International Journal of Medical and Health Research
ISSN: 2454-9142
Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 3; Issue 9; September 2017; Page No. 33-35

Harlequin ichthyosis: Case report

[*1] Najla Alrumaih, [2] Saad Alqasem, [3] Ali Algonaim, [4] Faeza Almatari
[1] College of Medicine, King Saud University, Riyadh, Saudi Arabia
[2, 3] College of Medicine, Prince Sattam bin Abdulaziz University, Alkharj, Saudi Arabia
[4] Al-imam Abdulrahaman Al-faisal Hospital, Riyadh, Saudi Arabia

Abstract
Harlequin ichthyosis (HI) is a rare autosomal recessive disorder characterized by thick, fissured armor-plate hyperkeratosis, ears and nose deformities, ectropion, eclabium with fish mouth appearance, flexion deformities of all joints and hypoplastic digits. The first reported case was in 1750. HI has a poor prognosis with high mortality rate mainly due to infections and metabolic abnormalities. HI has an incidence rate of 1 in 300,000 births. The mainstay of management is supportive care and systemic retinoid therapy in Neonatal Intensive Care Unit. We report a case of newborn girl in Saudi Arabia with HI born to relative parents. She was delivered by cesarean section due to breech presentation of at 35+ gestational age with labor pain. We recommend to have a genetic screening and counseling in all high risk couples e.g. consanguinity marriages as well as having more studies to determine the best mode to deliver a baby with HI.

Keywords: harlequin icthyosis, autosomal recessive, skin disorder, abca12 gene mutation

Introduction
Harlequin ichthyosis (HI) is the most severe form of rare, autosomal recessive congenital ichthyoses (ARCI), with an incidence of about 1 in 300,000 births [1, 2]. It is lethal disease especially in the early period of babies life [3]. The first case was described by Hart in 1750 [4].
Newborns with HI present with thick, fissured armor-plate hyperkeratosis, ears deformity or may be absent entirely, as may the nose, everted eyelids (ectropion), the lips are pulled back by the dry skin (eclabium) with fish mouth appearance, flexion deformities of all joints due to extreme inelasticity of the skin and hypoplastic digits [2, 3].
However, improved survival has been achieved with intense supportive care and systemic retinoid therapy in the neonatal period. Death in these cases is commonly caused by an increased risk of life-threatening infection, respiratory failure and electrolyte abnormalities [5].
The underlying genetic abnormality in HI is associated with a mutation in the gene, the lipid-transporter gene adenosine triphosphate-binding cassette transporter A12 (ABCA12) on chromosome 2 (ABCA12) [1]. ABCA12 is a keratinocyte lipid transporter associated with lipid transport in lamellar granules [2]. In HI skin, loss of function of ABCA12 results in defective permeability of the skin barrier due to impaired lipid lamellar membrane formation in the cornified layer [2].

Case Report
A 39-year-old pregnant woman was admitted to Al-Imam Abdurrahman Al Faisal Hospital in Riyadh for her seventh pregnancy due to preterm, premature rupture of membrane and obstetric pain. Gestational age was approximately 35 weeks and 4 day based on both the first day of the last menstrual period and ultrasound. Patient was un-booked and at time of delivery, the fetus showed breech presentation on ultrasound. Female baby with Harlequin Ichthyosis was born via caesarean section. Her birth weight, length, and head circumference was 2.75 kg, 45cm, and 35 cm respectively. Apgar score was 3 at 1 min after that the baby intubated.
Generalized edema, thick skin with deep fissures, general hyperkeratinization, facial distortion secondary to taut scales, diffuse alopecia ectropion, left nostril closed by membrane, immature eyes and auricles, eclabium, tongue tie, dystrophic and ischemic nails were noted in the physical examination (Figure 1). Antibiotic therapy and conservative treatments were started after admission to the neonatal intensive care unit.
The patient had three healthy children after normal vaginal deliveries from the first marriage (two males and one female, the parent had a distant relationship), and in the second marriage parents had a nearly relationship and had two previously normal healthy children (one male and one female) after normal vaginal deliveries. The parents had a family history of other genetic disorders like Down syndrome and Sickle Cell Anemia but no inherited skin disorder. At the time of writing this report the baby is now 35 days old and she is in isolation room for treatment of sepsis (Figure 2).

Fig 1: The baby at time of delivery showing thick armour-like scales with fissuring, areas of erythema, ectropion and eclabium.

Fig 2: The baby at 35 days old in isolation room showing shedding of collodion membrane.

