Case Series

Congenital ichthyosis presentation and outcome - A case series

Qudsiya A. Ansari, Vinaya A. Singh, Kailas G. Randad, Prasoon Bansal

Department of Paediatrics, Topiwala National Medical College, Mumbai, Maharashtra, India

Abstract

The ichthyosis, also called disorders of keratinization or cornification, are heterogeneous group of disorders characterized by a generalized scaling of the skin of varying severity. The majority of ichthyosis is inherited but acquired forms can develop in the setting of malignancy, autoimmune or infectious disease, and nutritional deficiency. Autosomal recessive congenital ichthyosis, which include lamellar ichthyosis, congenital ichthyosiform erythroderma, and harlequin ichthyosis, are rare; their overall incidence has been estimated at approximately 1 in 300,000 births. In this article, we described four cases of congenital ichthyosis, their potential complications, causes of morbidity and mortality, and discussed the management and importance of genetic testing for diagnosis as definitive diagnosis is important for long-term management and counseling of the parents.

Keywords: Congenital ichthyosis, eclabium, ectropium, lamellar ichthyosis

Introduction

Collodion baby is used to describe a newborn covered with translucent, parchment like skin sheet, it is not a single entity but a newborn phenotype who will eventually demonstrate lamellar ichthyosis or congenital ichthyosiform erythroderma. It is a disorder of cornification, may be associated with systemic symptoms. There can be an abnormal quality or quantity of scale production, abnormal thickness of stratum corneum or keratinocyte kinetics, and associated with skin inflammation. Autosomal recessive congenital ichthyosis includes several forms of nonsyndromic ichthyosis.[1] Clinical presentation of congenital ichthyosis varies in severity, ranging from harlequin ichthyosis, the most severe and often fatal form, to lamellar ichthyosis and congenital ichthyosiform erythroderma. These phenotypic descriptions are useful to know for prognosis and management.[2]

Address for correspondence: Dr. Qudsiya A. Ansari, 45/B Baldiwala Apartments, Rippon Road, X Lane, Off M.A Road, Mumbai - 400 008, Maharashtra, India.
E-mail: ansari.qudsiya31@gmail.com

Received: 30-06-2023 **Revised:** 01-09-2023
Accepted: 12-09-2023 **Published:** 21-11-2023

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_1080_23

Case 1

A late preterm female neonate born at 36 weeks of gestational age with a birth weight of 1.8 kg delivered by lower segment cesarean section (LSCS) to a primigravida mother with a history of third-degree consanguinity was noted. Antenatal period was uneventful. Baby was small for gestational age, with normal length and head circumference (44 cm and 32 cm, respectively). On examination, the vitals were stable. On physical examination, entire body was covered with parchment like taught membrane with peeling all over the body, eversion of eyelids (ectropion), her mouth was wide open like a fish (eclabium), with restricted joint mobility. The newborn had generalized erythema and edema over the body [Figure 1]. Rest systemic examination was normal. Baby was started on ryles tube feeds, emollients were applied and artificial tears were instilled. Hypernatremia, hyperbilirubinemia, and neonatal sepsis (blood culture: *E. coli* positive) were successfully treated during the initial 3 weeks of life and oral breastfeeding was established gradually. Whole exome sequencing revealed ALOX12B gene mutation. There was gradual shedding of the colloidan membrane over 3 weeks of hospitalization with improvement in ectropion and eclabium [Figure 2]. At 3 months of age, the baby was

How to cite this article: Ansari QA, Singh VA, Randad KG, Bansal P. Congenital ichthyosis presentation and outcome - A case series. J Family Med Prim Care 2023;12:2990-3.

admitted with sepsis and failure to thrive. Baby succumbed to staphylococcal sepsis induced multiorgan dysfunction.

