Annals of Tropical Paediatrics (2011) 31, 247–249

Management of harlequin ichthyosis in low-income countries

G. ROSSI & D. MESIA*

*Médécins sans Frontières, Rome, Italy and *Médécins sans Frontières, Brussels, Belgium*

(Accepted March 2011)

Abstract Harlequin ichthyosis (HI) is a very rare severe form of autosomal recessive congenital ichthyosis, usually associated with stillbirth and early neonatal death. A newborn girl with HI is described. She presented in a critical condition with severe universalis hyperkeratosis, diffuse scales and deep erythematous fissures. She received preventive systemic antibiotics and hygienic nursing with skin and eye care, feeding and appropriate hydration. She was discharged at 28 days in good general condition.

Introduction

Severe types of congenital ichthyosis presenting in the newborn with intense hyperkeratosis over the whole body are rare and characterised by a variable phenotype expression which mirrors the complexity of the underlying genotype determinants. The birth of an infant affected by congenital ichthyosis is a challenge both for parents and clinicians. In poor medical settings typical of low-income countries, the lack of proper diagnostic laboratory and therapeutic facilities are major constraints in managing severe dermatological conditions.

An infant with congenital ichthyosiform erythroderma is presented.

Case Report

A female infant was delivered in the Médécins sans Frontières (MSF)-supported Paediatric Clinic in Dakoro Hospital in the Maradi Region of Niger. She was born at term (birthweight 3170 g), without complications, to consanguineous parents. Her mother was primiparous. There was no family history of skin disorder or mention of previous neonatal deaths.

On examination, the patient was in a critical condition with severe ichthyosis with hyperkeratosis, scales and deep erythematous fissures over a large part of the body surface and severe bilateral ectropion. The face was expressionless with an open mouth and eclabium (Fig. 1).[1] The hands and feet were swollen because of circumferential skin constriction. The fingers and toes were ischaemic (Fig. 2). A diagnosis of harlequin ichthyosis (HI) was made. Systemic antibiotics (ceftriaxone 60 mg/kg/day i.v. and cloxacillin 75 mg/kg/day BID i.v) and tetracycline eye ointment were prescribed. Intensive skin care was undertaken, mainly by daily moisturising and greasing with a topical preparation made of vaseline oil (70%), zinc oxide (20%) and aureomicine pomate (10%). Over the next few days, her general condition improved and complete desquamation of the hypercheratotic skin, accompanied by bloody secretions, occurred

Corresponding author: Dr Gabriele Rossi, Médécins sans Frontières, via Como 17, 20095 Cusano Milanino, Italy. Fax: +39 2 619 3038; email gab.rossi@tiscali.it

DOI: 10.1179/1465328111Y.0000000020

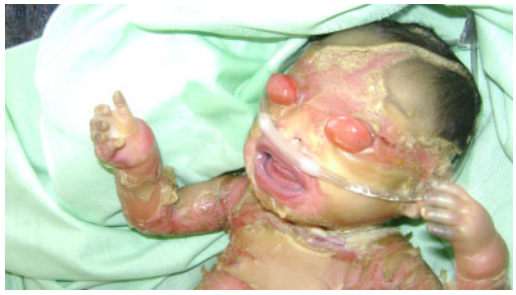

FIG. 1. Day 1: Classical facial presentation of harlequin ichthyosis with severe ectropion and eclabium.

(Figs 3 & 4). Clinical management included (i) regular observations (temperature, heart rate, activity level, feeding); (ii) avoidance of hypothermia by ensuring regular wrapping, especially at night-time, and an overhead heater if necessary; (iii) encouraging early and frequent (3–4 hours initially) breastfeeding (comprising a total fluid input of 60 ml/kg/day the 1st day, increasing to 180 ml/kg/day within 1 week); (iv) continuous monitoring for and timely treatment of hypoglycaemia (possibly associated with hypothermia and sepsis); and (v) asepsis and hygienic care were closely monitored and adhered to by the nursing staff.

The following was given to the mother in preparation for discharge: (a) soap and explanation of the rules of hand hygiene; (b) the importance of regular medical follow-up was stressed; (c) use of insecticide-impregnated bed nets to decrease the risk of malaria was advised and three bed nets were provided for the family; (d) the importance of boiling water to decrease the risk of gastro-enteritis was stated; and (e) information and

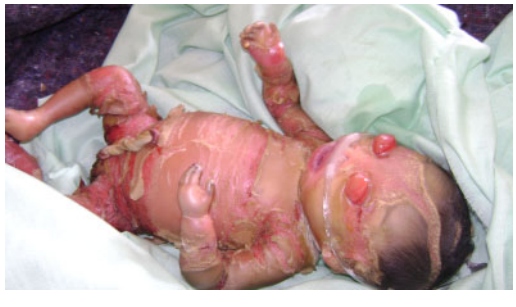

FIG. 2. Day 1: Several hyperkeratotic plaques with a diamond-like configuration, resembling a harlequin clown's costume. Limbs are in a rigid fixed position.

