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Case Report

Harlequin Ichthyosis: A Fatal Disease

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ABSTRACT

Harlequin ichthyosis (HI) is a rare and severe form of congenital ichthyosis that is inherited in an autosomal recessive manner. Affected newborns are frequently premature, and this illness may be fatal at birth. Severe hyperkeratosis, widespread fissuring, and varying degrees of cutaneous abnormalities are the disease's hallmarks. Here a case of a harlequin baby is reported who was born prematurely and to consanguineous parents. She had typical manifestations of harlequin ichthyosis. Conservative treatment was given, but the baby died on the eighth day of her life.

Keywords: *Harlequin ichthyosis, Autosomal recessive, ABCA12 gene mutation*

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INTRODUCTION

With a frequency of 1 in 300,000 live births, harlequin ichthyosis (HI) is a rare and lethal disease[1]. It is inherited in an autosomal recessive manner. The majority of mutations in the keratinocyte lipid transporter adenosine triphosphate binding cassette A12 (ABCA12) that lead to functional abnormalities are linked to HI[2,3]. A dysfunctional or absent adenosine triphosphate-binding cassette A12 (ABCA12) protein causes abnormal lamellar granule lipid and protease transport in granular layer keratinocytes, resulting in epidermal hyperkeratinization and ineffective desquamation[4,5].

The skin on HI's entire body is severely thickened and scaly. Other clinical characteristics of the HI include ectropion, lack of development of the external regions of the nose and ears, eclabium and open mouth, hypoplastic fingers, anonychia, and restricted joint mobility[6,7,8]. Hypo/hyperthermia, dehydration, respiratory distress, hypoventilation, malnutrition, hypernatraemia, seizures, and skin infections are all serious risks for HI patients. HI is linked to premature birth and frequently results in death from neonatal problems such as fluid loss and septicaemia[9].

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CASE REPORT

A 30-minute-old female baby, 1st issue of her consanguineous parents, weighing 1810 grams, was admitted to the paediatrics department of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, with complaints of a small baby delivered before term. The baby was delivered by LUCS during 34 weeks of gestation due to premature rupture of the membrane for 2 days at JRRMCH on July 30th, 2021. On admission,

the baby′s heart rate was 110 beats per minute, respiratory rate was 52 breaths per minute, temperature was 99°F, chest indrawing was present, reflexes were poor, and OFC and length were within normal limits. Baby′s skin was thick with deep fissures, facial disfigurement with severe ectropion, and the nose and ears were flattened. The mouth was widely open and the lips were everted. Nails were absent and a very small amount of hair was present over the scalp. There was restricted joint movement and the hands and feet appeared to be fixed, oedematous. Fingers and toes were deformed (Figure 1). So, the patient was initially diagnosed as preterm (34 weeks) low birth weight baby (1810 grams) with harlequin ichthyosis. The baby was kept in neonatal ward, umbilical catheterization was done. Her treatment was started by keeping her nothing per oral, I/V fluid, parenteral antibiotics, O_2 inhalation through the head box. Consultation with dermatology, paediatric surgery and ophthalmology departments were done. For skin care, Sodium Fusidate cream, 0.1% Tazarotene cream and white soft Paraffin + liquid Paraffin were applied. Regular dressing was done. For eye care, 0.5% Moxifloxacin hydrochloride eye drop, 1% Carboxymethylcellulose sodium eye drop and 1% Fusidic acid eye drop were given. On the 5th day of life, as her condition was stable, a small amount of feeding was started. She developed severe respiratory distress with feeding intolerance on the seventh day. Unfortunately, she passed away on the eighth day of

Figure-1: *Features of harlequin ichthyosis at birth*

DISCUSSION

One of the rare congenital diseases is harlequin ichthyosis, and it is often fatal. There is relatively little information available on this anomaly, and it mostly comes from case reports. A foetus with thickened and cracked skin over the whole body was first reported as HI by Reverend Oliver Hart of Charleston, South Carolina in 1750[6].

