Harlequin Ichthyosis the Most Severe Form of the Congenital Ichthyosis; A Case Report Study

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Abstract

Harlequin ichthyosis (HI) is a rare and the most severe form of the congenital ichthyosis with an autosomal recessive inheritance. At birth, the HI phenotype is striking with thick hyperkeratotic plate-like scales with deep dermal fissures, severe ectropion, among other findings. Although HI infants have historically succumbed in the perinatal period related to their profound epidermal compromise, the prognosis of HI infants has vastly improved over the past 20 years. The disease might be lethal at birth and the affected babies are often premature. The present study reports a new case with HI and adds to the collective knowledge of this rare skin disorder.

Keywords: *Harlequin ichthyosis, Gene, Mutation, Autosomal recessive, Case report, Iran*

Introduction

Harlequin ichthyosis (HI) is a genetic disorder that results in thickened skin over nearly the entire body at birth.[1] The skin forms large, diamond/trapezoid/rectangle-shaped plates that are separated by deep cracks. These affect the shape of the eyelids, nose, mouth, and ears and limit movement of the arms and legs.[2] Restricted movement of the chest can lead to breathing difficulties. These plates fall off over several weeks.[3] Other complications can include premature birth, infection, problems with body temperature, and dehydration. The condition is the most severe form of ichthyosis, a group of genetic disorders characterized by scaly skin.[2]

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HI is caused by mutations in the *ABCA12* gene. This gene codes for a protein necessary for transporting lipids out of cells in the outermost layer of skin. The disorder is autosomal recessive and inherited from parents who are carriers.[4] Diagnosis is often based on appearance at birth and confirmed by genetic testing.[5]

Before birth, amniocentesis or ultrasound may support the diagnosis.[4] Newborns with HI present with thick, fissured armor-plate hyperkeratosis. Sufferers feature severe cranial and facial deformities.[6] The ears may be very poorly developed or absent entirely, as may the nose.[2] The eyelids may be everted (ectropion), which leaves the eyes and the area around them very susceptible to infection. Babies with this condition often bleed during birth. The lips are pulled back by the dry skin.[7]

Joints are sometimes lacking in movement, and may be below the normal size. Hypoplasia is sometimes found in the fingers. Polydactyly has also been found on

occasion.[3] In addition, the fish mouth appearance, mouth breathing, and xerostomia place affected individuals at extremely high risk for developing rampant dental decay.[2]

Patients with HI are extremely sensitive to changes in temperature due to their hard, cracked skin, which prevents normal heat loss. Respiration is also restricted by the skin, which impedes the chest wall from expanding and drawing in enough air.[8] This can lead to hypoventilation and respiratory failure. Patients are often dehydrated, as their plated skin is not well suited to retaining water.[3]

There is no cure for the condition. Early in life, constant supportive care is typically required. Around half of those affected die within the first few months; however, retinoid treatment can increase chances of survival.[9] Children who survive the first year of life often have long-term problems such as red skin, joint contractures and delayed growth.[7]

Case presentation

A 26-year-old woman, gravida 3, was admitted to Kosar Hospital in Urmia, Iran at 29 weeks of gestation because of oligohydramnios. There was no family history of harlequin ichthyosis. Ultrasound examination showed a 28 gestational weeks fetus with oligohydramnios. A male baby with HI was born via normal spontaneous vaginal delivery. Her birth weight, length, and head circumference was 2.4 kg, 43 cm, and 28 cm, respectively [see 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 newborn died after two weeks.

Figure 1: The newborn with open wide mouth, abnormal eyes, and flatted nose and e

Discussion

HI is a rare and extremely severe form of congenital ichthyosis, with an incidence of about 1 in 300000 births.[10] Prenatal diagnosis is usually difficult because of nonspecific signs in the ultrasonographic examination and rareness of the disorder. Delivery of a child with congenital ichthyosis identifies a family at risk, and for subsequent pregnancies prenatal diagnosis can be offered. This report is a typical example of all of these issues.

Mutations in the ABCA12 gene have been reported in the majority of HI patients.[5] This gene plays a major role in transporting lipids to cells that form the epidermis and the normal development of the skin.[6] At birth, infants are covered with hard hyperkeratonic armor, composed of large, thick, yellowish brown, and very sticky plates.[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.[8]

External auditory meatus and nostrils appear rudimentary and immature.[7] In addition, patients with HI have respiratory failure as a result of restricted chest expansion and skeletal deformities.[3] Feeding problems may result in low blood sugar, dehydration, and kidney failure. In addition, temperature instability and infection would be common.[11] Almost all these clinical features were observed in the current case.

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.[12] However, survival contributes to the type of mutations; victims with the compound heterozygote mutation survive more than those with the homozygote mutation.[13] In addition, advances in the postnatal treatments and cares improve the prognosis of the disease.[14] 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.

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Ethical Clearance: The study was undertaken after gaining Motahari medical research center/ Urmia Medical University's approval.

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