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Case Report

Jaundice in a baby with self-improving collodion ichthyosis and ALOX12B mutation- a challenging scenario

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ABSTRACT

Autosomal recessive congenital ichthyoses are a heterogeneous group of rare cornification diseases. Genetic mutations are responsible for the condition, with some causing a relatively milder phenotype such as 'self-improving collodion ichthyosis'. In most cases, affected babies are born with a thick parchment like membrane covering their body. These babies may have a problematic postnatal course, and are prone to complications. The authors present the report of a newborn collodion baby afflicted with ALOX12B mutation, who had a challenging post natal course. Difficulties in feeding, temperature control, hydration and electrolyte balance were encountered and required precise monitoring and formulation of an effective treatment strategy. Treatment of jaundice in the baby also presented a unique challenge, which was successfully managed.

Keywords: Collodion, Ichthyosis, Mutation, ALOX12B, Jaundice, ARCI, SICI, Autosomal recessive

INTRODUCTION

Autosomal recessive congenital ichthyoses (ARCI) are a rare group of heterogeneous non-syndromic, skin scaling disorders characterized by varying degrees of desquamation and erythema, and occur due to abnormal skin keratinization.[1] ARCI is diagnosed on the basis of skin findings at birth and in infancy.

Currently, nine genes are known to be associated with ARCI-TGM1, ALOXE3, ALOX12B, ABCA12, CYP4F22, CERS3, PNPLA1, LIPN and NIPAL4 (ICHTHYIN).[2] ARCI classically includes nonbullous congenital ichthyosiform erythroderma (NCIE), lamellar ichthyosis (LI), and harlequin ichthyosis (HI).[1] TGM-1 mutations account for 34%-55% of all ARCI and 90% or more of severe LI. ALOX gene mutations are responsible for an estimated 17% of individuals with ARCI, and are typically associated with NCIE or intermediate LI/NCIE phenotypes.[2]

In most cases, patients are born surrounded by a parchment-like membrane. Neonatal complications can occur in 45% of all collodion babies, leading to a mortality rate of ~11% in the first few weeks of life.[3] However, in about 10-25% of all cases, the membrane is shed without showing residual signs of ichthyosis-a condition known as "self-healing collodion baby"(SHCB).[4]

The term "self-improving collodion ichthyosis" (SICI) was proposed by Vahlquist et al, in lieu of SHCB ,who deemed it suitable for older children and adult patients who showed some remaining skin symptoms.[5] Bathing suit ichthyosis (BSI) and self-improving collodion

ichthyosis (SICI), thus, are 2 minor variants of ARCI. BSI is characterized by scaling of the skin in a bathing suit pattern, mainly limited to the trunk, whereas SICI is characterized by complete disappearance of the skin lesions.[6]

CASE REPORT

A male baby X, weighing 2.3 Kgs (25th centile) was born at 37 weeks gestation to south-Indian non consanguineous parents, where the mother was a primi gravida. The baby was delivered vaginally. APGAR scores at 1,5 and 10 minutes were 8, 9 and 9 respectively. Intrauterine growth retardation was observed with the head circumference being 34cms (25th centile) and length of 48cms (25th centile). The baby's posture was flexed. Limb movements were mildly restricted.

The baby was covered by a translucent parchment like membrane, appeared erythematous, and he also had features such as ectropion, small eyelids, thinned out eyebrows, sparse hair, wrinkled ears, eclabion, yellowish crusting in the nostrils and split skin predominantly on the flexures. Skin over the genitalia was also taut. All newborn reflexes were present. A nasogastric tube was inserted in anticipation of feeding difficulties.

Figure 1: (A) Neonate born with a collodion membrane. Ectropion, eclabion, wrinkled ears are seen. (B) Cling wrap applied on the baby helps in reducing insensible water loss.

