

Harlequin ichthyosis: Case report

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Harlequin fetus is a rare and the most severe form of the congenital ichthyosis with an autosomal recessive inheritance. Incidence of the disease is nearly 1 in 3,00,000 live births. The disease might be lethal at birth and the affected babies are often premature. Harlequin ichthyosis (HI) is marked by severe keratinized and alligator-like horned skin. The present study reports a new case with HI and adds to the collective knowledge of this rare skin disorder. HI has been linked to mutation in the *ABCA12* gene; therefore, genetic counseling and mutation screening of this gene should be considered.

Key words: *ABCA12* gene mutation, autosomal recessive, skin abnormalities

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INTRODUCTION

Harlequin ichthyosis (HI) is a lethal disease,^[1,2] but victims in very rare cases may survive for several months or years.^[3] HI appears with severe thickened and scaly skin on the entire body. In addition, ectropion, lack of development of the external parts of the nose and ears, eclabium and open mouth, hypoplastic fingers, anonychia and mobility limitation of the joints are some other clinical features of the HI.^[2,4,5] Patients with HI are at high risk for hypo/hyperthermia, dehydration, respiratory distress, hypoventilation, malnutrition, hypernatremia, seizure, and skin infection.^[2,6] HI is associated with preterm birth and often leads to death due to neonatal complications such as fluid loss and septicemia.^[3]

CASE REPORT

A 31-year-old pregnant woman was admitted to the Zabol Amir-Al-Momenin hospital for her third pregnancy due to preterm, premature rupture of membrane and obstetric pain. Gestational age was approximately 30 weeks and 1 day based on both the first day of the last menstrual period and ultrasound. No remarkable complication was noted in the last ultrasound examination at 28 weeks of pregnancy. A female baby with HI was born via normal spontaneous vaginal delivery. Her birth weight, length, and head circumference was 2.1 kg, 44 cm, and 29 cm, respectively [Figure 1]. Parents had a distant relation and had two other normal healthy children. Thick skin with deep fissures, general hyperkeratinization, cyanosis,

flat fontanels, ectropion, immature eyes and auricles, eclabium, bradycardia, bradypnea, and moaning were noted in the physical examination. Antibiotic therapy and conservative treatments were started after admission to the neonatal intensive care unit. However, the parents self-discharged their newborn daughter at the same day after birth.

DISCUSSION

HI is an inherited autosomal recessive disorder that characterized by congenital epidermis abnormality.^[4,5] Mutations in the *ABCA12* gene have been reported in the majority of HI patients.^[4,6] This gene plays a major role in transporting lipids to cells that form the epidermis



Figure 1: The patient with deep cracked skin, open wide mouth, abnormal eyes, and flatted nose and ear

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and the normal development of the skin.^[2] At birth, infants are covered with hard hyperkeratonic armor, composed of large, thick, yellowish brown, and very sticky plates.^[6,7] After birth, deep red fissures occur on these hard and inflexible plates that extend to the dermis, resulting in a joker-like skin. Infants with HI might have microcephaly, ectropion, and eclabium.^[4] External auditory meatus and nostrils appear rudimentary and immature.^[8] In addition, patients with HI have respiratory failure as a result of restricted chest expansion and skeletal deformities. Feeding problems may result in low blood sugar, dehydration, and kidney failure. In addition, temperature instability and infection would be common.^[4,6] Almost all these clinical features were observed in the current case.

Families with one or more children with HI have been previously reported. A boy with HI was born at 37 weeks of pregnancy with 2.9 kg in a Polish family. He was 6 months old at the reporting time. Another study has reported two cases with HI from Mashhad, Iran. The first case was a 2.0 kg premature girl who was delivered at 32 weeks of pregnancy and died 3 days after birth. She was the product of a first-cousin marriage. The second one was also a girl with a weight of 2.3 kg.^[7]

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.^[4] Microscopic examination of the amniotic fluid cells and ultrasound for assessment of the shape of fetal mouth at 17 weeks of pregnancy might be useful for the early detection.^[9,10] Prenatal diagnosis can also be feasible using skin biopsy at 24 weeks of pregnancy, especially among the families with a history of HI. Although ultrasonography can be useful in some cases but it might not be applicable due to delayed phenotypic expression and the rarity of the disease.^[3] Furthermore, sequence analysis of *ABCA12* should be done first for the individuals with HI history.^[4]

The mortality of HI is high and most of the victims die within a few weeks of birth because of secondary complications such as infection and dehydration.^[4] However, survival contributes to the type of mutations; victims with the compound heterozygote mutation survive more than those with the homozygote mutation.^[11] In addition, advances in the postnatal treatments and cares improve the prognosis of the disease.^[4,11] The survival rate increases to more than 50% with early prescription of oral retinoids. The patients' quality of life improves with supportive cares. In addition to the routine care such as checking vital signs, patients should be kept in a warm and humid incubator. Hydration should be performed.^[12] As accessing to the peripheral vessels can be difficult, an umbilical venous catheter might be needed. Taking shower twice per day, saline compresses and gentle

emollients must be used to keep the skin soft and to accelerate the desquamation. Water and electrolyte disturbances must be managed as well. Environment must be cleaned up to prevent infection; hence, repeated cultures of the skin would be essential to detect the hazardous microorganisms.^[4] In addition, genetic counseling and molecular investigation of the *ABCA12* gene should be considered.

CONCLUSION

The supportive care such as oxygen therapy, transporting to incubator, using normal saline to cleanse and moist the skin was performed early after birth. However, the patient was self-discharged by parents at the same day of birth, and there was no more information regarding her survival. The current case adds to the collective clinical knowledge of this rare skin disorder. We suggest that mutation screening of the *ABCA12* gene and genetic counseling of families would be important especially in families with a consanguinity marriage.

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