Harlequin fetus: a rare presentation

* Quddush R[1] Hasan MJ[2] ,Raushan A[3] Rahman M[4] , Rayen J[5] Sattar S[6] , Khan MK[7], Islam N[8]

Abstract

Harlequin fetus is the most severe form of congenital ichthyosis. Although autosomal recessive pattern of inheritance is seen mostly but a new autosomal dominant mutation may possibly be responsible. When diagnosed in a newborn, two forms can be identified: collodion baby and its most severe form, harlequin fetus or maligna keratoma. In both cases, clinical manifestations are thick and hard skin with deep splits The disorder has an ominous prognosis since the neonates usually die in the first hours or days of life. A case of harlequin fetus born to consanguineous parents is reported. It had typical skin manifestations. Supportive treatment was offered but it died on fourth hour of life.

CBMJ 2012 July: Vol 01 No 02: P: 59-62

Key words: *Harlequin fetus, congenital ichthyosis, collodion baby, maligna keratoma*

Introduction

Harlequin type ichthyosis is a rare genetic skin disorder characterized by massive thick skin plates that usually produce distorted field features and often deformities in other parts of the body[1] .

It was first described by Hart in 1750 on the basis of familial occurrences, the mode of inheritance is autosomal recessive[1,2]. Since then it has been referred to as "fetal ichthyosis", "ichthyosis intrauterina", "keratosis diffusa fetalis", "congenital diffuse maligna keratoma", "malignant keratosis", "alligator baby"[3].

It is usually fatal in the first few days of life but the development of one such fetus to age of 30 months has been reported[2,3,4] .

At birth, it is characterized by armour-like hyperkeratotic plates covering the entire body, ectropion, eclabium, poorly developed ears and contractures of hands and feet. Nails and hair may be absent and joint mobility is restricted[5,6,7].

Case history

A male baby was born full term by caesarian section following a breech presentation with 1 and 5 min Apgar score 5 and 6 in a local clinic in Mymensingh of Bangladesh presented with respiratory distress and abnormal appearance just after birth. No antenatal check was done, Tetanus toxoid was not given, having h/o rash at first trimester. The couple had lost one offspring in neonatal period with the same disorder. The pregnancy of the 20 years old mother was safe till she went into labor. She didn't take any medication during pregnancy period.

1. ** Dr. ASM Rushul Quddush*
Assistant Professor, Department of Pediatric, Community Based Medical College Bangladesh.
2. *Dr. Mahmud Javed Hasan*
Assistant Professor, Department of Nephrology, Community Based Medical College Bangladesh.
3. *Dr. Afsana Rowshan*
Assistant Professor, Department of OBG, Mymensingh Medical College Bangladesh.
4. *Dr. Masudar Rahman*
Associate Professor, Department of Radiology, Community Based Medical College Bangladesh.
5. *Dr. Junna Rayan*
Assistant Professor, Department of OBG, Addin Medical College Bangladesh.
6. *Dr. Shamima Sattar*
Lecturer ,Department of Pharmacology, Community Based Medical College Bangladesh.
7. *Professor Dr. Mahbul Ul Karim Khan*
Department of Pediatric, Community Based Medical College Bangladesh.
8. *Professor Dr. Md Nazrul Islam*
Department of Pediatric, Community Based Medical College Bangladesh.

** Address of Correspondence :*
E-mail: ruhulquddush@gmail.com
Mobile: +8801712123225.

On examination the baby was dyspneic, clinical appearance was striking like- skin was hard, thickened, waxy and yellowish in color, it was split irregularly to reveal erythematous moist fissures, the ears were crumpled and hypoplastic, there was severe ectropion and eclabium, the nose was flattened, hair was scanty, the nails were hypoplastic (Figure 1).

Figure 1 Thick armour-like scales with fissuring, areas of erythema, ectropion and eclabium, the ears crumpled and hypoplastic.

The baby's cry was abnormal and unable to suck effectively due to persistent opening of mouth. There was small penis, undescended testes and a rudimentary scrotum. The limbs were edematous with small hands and feet having circumferential constriction bands around & the nails were hypoplasic. Vital signs-respiratory rate 68/min, heart rate-154/min, activity was minimal, primitive reflexes (Moro, rooting, sucking) couldn't be elicited.

