



Case Report

A Rare Case of Harlequin Ichthyosis Born To Epileptic Mother

Arun Kumar S Bilodi^{1*}, Vijaya Kumari², Prakash V Jadhav³

¹Professor & HOD, Department of Anatomy, Velammal Medical College Hospital, Velammal Village, Madurai

²Associate Professor of Biochemistry, ESI Institute of Medical Sciences & Research Center, Rajajinagar, Bangalore

³Ex Assistant professor of Pathology, Mahatma Gandhi Medical College, Pilliyarkuppam, Puducherry

*Correspondence Email: drbilodi@yahoo.com

Received: 29/01/2013

Revised: 27/02/2013

Accepted: 04/03/2013

ABSTRACT

Aim: To report a rare case of Harlequin Ichthyosis born to Epileptic mother

Place of Study: This case was studied in the Teaching Hospital Raja Rajeswari Medical College, Bangalore and in the department of Anatomy at Raja Rajeswari Medical College, Bangalore. Case examined in ICU at Raja Rajeswari Medical College, Teaching Hospital and after death of the child, case was studied in the Department of Anatomy of Raja Rajeswari Medical College, Bangalore, Karnataka.

Period of Study: During the year 2007-2008, this Harlequin baby was examined and studied.

Case Study: A Harlequin Baby that was born in the Teaching Hospital of Raja Rajeswari Medical College constituted the material for the present study..Harlequin baby syndrome is one of the severe & rare neonatal ichthyosis seen in new borns. Here we present one such anomaly observed in a new born male baby who had generalized hyperkeratosis of skin with cracks and fissures. The skin was thickened, rigid and dry. Baby also had ectropion, Eclabium, flattened nose and ears, a thick and short fingers and poorly formed scrotal sacs. No microcephaly was seen. Stature was normal. Dissection was done on the baby with written consent that showed hyperkeratosis of epidermis with normal internal organs. This child was second born to second degree consanguineous couples.

Histopathology Reports showed Massive Hyperkeratosis stratum Corneum 20-30 times than that of Stratum Malphiji.

KEY WORDS: Neonatal ichthyosis, Harlequin ichthyosis, Ectropion, Eclabium, Hyperkeratosis.

INTRODUCTION

Excessive keratinization of skin is known as ichthyosis. It is a group of hereditary disorder inherited as autosomal recessive trait usually inherited, but may also be X-linked. [1] In granular layer of healthy skin lipids from the cytosol is transferred into lamellar granules by lipid transporter, ABCA12. Then there will be fusion of lamellar granules with cell

membranes at interface of the granular layer- stratum corneum and contents will be discharged into intercellular lamellae. In skin of the Harlequin ichthyosis, there is absence of ABCA12 & there is prevention of transfer of lipids into lamellar granules. So lamellar granules become abnormal in shape or are reduced in number or absent. So there is reduction of exocytosis of lamellar granules. Vacuoles are formed containing

abnormal lipids in the cytoplasm of corneocytes. As a result there is remarkable thickening of stratum corneum which does not desquamate. [2] So Harlequin ichthyosis is a disorder of severe form of keratinization that occurs in the neonatal period which may be lethal. It involves of skin characterized by thickening of keratin layer of skin in the form of dense armor like scale all over the body resulting in contraction anomalies involving eyes (ectropion), ears, & mouth (lips-eclabium). [2] There is defective lipid transport is due to mutation in ABCA12 which has caused an impact on normal development of skin barrier. Secretion of lipid has been recovered after corrective of ABCA12 gene transfer into patient's keratinocytes. ABCA12 deficiency can be corrected by genes transfer in patients with keratinocytes for the restoration of normal glucosylceramide cell distribution & formation of lamellar granules. [3] First Harlequin fetus was described by Warring in 1750 in United States in the diary of Reverend Osler Hart. [4]

CASE REPORT

A twenty one years old female of a middle class family from Bangalore delivered normally a male baby in the labor ward of Raja Rajeswari Medical College Teaching Hospital, Mysore Road ,

Histopathological Studies: Showed Hyperkeratic Stratified Squamous Epithelium. The sub epidermal tissue showed prominent blood vessels and sparse mono nuclear cell infiltrations.