The neonate was placed in NICU care and under a radiant warmer which was set to manual mode. Initial values for Complete blood count, CRP, serum electrolytes, TSH, serum Calcium, Tandem mass spectrometry, liver and renal function tests were normal. TORCH panel was negative. Imaging studies, including Chest X-ray, Echocardiogram and abdominal ultrasound did not reveal any significant abnormalities. The baby's temperature was regularly monitored, and kept within a range of 36.5^{0}C-37.4^{0}C (axillary) with appropriate modifications in the warmer settings. IV fluids were given and nasogastric feeds were initiated. Serum electrolytes were monitored daily.

A white soft paraffin based (15% w/w) skin emollient was applied once every 4 hours, under sterile conditions for the first 5 days of life. We used food grade plastic cling wrap to cover the denuded areas of the baby's trunk and limbs, up to four times a day. The cling wrap would be applied roughly two hours after the application of the emollient, and removed one hour prior to the re-application.

After the first six days of life, when the skin desquamation had accelerated, the frequency of emollient application and body cling wrapping was reduced to five times daily for a 72 hour period, subsequently to a thrice daily schedule for a further 3 days after which it was ceased. Skin swabs were taken at 24 hours, 96 hours and day 6 of life and did not yield any pathogens. Prophylactic Mupirocin cream was applied on the fissured skin twice daily from day 9 to day 14 of life.

Lubricating eye drops, which were initiated shortly after birth, were continued till two weeks. The first bath was given on day 8 and Kangaroo mother care (KMC) was initiated on day 9 of life.

A challenge presented itself in the form of exaggerated physiological jaundice at day 4 of life. Icterus was observed in the baby and the total bilirubin level was 20.6 mg/dL, indirect bilirubin was 16.9 mg/dL- necessitating double surface phototherapy (DSPT). We provided DSPT using a bili-blanket as well as an overhead CFL unit, for a 48 hour period, following which a satisfactory drop in serum bilirubin (Total) to 11.1 mg/dL was observed. The application of emollient and cling film was continued as per schedule even during the period of DSPT administration. Precise monitoring of body temperature, titration of IV fluids in order to compensate for the increased transdermal losses, and monitoring of serum electrolytes was required.

Skin biopsy of the collodion membrane was done, and analysis showed a thickened stratum corneum with granular prominence and edematous stratum spinosum. A skin-punch biopsy was planned, but deferred respecting the parent's wishes.

The baby's weight was monitored daily. Expressed breast milk (EBM) with human milk fortifier (HMF) was used for feeding initially and was given through the nasogastric tube for the first 6 days. IV fluids were also administered for the first 7 days of life. By day 7, the baby was able to accept spoon feeds, and progressed to breast feeds by day 16 with appropriate postnatal weight gain. He was transferred to the nursery on day 10 of life. He was discharged on day 22 in a stable condition. Denudation of the collodion membrane was near total by 4 weeks of life and was accompanied by fine scaling and mild erythema. Healthy looking skin was seen by the 5th

week of life. On follow-up at two months of age, only mild, whitish scaling was seen in the axillary region.

Figure 2: (C) Day 7 of life. Note the dermal denudation. (D) Day 10 of life. Ectropion and eclabion had resolved.

Genetic analysis for TGM-1 mutation was requested, and was reported as negative for mutations. This necessitated a second sample analysis for ALOX12B and ALOXE3 mutations (considering the milder phenotype and also being the second most common mutations responsible for ARCI). Analysis revealed a homozygous ALOX12B (p.Tyr521Cys)c.[1562A>G] mutation with A replacing G in position 1,562 resulting in cysteine replacing tyrosine at aa position 521. The parents were not willing for genetic analysis for themselves.

DISCUSSION

Our patient was managed in the NICU with a thermo-neutral environment and sterile precautions taken during handling. A humidified incubator was not available, but has been recommended in the management strategy.[7] Precise monitoring of the baby's temperature, vitals and urinary output are important measures. If placing the baby under a warmer, caution must be exercised in selecting the mode, as affixation of the probe on the peeling off membrane may lead to overheating and dehydration (in case of servo). We found it convenient to use manual mode, with set points so as to maintain the body temperature within an acceptable range.

Our patient received nasogastric feeds during the early course of hospitalization. Attempts at breast feeding or spoon feeding need to be carried out only after assessment by the treating physician, as the membrane around the mouth hampers normal feeding and enthusiastic attempts may cause aspiration. Nasogastric or orogastric tube feeding may be acceptable forms of feeding during the initial days.[8] Anticipating the increased requirement of calories and loss of proteins - we decided to use a human milk fortifier along with the mother's milk, which was tolerated well by the baby.

Application of petrolatum based emollients has been recommended, and creates a barrier for transepithelial water loss (TEWL).[7,9] As most emollients act maximally within thirty minutes to one hour after application, and usually do not persist for more than four hours, we decided to use food grade cling wrap to effectively 'lock-in' moisture which was being lost through the denuded areas. Trials conducted elsewhere have demonstrated its utility in reducing insensible water loss.[10] The monitoring of body temperature assumes even more significance in this case, as hyperthermia may result and it would be prudent to adjust the temperature of the warmer to a lower setting.

Administration of intravenous antibiotics is not necessary if there is no evidence of infection.[11] In the case of X, skin swab cultures were sterile and we considered application of a topical antibiotic only during the initiation of KMC, when the baby would be exposed to maternal skin florae. The presence of ectropion puts collodion babies at high risk for developing keratitis due to xerophthalmia.

X required phototherapy for the management of indirect hyperbilirubinemia. DSPT was administered for a 48 hour period, while the emollient and cling wrap applications were continued. In spite of these barriers, we evidenced a satisfactory drop in X's bilirubin levels. During routine DSPT, and especially with the use of CFL lamps, the issues that are compounded are water loss and increase in body temperature. A compensatory increment in fluid intake along with precise monitoring of body temperature may address this issues.[12]

The role of ALOX12B

The ALOX12B protein is coded by exons 1 to 15 of the ALOX12B gene on chromosome 17p13.1. Arachidonate 12-lipoxygenase, 12R type (12R-LOX) is encoded by the ALOX12B gene and is involved in the conversion of arachidonic acid to 12R-hydroxyeicosatetraenoic acid. In humans, 12R-LOX has been detected in keratinocytes, tonsil squamous epithelial cells, bronchial epithelial cells, and psoriasis scales, as well as in B cells. 12R-LOX has an important physiological role in the skin and maintains appropriate moisture by preventing TEWL.[13] In case of ALOX12B mutations among various ARCI diseases, ALOX12B is mainly, but not solely, involved in nonbullous congenital ichthyosiform erythroderma. Both ALOX12B and ALOX3E mutations are typically associated with a milder form of ichthyosis.[14] The affected skin generally improves during either childhood or puberty, and these patients have a normal life span. Missense, termination, and frameshift mutations may be seen.

CONCLUSION

The management of a collodion baby poses a significant challenge to the treating physician. Adequate preparation i.e. anticipating difficulties in feeding, thermoregulation, fluid and electrolyte balance, infections etc. can positively affect the outcome. Initial monitoring and treatment is ideally provided in an NICU setting. Careful monitoring and taking aseptic precautions during handling of the baby can prevent complications. Reducing TEWL and maintaining body temperature within an acceptable range should be important targets, and as such the management strategy is similar to that of a baby with burns. Prophylactic antibiotic therapy is not compulsory; however, a watch should be kept for the development of sepsis. It may be difficult to identify jaundice in a collodion baby. Appropriate investigations and management strategies need to be formulated by the treating physician in such cases. Fortification of mother's milk supplements proteins and calories, which are essential for babies with this condition. Counselling and the option for genetic analysis need to be given to the parents. Parents need to be educated about the proper skin care techniques and practices to be adopted while handling the babies.

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