Harlequin Baby : A Case Report

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Abstract

Harlequin fetus is a rare and the most severe form of congenital ichthyosis. Most of the infants die within a few weeks after birth due to sepsis and respiratory difficulties. The case of a female harlequin baby is reported. The baby survived because of good neonatal intensive care, topical emollients and oral etretinate. Now she is over three years old and the skin developed into congenital non-bullous ichthyosiform erythroderma. Unfortunately she had delayed growth and development. This is the first case report of a harlequin fetus in Thailand that had prolonged survival.

The harlequin fetus is rare and the most severe form of congenital recessive ichthyosis. The first case was reported by Reverend Oliver Hart in 1750[1], since then a number of cases have been described worldwide[2-5]. At birth the entire skin is covered with thick scales and extensive fissures. Ears and noses are flattened and underdeveloped with severe ectropion and eclabion. Other abnormalities reported in the harlequin fetus include nonspecific renal dysplasia, thymic aplasia or hypoplasia, thyroid aplasia, cervical hemivertebrae and hypoplasia of the lung[2,3,15]. The infants usually die within the first two weeks of life as a result of sepsis and respiratory difficulties[6]. We report the first case of a harlequin fetus in Thailand that has survived. The patient is now over three years old.

CASE REPORT

A 2,500 grams fullterm female baby was born normally to a 28 year-old-mother at a private clinic in Pichit. She was the first child of the family. The antenatal period had been uneventful. There was no family history of abnormal skin diseases and the parents were unrelated. Her family pedigree is shown in Fig. 1.

The infant was transferred to the Children's Hospital at the age of 4 days. The clinical appearance of the baby was striking. All of the body surface was covered by large, thick rigid

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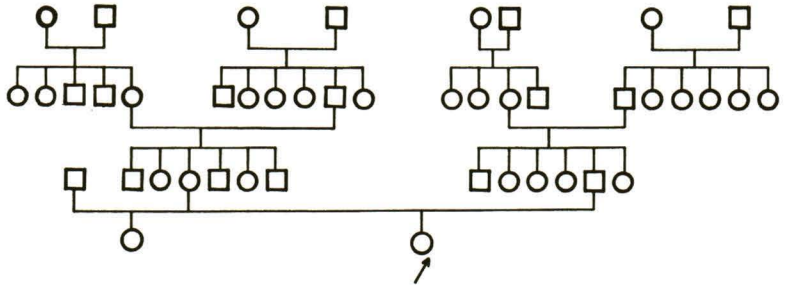

Fig. 1. Family pedigree of the patient.

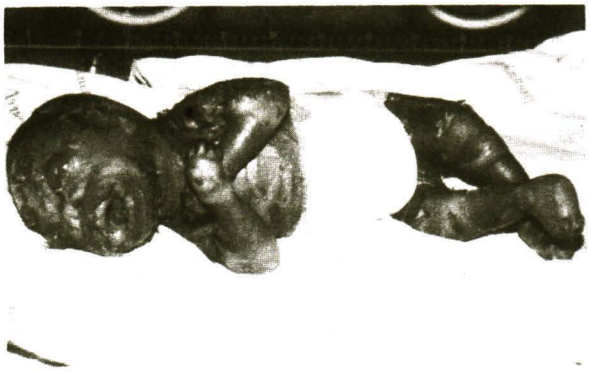

Fig. 2. Harlequin baby at the age of 4 days.

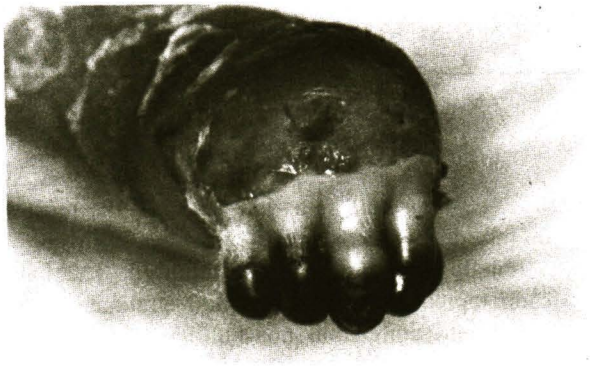

Fig. 4. Peripheral gangrene of all the digits.

