturbances, thermal imbalance and sepsis whereas the restricted movement restricts the survival of some patients with HI.

We report a case of HI in one of two dizygotic twins following in vitro fecundation.

CASE REPORT

A 29-year-old woman, gravida 2, para 0, aborta 1 with a dichorionic diamniotic twin pregnancy at 30 weeks of gestational age presented to the Labor and Delivery Unit complaining of abdominal pain and frequent loose stools. Her pregnancy was uneventful. She denied any history of illicit drug use or radiation exposure. There was neither consanguinity nor any family history of ichthyosis or other congenital anomalies. Her obstetrical history consisted of a first trimester spontaneous abortion that was followed by secondary infertility. A successful in vitro fertilization cycle resulted in the current twin dizygotic pregnancy.

On physical examination, the patient was afebrile with stable vital signs but diffuse abdominal tenderness was noted. Monitoring revealed reassuring fetal heart rates with regular preterm contractions. The laboratory workup revealed a C reactive protein of 33 mg/L and WBC value of 48/mm³ on urinalysis.

The patient was admitted to the hospital and amoxicillin-clavulanate was initiated. Tocolysis was attempted, however preterm labor progressed and the patient was rushed to the operating room for a primary cesarean section.

She delivered dizygotic twins: a healthy girl of 1.7 kg with APGAR scores of 10 at 1 and 5 minutes and a harlequin boy of 1.6 kg with APGAR scores of 8 and 10 at 1 and 5 minutes respectively. The amniotic fluid was clear and the cesarean section was uncomplicated.

The boy’s entire body was covered with thick hyperkeratotic plates separated by deep erythematous fissures (Figure 1). His ears were malformed and adherent to the scalp (Figure 1). He had eclabium (eversion of the lips) and severe bilateral ectropion (complete eversion of the eyelids with occlusion of the eyes) (Figure 1).
The scaling formed restrictive bands on all extremities resulting in edematous hands and feet and subsequent restricted movements of the limbs (Figure 1). He was admitted to the neonatal intensive care unit and placed on parenteral nutrition, systemic weight adjusted doses of ampicilline-cephotaxime and analgesics. Petroleum ointment was used every 2 hours to cover the scale plates. Topical Vitamin A was applied on the eyes six times a day.

Starting day 1, the baby boy received systemic acitretine at a dose of 1.6 mg/kg/24h. The neonatal intensive care unit stay was overall uneventful and the boy was discharged at 65 days of age.

DISCUSSION

HI is the most severe ichthyotic genodermatosis. It affects both genders equally with a mean gestational age at birth of 35 weeks. The survival rate is 56% and the major causes of death include fulminant sepsis (25%), respiratory failure (25%) or both (25%). Fifty percent of deaths occur within three days of life. Despite this poor prognosis, the reported age of the survivors ranges from 10 months to 25 years [1]. Sepsis is the product of HI’s defective skin barrier whereas the respiratory failure is due to restrictive chest movements caused by adherent scales on the thorax or a possible involvement of ABCA12 in lung physiology [1,6].
Since it was first described in Charleston, South Carolina, in 1750 by Reverend Oliver Hart, HI has known many advances notably in 2005 when ABCA12 was identified as the underlying causative gene. This gene encodes a protein that transports the glucosylceramide into the lamellar granules of the upper epidermal keratinocytes to be processed and secreted into the stratum corneum [4,5]. When mutated, skin development is altered in utero. Homozygous mutations in the ABCA12 gene have been shown to cause the harlequin phenotype whereas heterozygous mutations result in collodion babies, congenital ichthyosiform erythroderma and lamellar ichthyosis [1,5]). Nowadays, a prenatal diagnosis can be established using direct ABCA12 sequence analysis of fetal DNA obtained from amniocentesis fluid or chorionic villus sampling material in pregnancies at risk. In addition, there are two-dimensional ultrasound features suggestive of HI such as a large persistently open mouth, atypical nasal and ear dysmorphism, minimal fetal movement with semiflexed extremities and a hyperechogenic amniotic fluid. Three- and four-dimensional sonography are essential to confirm the diagnosis in these cases [7].

At birth, the neonate is covered with thick plate-like desquamation, separated by deep fissures. The defective cutaneous barrier leads to an increased vulnerability to infections. Other clinical findings caused by the thick epidermal plates include ectropion and eclabium. Later on, the thick stratum corneum sheds revealing a diffuse erythema with fine scaling [1,3]. A multidisciplinary approach and strong bonds with the family are key elements in optimal management of the affected neonate [8]. Our team was composed of a pediatric intensive care neonatologist, a dermatologist, an obstetrician, a geneticist, an ophthalmologist, a plastic surgeon and a psychologist as well as experienced NICU staff. Pictures of survivors were shown to the parents suggesting that the neonate will not be as severely affected once he survives the critical period.

There is no standard approach to manage the HI patient. Systemic retinoids have proven clinical efficacy in ichthyosis and ichthyosiform dermatosis [9,10]. In the setting of HI, studies have shown that oral retinoids could increase survival from 24% to 83% by promoting peeling and thinning of the stratum corneum [1]. Parenteral nutrition and heated high humidity incubators compensate for the difficulty in feeding and thermal imbalance. Supportive measures are primordial and include: regular emollient application to maintain skin hydration, lubrication of the cornea to prevent dryness, adequate analgesics and frequent blood draws and cultures to monitor for any electrolyte imbalances or signs of infection. Fluid balance and weights should be followed closely. Surgical release of constricting bands is an important adjunct to management in case of respiratory distress or extremity congestion [11].

CONCLUSION

In summary, a multidisciplinary approach and aggressive neonatal intensive care are key elements in the successful management of HI babies. Evidence of improvement in survival brings hope to burdened families. The revolutionary use of retinoid and the continuous advances in neonatal care strive to make harlequin ichthyosis a chronic condition rather than a fatal disease. Nonetheless, further studies are still needed to establish a standardized treatment protocol.

REFERENCES: