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Case Report

Harlequin ichthyosis – a disturbing disorder

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Abstract Harlequin ichthyosis is a severe variant of autosomal recessive congenital ichthyosis resulting from loss-of-function mutations in the ABCA12 gene on chromosome 2q35, a transporter protein responsible for the formation and function of the lamellar granules. The estimated prevalence is < 1/1,000,000. A day-old male baby, born to non-consanguineously married couple presented to the NICU with a rigid, taut, yellow brown, adherent skin. The prenatal and natal history was uneventful with normal anomaly scan and growth scans. It was a normal vaginal delivery with a birth weight of 2.2kg, normal cry and normal APGAR score. The first two siblings did not have similar complaints. On examination, deep fissures were noted at the site of stress, flexors and over the scalp. There was ectropion, eclabium, tethering of nose and ears. The hands and feet appeared edematous with restricted movements due to contractures. The conjunctiva appeared edematous. The baby appeared as if it was encased in a coat of armour. On day 2 of examination, there was mild decrease in the tautness of skin. Restrictive dermopathy and stiff skin syndrome were considered for differential diagnosis. But there was no associated skeletal abnormality and the clinical features distinctive of Harlequin ichthyosis. The baby was started on oral isotretinoin 1mg/kg along with adequate moisturizers for topical application. Genetic counselling was done to the parents and the complication of the disease explained. This case is presented for its rarity.

Key words
Harlequin ichthyosis, autosomal dominant.

Background

Harlequin ichthyosis (HI) is a severe variant of autosomal recessive congenital ichthyosis resulting from loss-of-function mutations in the ABCA12 gene on chromosome 2q35. The gene encodes for a membrane-based lipid transporter protein responsible for the formation and function of the lamellar granules.[1] The prevalence is estimated to be less than 1/1,000,000. HI is associated with <50% morbidity and mortality soon after birth.[2] We report a case of HI because of its rarity of presentation.

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Case Report

A newborn, male baby, born out of full-term gestation, to a non-consanguineous married couple presented to the NICU with a rigid, taut, yellow, adherent skin. The baby was born by normal vaginal delivery, weighed 2.2kg at birth, had normal cry and normal APGAR score. The mother was 4th para with 2 living children and 1 abortion. The first two pregnancies were uneventful with normal vaginal deliveries and first two children did not have similar complaints. Third pregnancy ended up in spontaneous abortion at 3rd month, cause being unknown. The present pregnancy had an uneventful prenatal and natal period with normal anomaly scan and growth scans.

On examination, the baby was encased in a thick, adherent, rigid skin, yellowish to brown in

Figure 1 Thick, adherent, rigid skin, yellowish to brown color with deep fissures.

Figure 2 Bilateral ectropion, eclabium of both the lips and hypoplastic auricle of left ear, flattened hypoplastic nose and fish-like mouth.

color with deep clefts **(Figure 1)**. Deep fissures were noted at the site of stress, flexors and over the scalp. There was associated ectropion of both the eyes, eclabium of both the lips **(Figure 2)**. The auricles were hypoplastic and appeared tethered to the skin **(Figure 2)**. The nose was flattened and hypoplastic. Fish mouth appearance was seen **(Figure 2)**. The hands and feet appeared edematous with restricted movements due to contractures. The conjunctiva appeared edematous. The baby was feeding well and maintained normal saturation. The respiratory rate and temperature were within normal limits. No other congenital anomalies were noted.

The newborn was placed in a humidifier to prevent hypothermia and respiratory rate was closely monitored. The baby was given regular feeds via nasogastric tube. Oral isotretinoin in a dose 1mg/kg body weight was started on day 1. Unfortunately patient was lost to follow-up.

Few conditions resembling HI like restrictive dermopathy, stiff skin syndrome, Neu-Laxova syndrome were considered for differentials. Restrictive dermopathy was ruled out as there was no associated skeletal and facial abnormalities.[1] Neu-Laxova syndrome is an autosomal recessive condition presenting with ichthyosis, marked intrauterine growth restriction, microcephaly, short neck and limb deformities.[1] In stiff skin syndrome, patient presents with rock-hard skin, limited joint mobility, and mild hypertrichosis in infancy or early childhood. The striking clinical finding of hyperkeratotic coat of armour encasing the baby prompted us to the diagnosis of Harlequin ichthyosis.[3]

Discussion

Harlequin ichthyosis was one of the first genodermatoses to be recorded. It is an autosomal recessive disease occurring due to missense mutation in the ABCA12 gene on chromosome 2q35. In the epidermis, ABCA12 binds to ATP and actively transports lipids across the cell membrane against a concentration gradient. This results in the formation of lamellar granules which contain polar lipids, proteases and their inhibitors, thereby playing a pivotal role in the development of epidermal barrier function.

The affected infant is premature or stillborn, encased in a rigid, taut, yellowish to brown colored tightly adherent hyperkeratotic coat of armour. Deep fissures are seen over the scalp and at site of stress with red fissures resembling

a harlequin's costume. There is associated ectropion, eclabium, rudimentary nose and ears. The patients are prone to various complications like respiratory insufficiency, hypoglycemia, hypothermia, dehydration and renal failure. The histopathology shows marked orthohyperkeratosis. Electron microscopy reveals abnormal keratohyalin granules with poorly formed intracellular lipid lamellae in the stratum coneum.[1]

Prenatal diagnosis with chorionic villus sampling (CVS) and amniotic fluid cells analysis is advised in women with previous affected baby. Antenatal 3D USG scan would reveal abnormal facial features with ectropion, eclabium, short foot length, incurved toes, clenched fist, poor delineation of nostrils and polyhydramnios.[4]

Unamuno et al.[5] described 4 premature infants born to consanguineously married couple. The infants were covered within a horny shell, similar to armor, with deep creases and large polygonal plates, rigid, semiflexed limbs.

Oliver Hart, a Charleston pastor, in his diary, described the first affected baby who survived for 2 days, in the year 1750.[1] Aggarwal *et al*.[6] reported two neonates of Indian origin with harlequin ichthyosis. The parents were found to have novel mutations in ABCA12 gene after neonatal demise.

We report this case for its classical presentation and for its rarity and conclude that the disease can be diagnosed prenatally by a simple ultrasound, amniocentesis and chorionic villus biopsy. The occurrence of the disease in future pregnancies can be prevented by adequate genetic counselling.

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