Case 2

A term 2.6 kg, male baby was born by normal vaginal delivery at home to a G3P2L2 mother. The baby cried immediately after birth. Antenatal history was uneventful. There was no history of consanguinity or family history of any inherited skin disorder. Admitted to neonatal intensive care unit (NICU) at 6 hours of life. On examination, the baby was irritable and was in shock. On physical examination, entire body was covered with parchment-like taught membrane with peeling all over the body, ectropion, eclabium, with restricted joint mobility [Figures 3 and 4]. Rest systemic examination has revealed no abnormalities. Baby deteriorated due to sepsis and expired on day 3.

Case 3

A term male neonate was delivered by LSCS i/v/o meconium-stained liquor to a primigravida mother with the parents being nonconsanguineous. Baby's birth weight was 2.1 kg, that is, small for gestational age. Antenatal and perinatal events were normal. At birth, the baby was covered with thin yellowish scaling skin. The limbs were held in a rigid semiflexion position. Other features included eclabion, small and rudimentary external ears, ectropion, absent eyebrow, and eyelashes [Figure 5]. Vitals signs and other systemic examinations were normal. The baby was admitted to the neonatal intensive care unit managed with adequate humidification. The dermatological opinion was taken and proper monitoring of body temperature was done and topical emollients were regularly applied. Tube feeding was started. Artificial tears were applied to prevent the drying of the eyes. The infant was closely monitored for any sepsis. Whole exome sequencing revealed ALOX12B gene mutation. There was gradual shedding of the colloidan membrane over 2 weeks of hospitalization with improvement in ectropion and eclabium [Figure 6]. Baby discharged from NICU on day life 15. On follow-up, the baby was asymptomatic and had adequate weight gain.

Case 4

A term female neonate was delivered by LSCS i/v/o cord around the neck to a G2P1L1 mother with the second-degree consanguineous marriage. The baby's birth weight was 3.2 kg.

Figure 1: Case 1 showing generalized erythema and edema all over the body on day of life 1

Figure 2: Case 1 shedding of the colloidan membrane after 3 weeks

Figure 3: Case 2 ectropion, eclabium, with restricted joint mobility

Figure 4: Case 2 entire body was covered with parchment like taught membrane with peeling all over the body

Antenatal and perinatal events were normal. The baby was referred from outside to our tertiary care center at day of life 4. There was peeling of the skin, thin shiny membrane was present. Other features included eclabion and ectropion. These were milder than compared to other three cases [Figure 7]. Vitals signs and other systemic examinations were normal. The baby was admitted in the neonatal intensive care unit managed with adequate humidification. The topical emollients were regularly applied. Tube feeding was started. Artificial tears were applied to prevent the drying of the eyes. The infant was closely monitored for any sepsis. There was gradual shedding of the colloidan membrane over 2 weeks of hospitalization with improvement in ectropion and eclabium. Baby discharged from NICU on day life 14. On follow-up, baby was asymptomatic and had adequate weight gain [Table 1].

