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Harlequin Ichthyosis: Case Report of a Rare Type of Ichthyosis

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Authors' contributions

This work was carried out in collaboration between all authors. Author AIG designed the study, author AT wrote the first draft of the manuscript and corresponding author, author ASK managed the literature searches, author AY revised article critically. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Aims: The purpose of this study is to present a case of Harlequin fetus, which is extremely rare.
Presentation of Case: A 27-year-old woman, gravida 3 para 1, was referred to the clinic with a diagnosis of preterm premature rupture of membranes. Upon ultrasound examination, a fetus with oligohydramnios at 30 weeks of pregnancy was determined. Fetal cardiac activity was present. The fetal nose and ears could not be visualized. The fetal mouth was opened wide and the lips were invisible. The wrists of the upper extremities were edematous. A cesarean section was performed, and a female fetus weighing 1140 g, 44 cm in length, and with *1st* and *5th* minutes Apgar scores of 6–8 was delivered. The fetal body was covered with dense keratin plaques, her eyes were in ectropion, and her nose and ears were also covered by thick keratin plaques. Eclabium lips, edematous wrists on the extremities, and the hands and feet in flexion were observed. The fetus died 24 hours later in the neonatal intensive care unit. The mother said that her second baby had the same conditions and died on postpartum day one.
Discussion and Conclusion: Harlequin ichthyosis is extremely rare and is a severe congenital

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anomaly that has autosomal recessive inheritance patterns. Prenatal diagnosis can be based on the ultrasound findings and parents' family history; this can contribute to our understanding of the disease and progress of pregnancy.

Keywords: Harlequin fetus; Ichthyosis; prenatal diagnosis.

1. INTRODUCTION

Ichthyoses are disorders of cornification that are characterized clinically by patterns of scaling and histopathologically by hyperkeratosis. The clinical types of ichthyosis depend on the mode of inheritance, as well as on the clinical and anatomic/pathological data [1]. Ichthyosis can be classified into one of three types: true ichthyosis, ichthyosiform states, and epidermolytic hyperkeratosis. There are several subtypes in each group. True ichthyosis includes the autosomal dominant, autosomal recessive, and X-linked recessive types.

Harlequin fetus (Harlequin ichthyosis) is one of the congenital forms of autosomal recessive inheritance ichthyosis that has an incidence rate of approximately 1 in 300,000 births [2]. This anomaly was first described by Oliver Hart in 1750. It had also been called ichthyosis intrauterina, keratosis diffusa fetalis, congenital diffuse malignant keratoma, malignant keratosis, and alligator baby. It is the most severe form of congenital ichthyosis. Clinical findings of the disease include thick and keratinized skin, ectropion, eclabium, flattened or undeveloped ears and nose, and different types of extremity anomalies. In general, these fetuses die due to prematurity, respiratory compromise, infection, hypothermia, and dehydration [3]. In the current case report, we presented a rare case of recurrent Harlequin ichthyosis in a 27-year-old female.

2. PRESENTATION OF CASE

In our case, a 27-year-old woman, gravida 3 para 1, had been referred to the emergency services of Dicle University with a diagnosis of repeated cesarean section and preterm premature rupture of membranes. Her physical examination was unremarkable. In the digital vaginal examination, the collum was 2.5 cm dilated, the effacement was 30%, and the amniotic fluid was actively leaking. The ultrasound showed a live fetus at 30 weeks with severe oligohydramnios. The mouth of the fetus was opened, the lips were oval and short, and the nose and ears could not be visualized. The wrists of the extremities were edematous. The right ankle was especially like a ball, and we suspected it was from pes equinovarus. From the history of the patient, we learned that in her second pregnancy she had similar findings, had no prenatal diagnosis, and had a cesarean delivery because of fetal distress. The baby had the same appearances and died one day later. There was a close kinship between parents (first cousins by marriage). In this pregnancy, she had monthly prenatal controls, and no pathologies were determined. We recommended that the patient have a vaginal delivery, but she rejected that suggestion. We then performed the cesarean section and delivered a female fetus weighing 1140 g, 44 cm in length, and Apgar scores at the 1st and 5th minutes were measured as 6 and 8, respectively. The body of the newborn was covered by thick and widespread keratin layers and, between these layers, there were erythematous fissures. There were ectropion and eclabium appearances. All of the extremities were swollen, edematous, and erythematous (Fig. 1). After the birth, the pediatrician evaluated the baby and transferred the baby to the neonatal intensive care unit (NICU).

