

A CASE REPORT : HARLEQUIN ICHTHYOSIS

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Abstract : Harlequin-type ichthyosis is a rare [genetic disorder](#) which results in thickened skin over nearly the entire body at birth .The skin forms large, diamond-shaped plates that are separated by deep cracks .They affect the shape of the eyelids, nose, mouth, and ears, and limit movement of the arms and legs. Restricted movement of the chest can lead to breathing difficulties.–These plates fall off over weeks. Harlequin-type ichthyosis is due to mutations of the [ABCA12 genes](#). It is [inherited](#) from a person's parents in an [autosomal recessive](#) manner.–Diagnosis is often based on appearance at birth and confirmed by [genetic testing](#). Before birth [amniocentesis](#) or [ultrasound](#) may support the diagnosis. There is no cure. Early in life constant [supportive care](#) is typically required. Treatments may include moisturizing cream, [antibiotics](#), [etretinate](#), or [retinoids](#). It affects about 1 per 300,000 births. Both sexes are affected equally commonly. Long term problems are common. Death in the first month is relatively common . The condition was first documented in 1750.

Alternative names for HI include - keratosis diffusa fetalis , ichthyosis fetalis , harlequin fetus , hyosis fetalis, ichthyosis congenita gravior ^[1]

KEYWORDS : [autosomal recessive](#), [ABCA12 genes](#), [genetic testing](#), [inherited](#), [supportive care](#)

I.Introduction

The disease has been known since 1750, and was first described in the diary of Rev. Oliver Hart from Charleston, South Carolina.^[2]

The *harlequin-type* designation comes from the diamond shape of the scales at birth (resembling the costume of [Arlecchino](#)).^[2]

It is a rare [genetic disorder](#) which results in thickened skin over nearly the entire body at birth.^[3] The skin forms large, diamond-shaped plates that are separated by deep cracks [Fig-1].^[3] These skin abnormalities affect the shape of the eyelids, nose, mouth, and ears, and limit movement of the arms and legs [Fig-2].^[3] It affects about 1 per 300,000 births.^[1] Both sexes are affected equally commonly.^[1] It is [inherited from a person's parents](#) in an [autosomal recessive](#) manner.^[1]

Here we are presenting a case of this rare condition.

II.Case Report

A new born infant (37weeks) born out of a consanguineous marriage to a primigravida mother, 31 years old in Gynaecology and inborn nursery pediatric department of our institute with thick deep fissured hyperkeratotic skin . His eyes and lips were pulled so tight because of the skin that they were flipped out , making them look bloody . Face was mask like. Joints were lacking movement , fingers and toes were hypoplastic .

Till the date of delivery pregnancy was uneventful .There was no history of any exposure of tobacco smoking , alcohol consumption or any exposure to other drugs or toxic substances . She underwent normal vaginal delivery of a live malformed male foetus of 2400 gm . After the baby was born cry was immediate though weak .There were restricted movements at the joints. Restricted movement of the chest lead to difficulty in breathing , grunt was also present . Oxygen with hood was started . Intravenous access was difficult due to leathered skin , umbilical catheterisation was done . Baby was referred to PGI Chandigarh for diagnosis and management . He was referred back due to guarded prognosis . Baby was continued on oxygen , skin was covered with warm saline gauge under radiant warmer to prevent hypothermia. Baby developed respiratory failure due to restricted chest movements shifted to CPAP as intubation was difficult due to restricted mouth opening , expired on 4th day of life due to respiratory failure .



Fig 1 : Showing Harlequin baby with thick skin forming large diamond shaped plates separated by deep fissures covering whole skin including scalp and genitalia giving a “coat of armour “ appearance . Clenched fists and incurved toes are also present .



Fig 2 : Shows thickened skin affect the shape of the eyelids , nose , mouth and ears.



Fig 3 : Shows there is no site for cannulation on skin for starting intravenous fluids . Umbilical catheterisation was done .



III. Discussion

Newborns with harlequin-type ichthyosis present with thick, fissured armor-plate [hyperkeratosis](#).^[1] Severe cranial and facial deformities are present in the new born .The ears may be very poorly developed or absent entirely, as may the [nose](#). The [eyelids](#) may be everted ([ectropion](#)), which leaves the eyes and the area around them very susceptible to infection.^[4] Babies with this condition often bleed during birth. The [lips](#) are pulled back by the dry skin ([eclabium](#)). 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. ^[1] In addition, the fish mouth appearance, mouth breathing, and [xerostomia](#) place affected individuals at extremely high risk for developing rampant dental decay.^[5] Patients with this condition 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. This can lead to [hypoventilation](#) and [respiratory failure](#). Patients are often [dehydrated](#), as their plated skin is not well suited to retaining water. The diagnosis of harlequin-type ichthyosis relies on both physical examination and certain laboratory tests. Physical assessment at birth is vital for the initial diagnosis of harlequin ichthyosis. Physical examination reveals characteristic symptoms of the condition especially the abnormalities in the skin surface of newborns.