The stratum corneum was 20 -30 times thicker than stratum malphigii The stratum granulosum was significantly flattened. Epidermal areas showed Papilomatosis. The features are consistent with neonatal ichthyosis.

Bangalore with birth weight of 2kg Mother of the new born was known epileptic & she was on drugs but the name of the drugs & duration is not known. All her parameters were within limits. This was her second child, which was alive for one day and died on second day in the neonatal intensive care unit. The couple had a consanguineous marriage. There was no history of similar complaints in the past but there was history of death of the first male child due to imperforate anus.

Clinical Findings

On examination child has cracks & fissures all over the body with ectropion (eversion of eyelid) & eclabium (gaping of lips), flattening of ears and nose alopecia over the scalp, Short and thick contracted fingers All digits were in the attitude of flexion causing restrictions of movements associated with small and poorly developed scrotal sacs. There was no other anomaly seen in the body. With the written consent from parents and from the consent of head of department of obstetrics and gynecology and head of department of Anatomy, the body was dissected carefully to see any other anomalies. All the internal organs were normal. It was only the skin which was involved showing hyperkeratosis with sub epidermal tissue showing prominent blood vessels.

DISCUSSION

Harlequin type of ichthyosis are caused by several mutation in the ABCA 12 genes These are said to have lead to absence of ABCA 12 proteins or extremely small version of protein which cannot transport lipid properly. A functional loss of ABCA 12 proteins causes various problems in the development of epidermis before or after birth. These abnormalities of lipid transport prevent in the formation of skin as a effective barrier. As a result there is formation of thick hard scales which are

important characteristic features of Harlequin ichthyosis. [5]

Lipid processing in the skin is very important to protect the function of stratum corneum which is the outer layer of epidermis. [6] Lamellar granules which are lipid rich organelles present in the epidermal granular cells that derive lipid lamellae originate from trans-Golgi network. These lamellar granules contain cholesterol sulfate, phospho lipids sphingomyelin, and glucosylceramide which are polar lipids. These granules also transport many enzymes like proteases & their inhibitors & also play a role in the barrier permeability & desquamation process control. [7] Electron microscopy studies have revealed that there is absence of lamellar granules or there is abnormality in lamellar granules & there is also absence of inter cellular lamellae. [8] The defect in lipid processing enzymes have known to cause different types of ichthyosis. They are steroid sulfatase in X-linked recessive ichthyosis, [9] fatty aldehyde dehydrogenase in Sjogren-Lasson syndrome [10] Lipoxygenase-3&12R Lipoxygenase in autosomal-recessive congenital ichthyosis. [11]

A case of pre term Harlequin has been reported from the department of pediatrics in a female child, from Jaykaylon Hospital S.M.S. Hospital, Jaipur. This female child was 34 to 36 weeks size with 4-5 cms plaques separated by deep fissures. There was also eversion of eyelids known as Ectropion and round fish like mouth known as Eclabium and the skin showed the state of contractures in flexed position. There was also restriction of movements of all fingers. In spite of all supportive managements like hydration, emollients, orogastric feedings, this female child died on third day. [12]

Another case of harlequin baby was reported from Sialkot, Pakistan in a multiparous woman of low socioeconomic status. She delivered a female child

weighing 1.8kg with APGAR score 6/10 at CMH hospital Hyderabad, Pakistan. This female child also had deeply cracked fissures with eclabium boggy scalp, associated with cleft palate rudimentary nose, deformity of hand & feet died on 10th day. Child was 4th to her parents but other sibilings were normal. There was no history of any skin disorders, any ichthyosis, or neonatal deaths in the family. [13]