In the majority of HI patients, there are mutations in the ABCA12 gene[3,7]. The transfer of lipids from the cytosol of the keratinocytes into lamellar granules is made possible by this ABCA12-mediated lipid transfer pathway. ABCA12 is mostly found in keratinocytes of the granular layer and localizes to LGs near the cell periphery throughout the whole Golgi apparatus. In the granular cell's LGs, ABCA12 is involved in the transfer of lipids from the Golgi apparatus. The contents of the lamellar bodies are extruded into the intercellular space at the transition between stratum granulosum, the third layer of the epidermis, and stratum corneum to create protective lipid sheets that provide the hydrophobic barrier on the skin[6].

Hallmarks of the diagnosis are consanguinity and a family history of the same and other skin diseases. There is a family history of psoriasis, juvenile rheumatoid arthritis and hypothyroidism with Harlequin babies were reported[10]. The inheritance is autosomal recessive in manner, and affected babies are usually homozygous for the mutation[11]. In this case, there was consanguinity between the parents. There was presence of consanguinity in the parents in the case reported by Tahir et al[12]. But in some case reports, which were reported by Abbas et al.[13] and Quddush et al.[14], there was no consanguinity in the parents.

Babies with HI are usually born prematurely and do not have any abnormalities in their brain or internal organs[15]. In this current case, the baby was born prematurely. Similar cases were reported by Tahir et al.[12] and Salehin et al[16]. But there were some cases reported as in term babies by Abbas et al.[13] and Quddush et al[14]. On ultrasonography of both eyes, there was a bilateral absence of eyeball in the case report of Abbas et al[13].

Infants are born with strong hyperkeratotic armour, made of massive, thick, yellowish brown and extremely sticky plates[3,17]. Deep red fissures form on these rigid, unyielding plates after birth giving the skin a characteristic and alarming appearance. Microcephaly, ectropion and eclabium may be present in infants with HI[7]. Nostrils and the external auditory meatus seem primitive and underdeveloped[18]. In

the initial stage of the disease's early identification would be a prenatal diagnosis. Early detection methods include microscopic analysis of the cells in the amniotic fluid and ultrasound evaluation of the foetal mouth form at 17 weeks of pregnancy[11,15]. Additionally, people with HI histories should first perform ABCA12 sequencing analysis[7]. A skin biopsy is a part of postnatal diagnosis and is likely to show structural abnormalities of lamellar granules and epidermal keratin expression. In this case, based on the gross appearance of the baby, the diagnosis was made.

A multi-disciplinary approach is necessary due to the nature of the complications and co-morbidities. Early treatment of HI typically entails the use of a humidified incubator to prevent transcutaneous water loss, maintaining a stable body temperature, caring of skin and eyes, administering analgesics to treat painful deep fissures, proper infection control and maintaining nutritional status. An umbilical venous catheter might be needed due to difficulty in accessing the peripheral vessels. To keep the skin moist and hasten the desquamation, twice-daily showers, saline compresses, and mild emollients are required. Management of water and electrolyte disturbances must be done. In order to prevent infection, the environment must be cleaned up and frequent cultures of skin are required to find any potentially dangerous microorganisms[7].

Most patients died within a few weeks of birth as a result of secondary complications such as infection and dehydration[7]. Survivorship, however, is dependent on the type of mutation; victims with compound heterozygote mutations have a better chance of survival than those with homozygote mutations[19]. In addition, the prognosis of the disease can be improved by advances in the postnatal treatments and cares[7,19]. In addition, genetic counselling for families with consanguinity marriages, as well as molecular research on the ABCA12 gene, should be considered.

CONCLUSION

The most severe type of congenital ichthyosis is called harlequin ichthyosis. A harlequin baby's phenotypic characteristics were present in our patient. Amniotic fluid collection can be used to provide a prenatal diagnosis as early as week 17 of pregnancy. Prenatal diagnosis of this illness is possible with the aid of ultrasonography and electron microscopic analysis of the foetal skin sample in order to prevent its severe effects. Particularly in families with a consanguinity marriage, mutation screening of the ABCA12 gene and genetic counselling of families would be crucial. The cornerstone of treatment, employing a multidisciplinary approach, continues to be supportive therapy. The prognosis is poor, and fulminant sepsis is still the main cause of death.

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