Abnormal findings in physical assessments usually result in employing other diagnostic tests to ascertain the diagnosis. Genetic testing is the most specific diagnostic test for harlequin ichthyosis. This test reveals a loss of function mutation on the ABCA12 gene. This gene is important in the regulation of protein synthesis for the development of the skin layer. Mutations in the gene may cause impaired transport of lipids in the skin layer and may also lead to shrunken versions of the proteins responsible for skin development. Less severe mutations result in a collodion membrane and congenital ichthyosiform erythroderma-like presentation.^{[6][7]} ABCA12 is an ATP binding cassette (ABC) transporter, and is a member of a large family of proteins that hydrolyze ATP to transport cargo across membranes. ABCA12 is thought to be a lipid transporter in keratinocytes necessary for lipid transport into lamellar granules during the formation of the lipid barrier.^[8] Biopsy of skin may be done to assess the histologic characteristics of the cells. Histological findings usually reveal hyperkeratotic skin cells, which leads to a thick, white and hard skin layer.^[1] Constant care is required to moisturize and protect the skin. The hard outer layer eventually peels off, leaving the vulnerable inner layers of the [dermis](#) exposed. Early complications result from infection due to fissuring of the [hyperkeratotic plates](#) and [respiratory distress](#) due to physical restriction of chest wall expansion. Management includes supportive care and treatment of [hyperkeratosis](#) and [skin barrier dysfunction](#). A humidified incubator is generally used. [Intubation](#) is often required until [nares](#) are patent. Nutritional support with tube feeds is essential until [ecclabium](#) resolves and infants can begin nursing. [Ophthalmology](#) consultation is useful for the early management of [ectropion](#), which is initially pronounced and resolves as scales are shed. Liberal application of [petrolatum](#) is needed multiple times a day. In addition, careful [debridement](#) of constrictive bands of [hyperkeratosis](#) should be performed to avoid [digital ischemia](#). Cases of [digital autoamputation](#) or [necrosis](#) have been reported due to [cutaneous constriction](#) bands. Relaxation incisions have been used to prevent this morbid complication.^[11] In the past, the disorder was nearly always fatal, whether due to [dehydration](#), [infection \(sepsis\)](#), restricted [breathing](#) due to the plating, or other related causes. The most common cause of death was systemic infection and sufferers rarely survived for more than a few days. However, improved [neonatal intensive care](#) and early treatment with [oral retinoids](#), such as the drug [Isotretinoin](#) (Isotrex), may improve survival.^[9] Early oral retinoid therapy has been shown to soften scales and encourage desquamation.^[10] After as little as two weeks of daily oral isotretinoin, fissures in the skin can heal, and plate-like scales can nearly resolve. Improvement in the ecclabium and ectropion can also be seen in a matter of weeks. Children who survive the neonatal period usually evolve to a less severe phenotype, resembling a severe [congenital ichthyosiform erythroderma](#). Patients continue to suffer from [temperature dysregulation](#) and may have heat and cold intolerance. Patients can also have generalized poor hair growth, scarring [alopecia](#), [contractures](#) of digits, [arthralgias](#), [failure to thrive](#), [hypothyroidism](#), and [short stature](#). Some patients develop a [rheumatoid](#) factor-positive [polyarthritis](#).^[11] Survivors can also develop fish-like scales and retention of a waxy, yellowish material in [seborrhic](#) areas, with ear adhered to the scalp.

The oldest known survivor is Nusrit "Nelly" Shaheen, who was born in 1984 and is in relatively good health as of March 2017.^[12] The maximum lifespan of patients with this disease has not yet been determined with the new treatments.

A study published in 2011 in the Archives of Dermatology concluded: "*Harlequin ichthyosis* should be regarded as a severe chronic disease that is not invariably fatal. With improved neonatal care and probably the early introduction of oral retinoids, the number of survivors is increasing."^[13]

Two cases have been reported in India till this time :

- A female baby born in [Nagpur](#), India in June 2016 died after two days. She is reported as the first case in India.^[14]
- What is believed to be the second case in India was reported in January 2017 in [Patna](#), the capital of [Bihar](#).^[15] Deputy superintendent of Paliganj sub-divisional hospital Dr Shiv Lal Chaudhary, who is also in charge of Paliganj PHC, said the baby was born through a normal delivery. The baby was born four weeks prematurely. The couple's other child, aged 18 months, is not reported to have the disease.

IV. Conclusion

Harlequin ichthyosis is a rare but debilitating condition occurring due to consanguineous marriages can be diagnosed early during antenatal period by karyotyping in mothers with previously affected babies can be terminated. Characteristic features on prenatal USG tend to appear late.^[16] Antenatal counselling should be done. Chances of survival has increased with improved neonatal care.

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