**Prenatal Diagnosis of Harlequin Ichthyosis: Report of a Case**

Harlequin Ichthyosis

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Abstract
Harlequin ichthyosis (HI) - the most severe form of keratinizing disorders, often lethal in the neonatal period - is characterized by a profound thickening of the keratin skin layer, a dense armor-like scale that covers the body, and contraction abnormalities of the eyes, ears, and mouth. Here, we report a recurrent case of fetal HI and its prenatal ultrasonographic diagnosis in a Turkish consanguine couple.

Keywords
Ichthyosis; Prenatal Diagnosis; Prenatal Ultrasonography; Consanguinity

**Özet**
Sıklıkla neonatal döneminde ölümle sonuçlanan ve keratinizasyon bozukluklarının en ciddi formu olarak kabul edilen Harlequin iktiyozisi (HI), cildin keratin tabakasında derin yarıklar, vücudu zırh gibi kaplayan yoğun bir kabuk ve gözü, kulağı ve ağzı etkileyen kontraksiyon anormallikleriyle karakterizedir. Bu olgu sunumunda, akraba olan bir Türk çiftte tekrarlayan fetal HI ve prenatal ultrasonografik tanısı sunulmaktadır.

Anahtar Kelimeler
Iktiyozis; Prenatal Tanı; Prenatal Ultrasonografi; Akraba Evliliği

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Introduction
Harlequin ichthyosis (HI) is a severe disorder of keratinization caused by mutations in the ABCA12 gene with autosomal recessive inheritance [1]. The mutations lead to defective lipid transportation which negatively affects the correct development and function of the skin [2]. The characteristic clinical features of HI include thick, plate-like scales over the entire body with ectropion, eclabium and flattened ears [3]. The overall survival rate of this severe disorder is 56% [4]. Retinoids (etretinate, acitretin) are the major drugs that are generally preferred in postnatal management of HI [5]. Today, with the advents in technology, the prenatal diagnosis of this entity is possible. Here, we report the prenatal ultrasonographic features and diagnosis of a case with HI.

Case Report
A 23-year-old gravida 2 para 1 woman, at the 26th week of gestation, was referred to our perinatology unit for second opinion ultrasound (US). The couple was third degree consanguine and their first baby died on the fifth day of life, with the diagnosis of HI. Her personal and family history was otherwise unremarkable. In the present pregnancy, she did not report any medication use, had no history of fever (with or without rash), ionizing radiation exposure during the first trimester. First trimester screening for aneuploidy revealed a risk of 1:1818 for Down syndrome. Her routine pregnancy follow-up was eventless but she did not have a second trimester ultrasonographic examination for abnormality screening.

On 2-dimensional (2D), 3-dimensional (3D) and 4-dimensional (4D) US, polyhydramnios, intrauterine fetal growth retardation (EFW below the 10th percentile), facial dysmorphism with distortion of the lips (eclabion), ectropion - conjunctival protrusion associated with severe chemosis, skin fissures, short digits, flat nose, severe edema on the dorsal surfaces of hands and feet were detected. These findings were considered as sonographic features of HI. (Figure 1-5). After proper counselling about the postnatal course of the disease and the risks of amniocentesis,
A male infant with HI (birth weight, 2130 gr) was delivered by cesarean section for breech presentation and preterm labor following premature rupture of the fetal membranes at 32 weeks of gestation. The infant manifested malformations, which were detected on antenatal US and additionally had poorly developed ears (Figure 6, Figure 7). He was hospitalized at the intensive care unit for 20 days and received regular application of emollients. The baby is now alive and 12 months old, receiving physiotherapy for extremities, routine pediatric and dermatologic follow-up and preventive care for infections and dehydration.

Discussion

HI is an overwhelming disorder and the phenotypical appearance of the neonate is devastating for both parents and health care providers. Therefore, early prenatal diagnosis of this disorder is particularly important. Although it was previously reported that the inheritance of HI is autosomal recessive, in a large number of cases, the inheritance pattern cannot be ascertained, and the disorder could be due to a new dominant mutation [6]. Unfortunately, as in our case, autosomal recessively inherited disorders are relatively common probably secondary to high percentage of related marriages in Turkey.

To date, various ABCA12 mutations have been reported in HI patients [7]. Although some attempts were made to use DNA-based analysis for earlier (i.e., first trimester) prenatal testing [6], US and fetoscopic- or ultrasound-guided fetal skin biopsies are generally preferred for prenatal diagnosis. With the widely usage of 3D and 4D ultrasound, the characteristic suggestive features of HI as eclabion, ectropion, rudimentary ears, flexion contractures at the knees, and dense floating particles in the amniotic fluid, are reported to be detected with higher frequency [8-11]. Moreover, some promising therapeutic interventions based on targeted molecular therapy and gene therapy strategies are also defined [12].

In conclusion, prenatal diagnosis was relatively straightforward in our case due to recurrence, enabling targeted US. The US markers for HI should be kept in mind, particularly for early and accurate antenatal diagnosis of this condition.

Competing interests

The authors declare that they have no competing interests.

References


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