CASE REPORT

Prenatal Diagonsis of Harlequin Icthyosis

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ABSTRACT

Harlequin ichthyosis is a very rare congenital disorder. This is the most fatal form of autosomal recessive congenital ichthyosis. It is characterized by very thick keratin layer of skin, flattened ears, fish mouth appearance of the eclabium and diffuse plate like hexagonal scales (similar to the costume of the comic character Archetypal Harlequin. The affected babies usually cannot even survive first few days of life. Fortunately, this condition can be detected by the ultrasonologist during prenatal ultrasound examination.

Our aim is to contribute to the knowledge pool which could help our peer group of radiologists to get familiarize with the findings in order to increase the chances of diagnosing this condition prenatally.

Key words: Ichthyosis; Antenatal ultrasound; Autosomal recessive disorder; Fish mouth.

Introduction

Harlequin ichthyosis is a very rare disorder. This is the most fatal form of autosomal recessive congenital ichthyosis (1). It is characterized by very thick keratin layer of skin, flattened ears, fish mouth appearance of the eclabium and diffuse plate like hexagonal scales (similar to the costume of the comic character Archetypal Harlequin (2). The affected babies usually cannot even survive first few days of life (3).

Our aim is to contribute to the knowledge pool which could help our peer group of radiologists to get familiarize with the findings in order to increase the chances of diagnosing this condition prenatally.

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Case report

A 26 yr. old primigravida came to our hospital for her first antenatal scan at 25 weeks of gestation. The ultrasound showed a single live intrauterine fetus andsonological findings of the fetus were irregularity of skin surface, thickened fetal abdominal wall and thickness scalp,symmetric swellings infront of orbits with swollen eyelids, swollen and everted lips (eclabium) giving rise to fish mouth appearance. The rest of the fetal anatomy was normal.

With these findings the patient was referred to a multidisciplinary team comprising of neonatologist, obstetrician andgeneticist who upon confirming the diagnosis of Harlequin ichthyosis counseled parents for termination of pregnancy in view of poor prognosis.

Post termination, the postnatal findings were consistent with

the Harlequins ichthyosis. The skin was fissured and thick, Ectropion, eclabium were well appreciated, swollen lips werepresent and limb movements were restricted.However, the baby died within few hours due to respiratory distress.

Discussion

Harlequinichthyosis is a very rare congenital ichthyosis with an incidence of 1 in 3, 00,000 of live births (3). First clinical case was documented in 1750 by Reverend Oliver Hart with similar findings. First case of prenatal diagnosis of Harlequins ichthyosis was reported in 1983 by Blanchet-Bardon et al based on fetal skin biopsies under fetoscopy. The first case of prenatal sonographic diagnosis of Harlequins ichthyosis was reported by Mihalko et al in 1989 (4).

Mutation in the ABCA12 gene encoding the adenosine triphosphate binding cassette transporter results in Harlequins ichthyosis. Sometimes, mutations in ABCA12 gene cause a deficiency of this epidermal lipid transporter. As a consequence, lamellar bodies are not properly formed and essential epidermal lipids (e.g., glucosylceramide) are abnormally processed and incompletely (or not) secreted in the intercellular spaces. These changes prevent the formation of lipid bi-layers in the stratum corneum and result in hyperkeratosis and abnormal barrier function (5).Moreover, ABCA12 deficiency impairs the transport of proteolytic enzymes like kallikrein proteases that are required for normal desquamation of the epidermis, thus leading to the massive build-up of stratum corneum in harlequin ichthyosis (1). The inheritance is autosomal recessive (3).

The clinical features of Harlequins ichthyosis include characteristic appearance of thick, shiny, white hyperkeratotic plates with deep erythematous diamond shaped cracks. Abnormal facies is due to thick and tight pulled up skin causing ectropion, eclabium, hypo plastic flat nose and rudimentary ear appendages. Massive skin thickening results in flexion contractures in upper and lower limbs leading to restricted mobility and a "coat of armour" appearance (3, 6 and7). Clenched fists and incurved toes are also present. Late phenotypic expression of this condition may lead to delayed or misdiagnosis on prenatal scans.

This condition is associated with preterm birth. Affected neonates usually not survive beyond first few days of life (3).

The known methods for diagnosis of Harlequins include fetal skin biopsy which is invasive and was used earlier only for at risk cases (2, 5). DNA analysis via amniocentesis and chorionic villous sampling in cases with positive family history for Harlequins icthyosis help in the prenatal diagnosis. Recently there is an increase in the number of prenatal sonographic diagnosis of Harlequins icthyosis.

Harlequin icthyosis is associated with high fatality rates (44%). With the improved modern medical care there are chances for increasing the survival rates among the babies affected with Harlequin icthyosis. Moist and hygiene environment should be provided to prevent skin dryness, dehydration and infections. Appropriate treatment for the infections is a big challenge. Further treatment includes keratolytic agents for thinning of stratum corneum, lubrication of cornea in cases of ectropion and cautious use of retinoids

A survival rate of 56% has been reported and is expected to further increase with improved neonatal intensive care and better treatment options such as early topical and systemic retinoids (8).In a study 25 cases out of 45 cases of Harlequins icthyosis survived with age ranging from 10months to 25years whereas 20 deaths occurred from day 1 to 52 either due to respiratory distress or sepsis.

Genetic counseling plays a major role as this condition is having autosomal recessive inheritance pattern. Carrier testing and prenatal testing should be carried out for pregnancies at risk if autosomal recessive congenital icthyosis related pathogenic variants have been identified in the family.

Conclusion

Harlequin icthyosis is a very rare but most fatal form of autosomal recessive congenital icthyosis. Our aim is to contribute to the knowledge pool which could help our peer group of radiologists to get familiarize with the findings of Harlequin Icthyosis in order to increase the chances of diagnosing this condition prenatally by ultra-sonography.

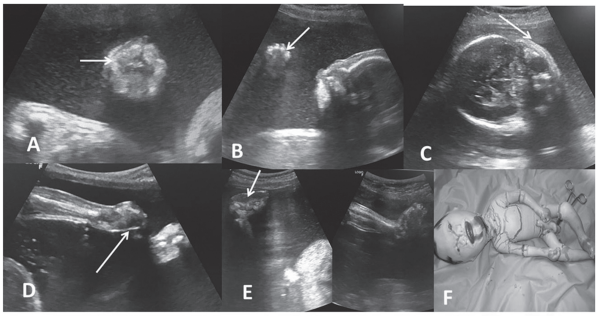

Fig. 1:

Ultrasound of fetus showing fish mouth appearance of lips(A),hypo plastic fingers and toes (B,D and E),thickened scalp (C) and thickened skin (D and E).Post natal image showing thickened and fissured skin ,swollen lips, hypo plastic hands and feet with clenched fist

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