Discussion

Congenital ichthyosis is a Mendelian disorder of cornification which is a large, clinically, and etiologically heterogeneous group characterized by patterns of scaling and histopathologically by hyperkeratosis. Defective formation of intracellular lipid layers leads to dysfunction of the epidermal barrier is the main cause of hyperkeratosis.[3] The consequence of this disrupted barrier can cause life-threatening complications with increased susceptibility to infection secondary to impaired skin integrity and dramatically increased metabolic demands due to increased epidermal turnover and evaporative heat and water loss.[4] Clinical presentation and severity may vary significantly and sometimes there may be involvement of another system.[5] Congenital ichthyosis can be diagnosed antenatally by ultrasonography scan with the features like polyhydramnios, echogenic amniotic fluid, fetal growth restriction, eyes closed with eversion of the eyelids (ectropion) and lips (eclabion), flat nose, mouth wide open, ears not well formed, flexion of extremities, mottled, breached skin of the face and limbs, hyperflexion of fingers and toes, and restriction of movements of fingers. This condition is better diagnosed by a three-dimensional scan. In some cases, there may be low unconjugated estriol levels which are tested on maternal serum screening during the second trimester.[6] Prenatal diagnosis of ichthyosis also includes chorionic villus sampling, fetal skin biopsy, and preimplantation testing. In the neonatal period, a diagnosis is mainly on clinical grounds alone but sometimes confirmation of diagnosis can be made by relatively simple diagnostic tests. Skin biopsy findings are often nonspecific and therefore helpful only in a minority of cases, but genetic diagnosis becomes particularly useful in the setting of future family planning.[7] The 12 genes known to be associated with congenital ichthyosis are ABCA12, ALOX12B, ALOXE3, CASP14, CERS, CYP4F22, LIPN, NIPAL4, PNPLA1, SDR9C7, SLC27A4, and TGM1.[8] Neonatal management includes a moist environment, hygienic handling to prevent infection, and treatment of infections; petrolatum-based creams/ointments to keep the skin soft, supple, and hydrates, lubrication, and keratolytic agents to promote peeling and thinning of the stratum corneum. Lubrication of the cornea is required for those with ectropion and oral retinoids for those with severe skin involvement.[9] Gene and cell therapies are evolving as a promising therapy for congenital ichthyosis that can correct the functional activity of altered proteins.[10]

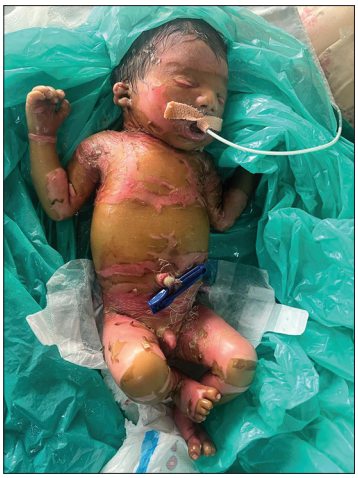

Figure 5: Case 3 scaling skin, eclabion, ectropion, absent eyebrow and eyelashes

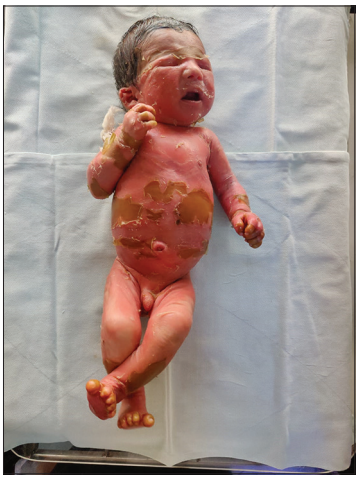

Figure 6: Case 3 shedding of the colloidan membrane after 2 weeks

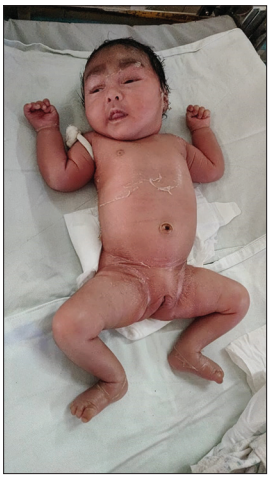

Figure 7: Case 4 peeled skin with thin shiny membrane

Table 1: Compare the presentation and outcome of the cases

	Case 1	Case 2	Case 3	Case 4
Gestational age	Late preterm 36 weeks	Term	Term	Term
Weight	SGA 1.8 kg	AGA 2.6 kg	SGA 2.1 kg	AGA 3.2 kg
Gender	Female	Male	Male	Female
Consanguinity	Third-degree consanguinity	No consanguinity	No consanguinity	Second-degree consanguinity
Sepsis	*E. coli* and *Staphylococcus sepsis*	Septic shock	No sepsis	No sepsis
Genetic workup	ALOX12B gene mutation	Not done	ALOX12B gene mutation	Not done
Outcome	Died at 3 months of age	Neonatal death	survived	survived

Conclusion

Congenital ichthyosis has a poor prognosis with varied complications and variable survival rates ranging from 10 months to 25 years depending on the severity of the disease. The supportive care is the mainstay of management for colloidian babies like maintenance of hydration by intravenous fluid or tube feeding, prevention of hypothermia, electrolyte imbalance, and septicemia. A gene panel that includes these genes of congenital ichthyosis is the diagnostic test of choice and skin biopsy is not necessary to establish the diagnosis.