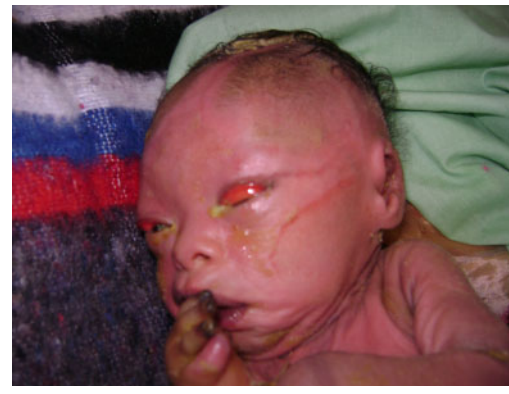

FIG. 3. Day 22: Desquamation of facial lesions. Improvement of the ectropium and resolution of the eclabium.

education on timely recognition of four main danger signs in the child (lethargy, not able to feed, vomiting and seizures).

The infant was discharged on day 28 weighing 4110 g and in good general condition, and the mother was given a supply of topical moisturising cream. At that time, the skin showed some signs of hyperkeratosis. The family lived in a distant rural area and did not return for follow-up.

Discussion

HI is a severe and usually fatal form of congenital ichthyosis; it belongs to the family of genodermatoses and has an autosomal

FIG. 4. Day 22: Almost complete desquamation of the whole body. Partial resolution of the postural fixed position of the limbs and fingers.

recessive inheritance pattern.[1] This is the most severe form of congenital ichthyosis with an incidence of 1 : 300,000 births. The name of the skin disorder derives from the typical presentation at birth, characterised by thick, whitish, armour-like skin, crossed by deep reddish fissures which often create diamond-shaped cutaneous forms resembling a harlequin costume (there are rhomboid scales, typical of the harlequin costume of a carnival clown). Facial anomalies include bilateral ectropion and eclabion (eversion of the lips), and usually there is malformation of the external ears and nasal hypoplasia. The limbs are short and surrounded by a rigid sheath with hypoplastic fingers, toes and nails.[2] The newborn appears to be encased in a tight membrane that holds the limbs in a semi-flexed position. The mouth remains permanently open, rendering the infant at times unable to suckle.

The gene underlying HI was identified in 2005.[1] It is responsible for production of the protein ABCA12, a transporter which belongs to the ATP-binding cassette (ABC) transporter superfamily.[3] ABCA12 protein, physiologically, transfers lipids from the cytosol of the keratinocyte into lamellar granules and discharges their contents into the intracellular space, forming lipid lamellae in the stratum corneum. Mutations of the gene ABCA12 cause loss of function of the protein, thus leading to a defective barrier in the stratum corneum and HI phenotype.[1,3]

The diagnosis is mainly clinical. Where there is a family history of HI, prenatal diagnosis is now possible through direct sequence analysis and restriction enzyme digestion analysis using the fetal genomic DNA from amniotic fluid cells at 16 weeks gestation.[4]

Before 2005, prenatal diagnosis by fetal skin biopsy histological analysis, although technically difficult and with low reliability, was the only available method. Skin biopsies were characterised by abnormalities, including a large number of lipid droplets in the keratinised cells and abnormal or absent lamellar granules. Prenatal diagnosis by ultrasound 2D and 3D imaging can detect features suggestive of a harlequin fetus in the 1st to 2nd trimester of pregnancy.[5]

There is no standard, accepted therapy for this disease. HI is usually associated with stillbirth and early neonatal death owing to respiratory compromise, infection, dehydration and hyponatraemia. Since Lawlor and Peiris's report in 1985 of a patient who survived,[6] a few other survivors have been reported. Outcome is variable with most cases evolving to severe, non-bullous ichthyosiform erythroderma. Interestingly, all the cases who have survived beyond the 1st year of life (including Lawlor and Peiris's) have received oral retinoids for a short period or intermittently.[7]

This case demonstrates that, with the use of essential hygienic nursing care along with prevention of infection and appropriate feeding, a regimen for skin and eye care and hydration, infants with conditions as severe as HI can be managed in low-income countries with basic medical facilities.

References

1 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.

2 Kouskoukis C, Minas A, Tousimis D. Ichthyosis congenital fetalis (Harlequin fetus). *Int J Dermatol* 1982; **21**:347–8.

3 Kelsell DP, Norgett EE, Unsworth H, *et al.* Mutations in ABCA12 underlie the severe congenital skin disease harlequin ichthyosis. *Am J Hum Genet* 2005; **76**:794–803.

4 Akiyama M, Titeux M, Sakai K, *et al.* DNA-based prenatal diagnosis of harlequin ichthyosis and characterization of ABCA12 mutation consequences. *J Invest Dermatol* 2007; **127**:568–73.

5 Bongain A, Benoit B, Ejnes J, *et al.* Harlequin fetus: three-dimensional sonographic findings and new diagnostic approach. *Ultrasound Obstet Gynecol* 2002; **20**:82–5.

6 Lawlor F, Peiris S. Harlequin fetus successfully treated with etretinate. *Br J Dermatol* 1985; **112**:585–90.

7 Singh S, Bhura M, Maheshwari A, Kumar A, Singh CP, Pandey SS. Successful treatment of harlequin ichthyosis with acitretin. *Int J Dermatol* 2001; **40**:472–3.