Incidence of neonatal ichthyosis is seen in 1 in 30,000 children. [14] Epileptic fits occur upto 49.2% in less than 36 weeks of pregnancy causing fetal morbidity and mortality. [15,16] In United States, magnesium Sulfate are given as prophylaxis for attack of seizure and also used as therapy for women with preeclampsia and eclampsia. [17]

Present Study

A Harlequin ichthyosis in a new born male child which later died on second day due to respiratory failure. This baby had plaques of skin all over the body with cracks & fissures. There was eclabium, ectropion, shortening of fingers with flattened nose & poorly developed scrotal sacs. Baby cried well on first day with shrill voice & there was restriction of movements of fingers & digits due to contractures. Dissection of the body showed normal internal organs. Only skin was involved. Biopsy of skin showed hyperkeratosis of skin. Mother of the new born was a known epileptic since many years & she was on antiepileptic drugs (name of drug not known). But mother did not have any convulsion during labor. Here neither the amniocentesis nor ultrasound done during antenatal period, but there was second degree of consanguinity. Her first child also died of imperforate anus. So it may be second degree of consanguinity & epilepsy may be the contributing factors for the development of anomalies in her children.

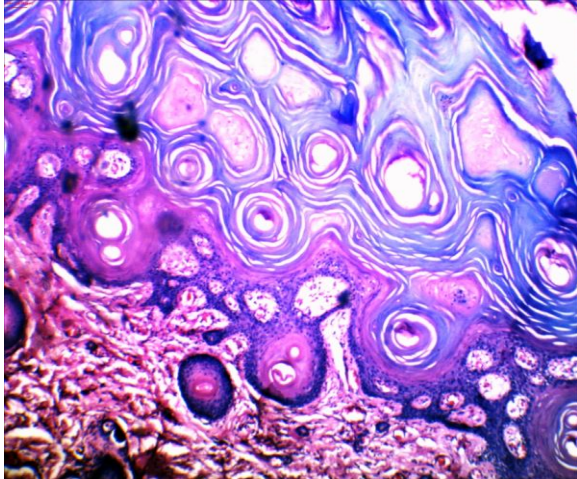


Fig. 1. Showing skin with massive hyperkeratosis .The stratum corneum is 20-30 times thicker than stratum malphigii. The stratum granulosum is significantly flattened. Epidermal areas show Papillomatosis .Features consistent with Neonatal ichthyosis.



Fig-2. Harlequin baby showing cracks, and fissures of skin present all over the body along with Eclabium (fish like round mouth) and ectropion (eversion of eyelids)

CONCLUSION

This study on Harlequin Ichthyosis gives awareness to public regarding effect of consanguineous marriages. This awareness can be done by educating people especially for mothers who have given birth to anomalous babies in rural population through volunteer organization, NGOs, health workers & department of community medicine. The agony of parents can be minimized by detecting anomalous babies by ultrasound or MR during antenatal period.

Anomaly cell can be constituted by the government both at state & central level like in other countries to detect, to treat and to control the incidences of anomalies by monitoring mothers and treating the anomalous babies. So this anomaly cell can bring down the rate of morbidity & mortality of anomalous babies. Hence this study on Harlequin Ichthyosis has been done and reported.

ACKNOWLEDGEMENTS

Our sincere thanks to

1) Medical Director of Raja Rajeswari Medical College, and Hospital, Bangalore, for giving

permission to examine the cases in our teaching hospital.

2) Medical Superintendent of Rajeswari Medical College Hospital, Bangalore also gave permission to examine the case in our teaching hospital.

3) Professor and Head of Department of Obstetrics and Gynecology and Anatomy of Raja Rajeswari Medical College ,and Hospital, Bangalore gave permission to examine this case in neonatal Intensive Care Unit where child was alive for one day .

4) Professor and Head of Department of Anatomy of Raja Rajeswari Medical College ,and Hospital, Bangalore gave permission to dissect the new born dead baby for the purpose of study.