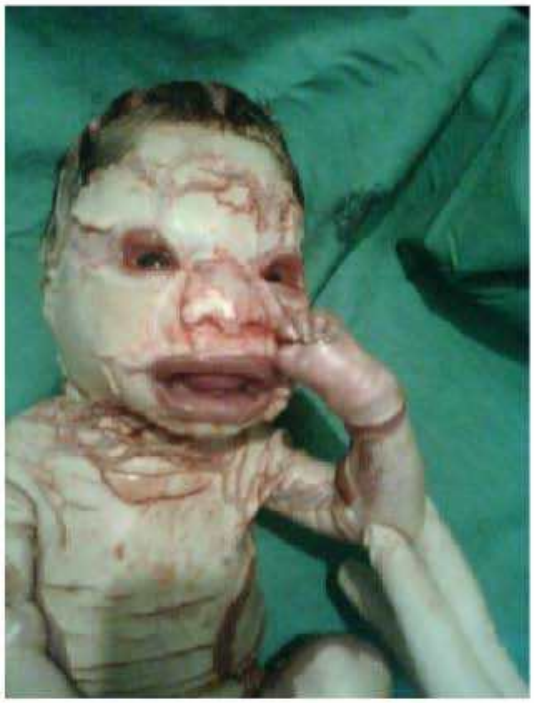

Figure 2 : Limbs edematous with small hands and feet, circumferential constriction bands around and the nails were hypoplasic.

The father was counseled about the referral of the patient in facility based tertiary level hospital but he did not agree because of some superstitions and also the grave condition of the patient. Immediately after resuscitation of the patient an umbilical venous line was set up as peripheral venous access was difficult. An extra 25% allowance was provided for fluid and calorie requirements, antibiotics were commenced in order to prevent infection, vaseline containing local antiseptics were applied topically. Liquid paraffin was applied on the skin locally. Ectropion was covered with eye pads and antibiotic ointment was applied.

After all resuscitation and management as much as possible in that settings some clinical symptoms and signs such as grunting, respiratory distress appeared spontaneously and ultimately the baby died within 3 hours of his life due to cardio respiratory failure and the parents did not allow for any pathologic biopsy, autopsy and further investigations.

This Harlequin Ichthyosis possibly the first case in Bangladesh is to be reported.

Discussion

Harlequin fetus is a rare disorder with the incidence of 1: 300,000 births[8]. The first report is from the diary of Oliver Hart, of Charleston, South Carolina who described these features in 1750[6] .

These children are at great risk during the neonatal period and often die shortly after birth from the undernourishment caused by the rigidity of the lips, and underventilation and pneumonia because of respiratory distress. Abnormal water loss through the skin and poor temperature regulation lead to risk for infection beginning in the skin, but at the same time, because of poor temperature regulation, do not show the usual signs of infection. The taut skin may restrict normal respiration[5].

More than 100 cases have been reported. Neither racial or gender predilection is known[9]. This disorder has been reported from different ethnic groups. Mutations in ABCA12 gene underlie the severe congenital ichthyosis. ABCA12 gene may play a critical role in the formation of lamellar granules and the discharge of lipids into the intercellular spaces and its mutation causes different lipid transport that significantly impacted normal development of the skin barrier. This finding paves the way for early prenatal diagnosis[10,11,12].

Consanguinity and family history of the same and other skin disorders are hallmark of the diagnosis. Harlequin babies with family history of psoriasis, juvenile rheumatoid arthritis and hypothyroidism have been reported[7]. There have been reports of several families with siblings affected with harlequin ichthyosis[13]. Twins affected by harlequin ichthyosis have also been reported[6]. Occurrence of consanguinity in same parents and of harlequin icthyosis in siblings suggest an autosomal recessive mode of inheritance[14,15].

However, consanguinity has not been observed in a large number of cases which makes it difficult to explain as an autosomal recessive mode of inheritance[16]. A new dominant mutation may possibly be responsible for the disorder.

Clinically, harlequin fetus is characterized by severely thickened skin with large, shiny plates of hyperkeratotic scale, severe ectropion, small and rudimentary pinnae, eclabium and nasal hypoplasia. Flexion contractures of limbs with circumferential constriction bands, hypoplasia of the fingers, toe- and fingernails have been reported. Temperature dysregulation, dehydration, respiratory compromise and central nervous system depression are the known complications of this disorder[17].

Diagnosis is essentially clinical, supplemented by histological findings[18,19]. Prenatal diagnosis has been accomplished by fetal biopsy and sonographic finding at 16-21 weeks of gestational age.

In 1994 some studies on amniocentesis between 16-21 week of gestational age identified specific histological changes such keratinized and with increased abnormal growth and fat drop in affected fetus [20].

Treatment includes adequate humidification use of emollients, adequate hydration and maintenance of temperature, prevention of infection. Clinical improvement can be induced by oral retinoid but the prognosis remain grave[19].

Neonatal morbidity and mortality may be due to cutaeneous infection aspiration, (preumonia squamous material) or hypernatremic dehydration from excessive transcutaneous fluid losses due to increased skin permeability.

