

## Harlequin Ichthyosis: A Rare Disorder

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Received: 01 July 2016

Initial Review: 20 July 2016

Accepted: 02 August 2016

Published Online: 18 August 2016

### ABSTRACT

Harlequin ichthyosis (HI) is the rarest and the most severe form of congenital ichthyosis. It is inherited in an autosomal recessive manner and associated with mutations in gene ABCA12. There have been reports of several families with siblings affected with harlequin ichthyosis. Affected infants have severe ectropion, eclabium, diffuse decreased range of motion, thick, dry hyperkeratotic plates, over entire body and scalp and associated deep erythematous fissures. Infants with HI have historically succumbed in the perinatal period to sepsis, respiratory failure and infections, poor nutrition and electrolyte imbalances. It is a rare entity. We report here a case of harlequin Ichthyosis infant born to consanguineous parents whose 3 siblings were also affected with the same disorder.

**Keywords:** *Ectropion, Eclabium, Harlequin Ichthyosis*

Harlequin ichthyosis (HI) is the rarest and the most severe form of congenital ichthyosis, with the incidence of one in 300,000 births. This disorder has ominous prognosis invariably. More than 100 cases have been reported [1]. The earliest record of its description is from Oliver Hart in 1750 [2]. Inherited in an autosomal recessive manner, HI is primarily associated with mutations causing functional defects in the keratinocyte lipid transporter adenosine triphosphate-binding cassette ABC A12 [3]. Infants with HI have historically succumbed in the perinatal period to sepsis, respiratory failure, infections, poor nutrition and electrolyte imbalances. In the past 20 years, however, the prognosis of HI infants has improved due to advances in neonatal intensive care and targeted oral retinoids [4]. Early management of HI generally includes a humidified incubator, temperature regulation, nutrition replacement, skin and eye care, pain control, physiotherapy, and infection control.

There is no definitive treatment for this disease; however, topical steroids, oral vitamin A, locally administered liquid paraffin, and some lactic acid solutions are discussed as treatment options [3]. Being rare, we report here a case of harlequin fetus born to consanguineous parents, whose 3 siblings were also affected with the same disease.

### CASE REPORT

An hour-old female baby was referred to us from an outside hospital. She was full term and delivered vaginally. She was a product of second degree consanguineous marriage. Birth order of the infant was 5<sup>th</sup> and the first 3 siblings died with similar complaints. All 3 were preterm, born between 30 to 36 weeks and died within 24 hours of birth. Fourth issue was a full term female, normal child, now aged 2.5 years. During this pregnancy, mother had an uncomplicated antenatal course and antenatal ultrasounds

were normal. Any kind of antenatal counseling was not done regarding this disorder.

On examination, weight was 2.3kgs (below 10<sup>th</sup> centile), length was 45 cm (at 10<sup>th</sup> centile), and head circumference was 33.5 cm (between 50<sup>th</sup> – 75<sup>th</sup> centile). The baby's axillary temperature was 98.6<sup>o</sup> F, pulse rate was 148 per minute and respiratory rate was 42 per minute. She was noted to have generalized edema and thick, dry hyperkeratotic plates over her entire body and scalp. Skin was hard, thickened, waxy and yellowish in color. It was split irregularly to reveal erythematous moist fissures. She also had severe ectropion, eclabium, abd diffuse decreased range of motion, especially in the digits, wrists, elbows, knees and ankles secondary to skin tautness. Ears and eyes were underdeveloped. Hairs were scanty. The limbs were edematous with small hands and feet having circumferential constriction bands around. The nails were hypoplastic. Her systemic examination was unremarkable.