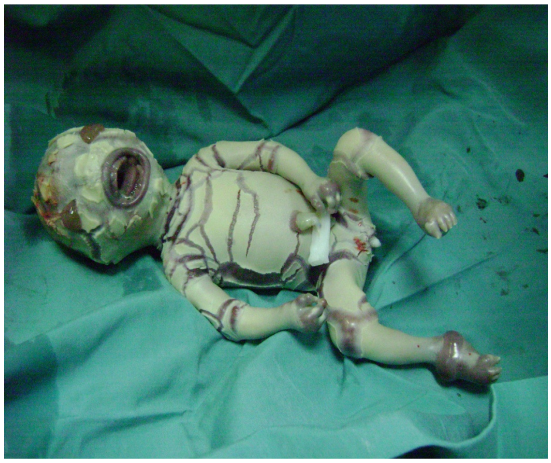

Fig. 1. The infant with thick and widespread keratine layers, open wide mouth, abnormal eyes, and flatted nose and ears

In the NICU, the patient was placed in a humidified incubator, started on IV antibiotics,

fluids, and electrolytes, and endotracheal surfactant and liquid paraffin were applied to the whole cutaneous surface. Narcotic analgesics were also given as needed to encourage normal breathing, but the baby died 24 hours later due to respiratory distress. Before discharge, we provided psychological support to the mother, and genetic counseling was recommended to the family.

3. DISCUSSION

Harlequin fetus is an extremely rare and fatal congenital anomaly. The data about this anomaly are so limited, and almost all of the data stem from case reports. The condition presents itself at birth with coarse and large plate-like scales with deep fissures, severe ectropion, eclabium, contractures of the digits, and flattening of the ears and nose. Patients are usually born prematurely and do not have any brain or internal organ abnormalities. Pain from the fissures can prevent patients from taking deep breaths, and respiratory infections can be a major cause of death in the neonatal period [4]. Our patient was also born prematurely, and we applied endotracheal surfactant and administered narcotic analgesics to reduce the pain and facilitate normal breathing. Despite these applications, the newborn was lost 24 hours postpartum due to respiratory distress.

Studies on the pathogenesis of this disease are new. It has been found that Harlequin ichthyosis is caused by mutations in the ABCA12 alleles. Akiyama et al. [3] and Yanagi et al. [5] expressed that the inheritance of this anomaly is autosomal recessive, and there are defects in both ABCA12. The product of this gene is a keratinocyte lipid transporter associated with lamellar granule formation. Loss of normal ABCA12 function leads to defective lipid transport by the lamellar granules in the upper epidermis, as well as to malformation of the stratum corneum lipid layers. It has also been reported that there are seven genes known to be associated with other autosomal recessive congenital ichthyosis [6]. We could not evaluate our case genetically; however, the similarity of the history of the previous pregnancy with the current one supports the inheritance pattern.

In the literature, ultrasonographic fetal skin biopsies investigated via electronic microscope are related to prenatal diagnosis [7]. Kudla and Timmerman reported some of the pathologic features observed during the prenatal ultrasound screening, including polyhydramnios, fixed flexion of the extremities, short digits, a flat nose, bilateral clubfeet, clenched hands, a short neck, a flat facial profile, thick lips, eclabium, open eyes, ectropion, cataracts, a constantly open mouth, micrognathia, hypoplasia of the ears, choroid plexus cysts, and a short umbilical cord [8]. Although our case had monthly prenatal care and had a similar previous pregnancy history, she had not been diagnosed and was referred to an advanced health center. We made the diagnosis just before labor, which was similar to that previously reported by Kudla and Timmerman at the current clinic at 30 weeks of gestation.

There is not a definitive treatment for this disease. However, topical steroids, oral vitamin A, locally administered liquid paraffin, and some lactic acid solutions are discussed as treatment options [9]. Harlequin fetuses usually die soon after birth. The survival rate increases to more than 50% with an early prescription of oral retinoids. The quality of life of these patients may be improved with supportive care [10]. In a recent case report, the authors reported that a 7-year-old boy with Harlequin ichthyosis is still alive following intensive care and with supportive treatment [11].

4. CONCLUSION

Harlequin ichthyosis is an autosomal recessive and fatal disease. During diagnosis, the most important points include the patient's history and ultrasonographic evaluation. Although there is no definitive treatment for this disease, supportive medical treatment may prolong the survival of these patients.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

Not applicable.

COMPETING INTEREST

Authors have declared that no competing interests exist.

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