Discussion

HI is a congenital disorder characterized by an autosomal recessive inheritance [6]. The first case reported in 1750 by Oliver Hart in South Carolina who described the feature of this disorder. Usually, it has fateful prognosis and most of HI babies die in first weeks of life [7]. Majority of the cases are reported due to ABCA12 gene mutation which is a gene responsible for transporting lipid to the epidermis in order to form a healthy normal skin [3, 6]. Infants at birth usually have thick, fissured armor-plate hyperkeratosis, ears and nose deformities, ectropion, eclabium with fish mouth appearance, flexion deformities of all joints and hypoplastic digits [2, 3]. Furthermore, restricted chest expansion and skeletal deformities may result in respiratory failure. Hypoglycemia, dehydration or even renal failure is common in these patients mainly due to feeding problems. In addition, hypo- or hyperthermia as well as infections are common [6, 8]. Most of these clinical features are present in this case. In addition, our case developed a sepsis which is one of the common complication and she shifted to isolation room for further care. The hallmark of the diagnosis are the family history of the same case, consanguinity and other skin disorders [4].

There are many cases of HI associated with family history of systemic diseases, Such as juvenile rheumatoid arthritis, hypothyroidism and psoriasis have been reported in Harlequin babies [7].

Our case has a positive family history of some genetic disorder like Sickle cell anemia, Down syndrome and a case of congenital anomalies with hydrocephalus.

The prevalence of HI is unknown yet. However, one study in Saudi Arabia was conducted by Al Zayir *et al.* in 2006 in a large university hospital using an OPD dermatology logbook have an estimated occurrence of 7/1000 but it doesn't provide a specific data [9]. Another study by Anwar A Mithwani *et al.* reported a prolonged survival of a patient with HI. A male baby was delivered at 37 gestational week of a consanguineous parents who didn't have any previous inherited skin disorders. The baby was managed as inpatient for 8 months with supportive treatments and lubrications then was discharged and now the patient is 7 years old and still having treatments for HI [1].

The management of HI is symptomatic. Using High-humidity environment and dressings with Vaseline helps in shedding of collodion membrane. Also, topical antiseptics, 5% lactic acid and liquid paraffin found to be effective in the management. Synthetic retinoids which is derived from vitamin A, has an effective rule in the treatment but the exact mode of action is unknown. It helps in control the differentiation and proliferation of keratinizing and non-keratinizing epithelia [1, 4].

Improved outcome was related to early administration of oral retinoid and heterozygous mutations [1]. In clinical outcome of

HI, Rajpopat *et al* reported a survival rate of 56%, out of 45 cases of HI, 16 cases surviving for 7 years or more and the longest surviving case reaching up to 25 years [10]. However the longest reported surviving case in Saudi Arabia was beyond 7 years [1].

The main aim of this report is to determine the best mode of delivery for baby with HI and to assert the importance of prenatal genetic diagnosis of HI in next pregnancy which is very important in all high risk pregnancies like our case. The diagnosis is usually done by taken a biopsy of fetal skin at 19 – 23 weeks of gestation with assistance of 3D or 4D ultrasonography or by direct sequence analysis of ABCA12 mutation from amniotic fluid cells [2].

Conclusion

With improvement in supportive clinical care, the use of oral retinoid and regular moisture of the skin the survival rate of patients with HI has increased. However, early diagnosis and genetic counseling of the parents is an important step in managing such patients. We recommend to have a genetic screening and counseling in all high risk couples e.g. consanguinity marriages as well as having more studies to determine the best mode to deliver a baby with HI.

References

1. Mithwani AA, *et al.* Harlequin ichthyosis: a case report of prolonged survival. BMJ Case Rep, 2014-2014.
2. Farhadi R, Kazemi SH. Harlequin ichthyosis in a neonate born with assisted reproductive technology: a case report. Med J Islam Repub Iran. 2013; 27(4):229-32.
3. Hovnanian A. Harlequin ichthyosis unmasked: a defect of lipid transport. J Clin Invest. 2005; 115(7):1708-10.
4. Javed T, FAM, Iqbal Khan H. Harlequin fetus: a case report. Journal of Pakistan Association of Dermatologists. 2005; 15:348-350.
5. Parikh K, *et al.* A case report of fatal harlequin ichthyosis: Insights into infectious and respiratory complications. JAAD Case Rep, 2016; 2(4):301-3.
6. Richard G, Balesj SJ. Autosomal Recessive Congenital Ichthyosis, in Gene Reviews(R), R.A. Pagon, *et al.* Editors. Seattle (WA), 1993.
7. Chan YC, TY Tan LK, *et al.* Harlequin ichthyosis in association with hypothyroidism and juvenile rheumatoid arthritis. Pediatric Dermatology, 2003; 20(5):421-426.
8. Kelsell DP, *et al.* Mutations in ABCA12 underlie the severe congenital skin disease harlequin ichthyosis. Am J Hum Genet. 2005; 76(5):794-803.
9. Al-Zayir AA. Al-Amro Al-Alakloby OM. Clinico-epidemiological features of primary hereditary ichthyoses in the Eastern province of Saudi Arabia. Int J Dermatol, 2006; 45(3):257-64.
10. Rajpopat S, *et al.* Harlequin ichthyosis: a review of clinical and molecular findings in 45 cases. Arch Dermatol. 2011; 147(6):681-6.