Immediately after transfer to our neonatal intensive care unit, umbilical catheterization was done to establish venous access. Appropriate fluids and antibiotics were administered. Liquid paraffin was applied on the skin locally. Analgesic drops were also given. Ectropion was covered with eye pads and ophthalmic ointments were applied as advised by ophthalmologist. Patient was started on acitretin (1 mg/kg/ per day) on day 2. Laboratory findings (complete hemogram, blood sugar, serum calcium and electrolytes) and chest X-ray were within normal range. Skin biopsy and genetic testing could not be done as facilities were not available in our setup. Initially, she was passing urine and stool normally but on 5<sup>th</sup> day of life, baby expired of septic shock.

## DISCUSSION

More than 100 cases of HI have been reported till date. Neither racial or gender predilection is known [1]. Mutations in ABCA12 gene underlie the severe congenital ichthyosis. There have been reports of several families with siblings affected with HI [5]. Twins affected by HI have also been reported [2]. Occurrence of consanguinity in parents and HI in siblings suggests an autosomal recessive mode of inheritance [6]. Prenatal diagnosis would be the first step for early detection of the disease. Therefore, obtaining the family history, consanguinity between the parents, and the presence of other skin

disorders in offspring would be very helpful for early diagnosis of the disease. Prenatal diagnosis is usually possible in families at risk but requires invasive fetoscopy for skin biopsy. The application of three-dimensional ultrasound enables a greatly improved analysis of the facial morphology and thus provides an important contribution to prenatal diagnosis [7].



**Figure 1: Harlequin baby showing generalized edema with thick hyperkeratotic plates over entire body, scalp and associated deep erythematous fissures**

Harlequin fetuses usually die soon after birth and most of the victims die within a few weeks of birth because of secondary complications such as infection and dehydration [8]. The survival rate increases to more than 50% with an early prescription of oral retinoids. The quality of life of these patients may be improved with supportive care [9]. Affected individuals with severe involvement can have ectropion, eclabium, scarring alopecia involving the scalp and eyebrows, and palmar and plantar keratoderma. Infants with HI are usually born prematurely and are encased in thick, hard, armor-like plates of cornified skin that severely restrict movements. Life-threatening complications in the immediate postnatal period include respiratory distress, feeding problems, and systemic infections.

Early management of HI generally includes a humidified incubator, temperature regulation, nutrition replacement, skin and eye care, pain control, physiotherapy, and infection control [10]. A humidified incubator with strict temperature regulation is essential for mitigating the large transcutaneous losses of water and heat caused by the dysfunctional epidermal permeability barrier. Even in the incubator setting, these losses, compounded by chronic inflammation, constitute a significant caloric drain for HI infants and can lead to growth retardation if calories are not replaced. Skin care is also a constant focus in these patients. Emollients should be generously applied to the skin multiple times per day to provide the infant with protection against foreign pathogens and help prevent transcutaneous water loss. Bathing and soaking can reduce the risks of skin infection, replenish moisture in the skin and promote the softening and shedding of the thick stratum corneum.

The deep cutaneous fissures of HI are very painful, making pain management an important issue in the care of these patients. Pain associated with truncal fissures discourages deep breathing and increases the risk of pulmonary complications. Sepsis remains a constant threat in the first month before the deep fissures have healed and continues to be a leading cause of death in these patients throughout infancy. For this reason, close monitoring for signs of sepsis and aggressive treatment of infections are essential. Creams or ointments are used to keep the skin soft and hydrated, keratolytic agents will promote peeling and thinning of the stratum corneum. Lubrication of the cornea in cases with ectropion prevents corneal drying. Weight gain and fluid intake must be carefully monitored. A multidisciplinary approach is vital in its management as it could prolong survival beyond the neonatal period.

## CONCLUSION

Harlequin Ichthyosis is a rare entity and as in our case, three siblings were also affected, and history of consanguinity was present, which favors an autosomal recessive inheritance.

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**How to cite this article:** Ramteke S Agrawal A, Shrivastava J. Harlequin Ichthyosis: A Rare Disorder. *Indian J Case Reports.* 2016; 2(3): 69-71.

*Conflict of interest: None stated, Funding: Nil*