5) Dr Anbalagan; Prof of Anatomy, Department of Anatomy, Mahatma Gandhi Medical College & Research Center, Pilliyarkuppam, Puducherry for assisting me.

REFERENCES

1. Sadler. T.W- Langman's Medical Embryology-11th edition- Lippincott Williams & Wilkins-South Asian,Wolters Kluwers India Pvt Ltd,New Delhi-P-346.
2. Alain Hovnian (2005)- Harlequin ichthyosis unmasked: a defect of lipid transport –Journal of clinical

- investigation;2005;115issue(7);1708-1710/ doi:10.1172/JCI25736.Published in Volume 115, Issue-7; (July 1, 2005)
3. Akiyama M et al .Mutation in lipid transfer ABCA12 In Harlequin Ichthyosis & functional recovery by the corrective gene transfer .J.Clin .Invest 2005,115:1777-1784- doi:10.1172/JC124834
 4. Warring J.J.Early mention of Harlequin fetus in America Am.J.Dis .Child 1932 .43:442.
 5. Kelsell D.P,Norgett.E.E,Unsworth.H, et al(2005):- Mutation in ABCA 12 underlie severe congenital skin disease Harlequin Ichthyosis-Am J Hum Genet 2005 76(5); 794-803.doi:10.1086/429844.PMC 1199369.PMID 15756637
 6. Madison K.C,.Barrier function of skin “la raison d etre” of the epidermis (review)-J.Invest Dermatol(2003):121:231-241.
 7. Elias PM,-The epidermal permeability barrier :from the early days at Horward to emerging concepts - J.Invest Dermatol 2004:122:xxxvi-xxxix.
 8. Milner,ME,O’Guin,WM,Holbrook,KA, Dale,BA;.Abnormal lamellar granules in harlequin ichthyosis,- J.Invest Dermato:1992:99:824-829..
 9. Webster,D,France,JT,Shapiro.LJ,Weiss. R: X linked Ichthyosis due to steroid sulphatase deficiency.Lancet 1978.1:70-72
 10. De Laurenzi,V,et al Sjogren –Lasson syndrome is caused by mutation in fatty aldehyde dehydrogenase gene .Nat.Genet ,1996,12;52-57.
 11. Jobard,F,et al Lipoxygenase - 3(ALOXE-3)& 12R Lipoxygenase (ALOX12B) are mutated in non bulbous congenital ichthyosiform erythroderma (NICE) linked to chromosome 17p13.1.Hum.Mol Genet 2002.11:107-113.
 12. Mukhopadhaya Sagori and Agarwal Ramesh (2006):Harlequin Ichthyosis – Indian Journal of Pediatrics ,Volume 73, April 2006: 351
 13. Naeem Raza,Asif Naseer(2005);- Herlequin baby –Pakistan Armed Forces Medical Journal(ISSN 0030 - 9648):March 2005 :Issue No-1:(5/11/2011),”Page numbers not given” (WWW.pafm.org/shows details.phpid=39...)
 14. Sheila,AU,Julie,P;Ichthyosis fetalis .An article in E. Medicine, Last updated 13,2003 .http://www.medicine.com
 15. Douglas.K.A,Redman.CWG(1994):Eclampsia in United Kingdom;BMJ:1395-1400.
 16. Siboi-BM-(1990):VIMaternal peronatal outcome in 254 consecutive cases -Am.J Obstet Gynaecol 1990 ;1049-55
 17. Andrew .C,Witlin,D.O.,Baha.M,Silai MD(1998)-Magnesium sulfate therapy in pre eclampsia and eclampsia:Journal of Obstret and Gynaecol:Vol:92:NO 5: 883-888.

How to cite this article: Bilodi AKS, Kumari V, Jadhav PV. A rare case of harlequin ichthyosis born to epileptic mother. Int J Health Sci Res. 2013;3(3):63-67.