Learning points

1) Congenital ichthyosis is inherited in an autosomal recessive manner as recurrence of this in the next pregnancy is 25%; therefore, genetic testing and counseling should be done for these cases.
2) Life-threatening complications including hypothermia, dehydration, supervening infections, and respiratory insufficiency should be prevented by appropriate measures.
3) At present, there is no curative therapy, but enzyme replacement and gene therapy are promising treatments for congenital ichthyosis and can correct the functional activity of altered proteins. But still, these approaches are at an early stage of development.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the guardians have given consent for their babies' images and other clinical information to be reported in the journal.

Acknowledgments

The authors thank Dean, Topiwala National Medical College and BYL Nair Hospital, Mumbai for giving opportunity to publish this manuscript.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Srivastava P, Srivastava A, Srivastava P, Betigeri AVK, Verma M. Congenital ichthyosis-collodion baby case report. J Clin Diagn Res 2016;10:SJ01-2. https://doi.org/10.7860/JCDR/2016/16397.7953.
2. Mazereeuw-Hautier J, Hernández-Martín A, O'Toole EA, Bygum A, Amaro C, Aldwin M, *et al.* Management of congenital ichthyoses: European guidelines of care, part two. Br J Dermatol 2019;180:484-95. https://doi.org/10.1111/bjd.16882.
3. Tahir A, Tariq SM, Haider SA, Hasan M. Ichthyosis congenita, harlequin type: A fatal case report. Cureus 2018;10:e3524. https://doi.org/10.7759/cureus.3524.
4. Mithwani AA, Hashmi A, Shahnawaz S, Al Ghamdi Y. Harlequin ichthyosis: A case report of prolonged survival. BMJ Case Rep 2014;2014:bcr2013200884. https://doi.org/10.1136/bcr-2013-200884.
5. Akiyama M, Sawamura D, Shimizu H. The clinical spectrum of nonbullous congenital ichthyosiform erythroderma and lamellar ichthyosis: Non-bullous CIE and lamellar ichthyosis. Clinical and Experimental Dermatology 2003;28:235-40. https://doi.org/10.1046/j.1365-2230.2003.01295.
6. Craiglow BG. Ichthyosis in the newborn. Semin Perinatol 2013;37:26-31. https://doi.org/10.1053/j.semperi.2012.11.001.
7. Youssefian L, Vahidnezhad H, Saeidian AH, Touati A, Sotoudeh S, Mahmoudi H, *et al.* Autosomal recessive congenital ichthyosis: Genomic landscape and phenotypic spectrum in a cohort of 125 consanguineous families. Hum Mutat 2019;40:288-98. https://doi.org/10.1002/humu.23695.
8. Mohamad J, Samuelov L, Malchin N, Rabinowitz T, Assaf S, Malki L, *et al.* Molecular epidemiology of non-syndromic autosomal recessive congenital ichthyosis in a middle-eastern population. Exp Dermatol 2021;30:1290-7. https://doi.org/10.1111/exd.14345.
9. Digiovanna JJ, Mauro T, Milstone LM, Schmuth M, Toro JR. Systemic retinoids in the management of ichthyoses and related skin types: Management of ichthyoses and related skin types. Dermatol Ther 2013;26:26-38. https://doi.org/10.1111/j.1529-8019.2012.01527.
10. Chulpanova DS, Shaimardanova AA, Ponomarev AS, Elsheikh S, Rizvanov AA, Solovyeva VV. Current strategies for the gene therapy of autosomal recessive congenital ichthyosis and other types of inherited ichthyosis. Int J Mol Sci 2022;23:2506. https://doi.org/10.3390/ijms23052506.