Prognosis is poor and survival of affected infants beyond the first year of life is uncommon. However the longest survival period reported was up to 2.5 years in a child who was treated with etretinate.

Conclusion

Harlequin fetus is a rare manifestation of severe congenital icthyosis. It is usually fatal in first few days of life. The above case born of a consanguineous parents died within 3 hours of life. Prenatal diagnosis has been accomplished by amniotic fluid samples obtained as early as 17 weeks' gestation. And also ultrasonography and the electron microscopic examination of the fetal skin biopsy permit the possibility of prenatal diagnosis of this disorder to avoid the graved consequences. Prognosis is poor and fulminant sepsis remains the most common cause of death in this infant.

References

1. *Vijayaragavan, S., S. Vishnu Bhat, S. Srinivasan R.K. Bhatnagar and A. Venugopal, 1990. Harlequin fetus with polydactyly and renal dysplasia (Brief reoport). Indian Pediatrics, 27: 874-876.*
2. *Watson, W.J. and L.M. Mabee Jr, 1995. Prenatal diagnosis of severe congenital ichthyosis (Harlequin fetus) by ultrasonography. J. Ultrasound Med., 14: 241-243.*
3. *Prasad, RS., R.K. Pejaver, A. Hassana, S.A.L. Dusari and M.A. Wooldridge, 1994. Management and follow-up of harlequin siblings. Br. J. Dermatol., 130: 650-653.*
4. *Singalavanija, S., V. Sangtawesin, S. Horpoapan and V. Ratrisawadi, 1998. Harlequin baby: A case report. J. Med. Assoc. Thai., 81: 365-370.*
5. *Darmstadt GL, Sidbury R. The skin. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson Textbook of Pediatrics, 17th edn. Philadelphia: WB Saunders; 2004. p. 2153-2250.*
6. *Dolunay G, Ilknur K, Merve B. A case of harlequin fetus with psoriasis in his family. J Pediatr and Neonatol 2001; 2: 1-7.*
7. *Chan YC, Tay YK, Tan LK et al. Harlequin ichthyosis in association with hypothyroidism and juvenile rheumatoid arthritis. Pediatr Dermatol 2003; 20: 421-6.*
8. *Rook A, Wilkinson D, Ebling F. Textbook of Dermatology. Blacwell: Oxford University press, 1972;1027-1039.*
9. *Sheila AU, Julitte S, Abby Van et al. Ichthyosis fetalis [online] 2005[cited 2005 Sep 27]. Available from:URL:http://www.emedicine.com/derm/topic192.htm.*
10. *Hovnanian A. Harliquen ichthyosis unmasked: a defect in lipid transport. J Clin Invest 2005; 115: 1708-10.*
11. *Kelsell DP, Norgett EE, Unsworth H et al. Mutations in ABCA12 underlie the severe skin disease harlequin ichthyosis. Am J Hum Genet 2005; 76: 794-803.*
12. *Akiyama M, Sugiyama-Nakagiri Y, Sakai K et al. Mutations in lipid transporter ABCA12 in harlequin ichthyosis and functional recovery by corrective gene transfer. J Clin Invest 2005; 115: 1777-84.*
13. *Multani AS, Sheth FJ, Shah VC, Chinoy NJ, Pathak S. Three siblings with harlequin ichthyosis in an Indian family. Early Human Dev 1996; 19: 229-33.*
14. *Malik NA, Ghauri AQ. Harlequin fetus. J Coll Physicians Surg Pak 2004; 14: 294-5.*
15. *Lawlor F. Progress of Harlequin fetus to nonbullous ichthyosiform erythroderma. Pediatrics 1988;82:870-873.*
16. *Dale BA, Kam E. Harlequin Ichthyosis, variability in expression and hypothesis for disease mechanism. Arch Dermatol 1993;129:1471-1477.*
17. *Suzimori K, Kanzaki T. Prenatal diagnosis of Harlequin Ichthyosis by fetal skin biopsy: Report of two cases. Prenatal Diagn 1991;141:451-457.*
18. *Soares, M.A. and U.L. Wagholikar, 1989. Harlequin ichthyosis. Indian J. Dermatol. Venereol. Leprol., 55: 61-63.*
19. *Baden, H.P., J. Kubilus, K. Rosenbaum and A. Fletcher, 1982. Keratinization in the harlequin fetus. Arch. Dermatol., 118: 14-18.*
20. *Elias, S., M. Mazur, R. Sabbagha, N.B. Esterly and J.L. Simpson, 1980. Prenatal diagnosis of harlequin ichthyosis. Clin. Genet., 17: 275-280.*