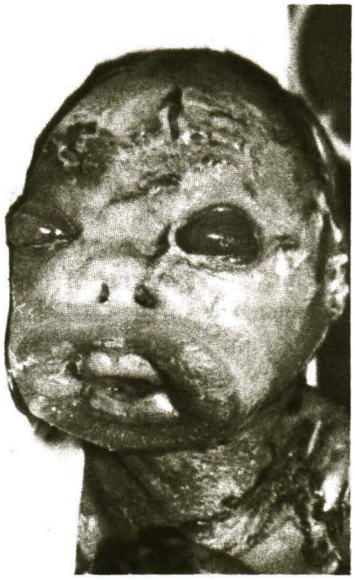

Fig. 3 Harlequin baby showed severe ectropion and eclabion.

scales that split to reveal moist fissures. There were severe ectropion and eclabion. The nose appeared to be absent, only nostrils were visible. Rudimentary ears were present and covered by hard keratin (Fig. 2, 3). Hands and feet were held in fixed flexion deformities with peripheral gangrene of digits and toes. (Fig. 4) Other physical examination was normal.

The baby was treated by placing in a humidified incubator. Tube feeding was started to provide adequate fluid and calories. Systemic cloxacillin and amikacin were given intravenously for 3 weeks due to superimposed bacterial skin infection.

Topical care of the skin consisted of topical emollients (Oilatum^{R}) for the whole body and topical mupirocin (Bactroban^{R}) was applied on the exposed and raw areas.

Ophthalmological examination showed marked ectropion of upper and lower eyelids in

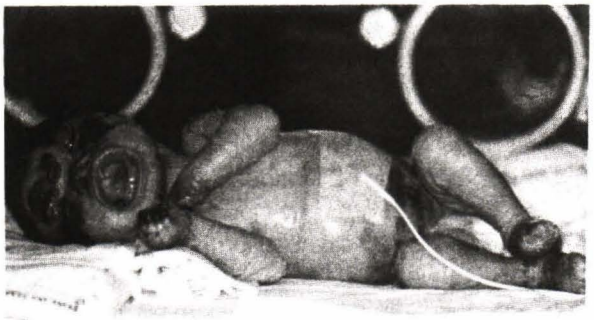

Fig. 5. At 1 month of age, ectropion and eclabion improved.

Fig. 6. At 3 months of age, the skin had improved remarkably with thinning of the scales all over the body.

both eyes with normal cornea and lens. The eyes were protected with antibiotic ointment and eye patch while the baby was asleep.

Ultrasound of the abdomen was performed to rule out the associated renal anomalies and the result was normal.

On day 7, etretinate in a dose of 0.5-1 mg/kg/day was given orally which was prepared

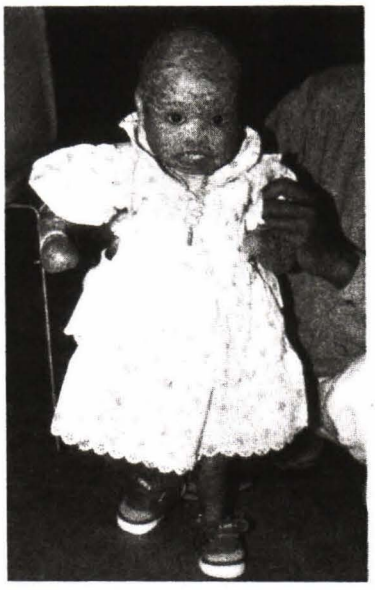

Fig. 7. The patient was 3 years of age.

by the hospital pharmacist. Complete blood count, electrolyte, liver function test and bone survey were done before the use of etretinate.

Skin biopsy was done at the lower leg on the 8th day. The result showed marked hyperkeratosis, regular acanthosis and normal granular layer with minimal superficial perivascular infiltration.

At the age of 1 month, the skin had improved remarkably with thinning of the scales almost all over the body. (Fig. 5) The infant was discharged from the hospital at the age of 3 months. (Fig. 6)

During infancy she had regular follow-up every 2 months until 1 year and then every 6 months thereafter. Etretinate was given continuously in a dose of 1 mg/kg/ day with regular monitoring of side effects including liver function test every 6 months and bone survey yearly. All the laboratory tests were within normal limits.

There was marked abnormality and delay in the growth and development. She could roll over at 6 months and walk at 1 year 5 months. Now she is over 3 years old and she can walk well and speak a few single words. Her height and weight are still below the third percentile (Fig. 7). The entire skin remained red and scaly, clinically resembling a congenital ichthyosiform erythroderma.

DISCUSSION

Although the clinical appearance of a harlequin fetus is distinct, the pathogenesis, biochemical defect, course and prognosis are unknown because survival beyond early infancy is rare.

Buxman et al reported that there was elevated level of cholesterol and triglyceride in the stratum corneum suggesting that the basic defect may be related to lipid metabolism[7]. Craig et al found that X-ray diffraction analysis of the stratum corneum of the harlequin fetus was beta keratin instead of normal alpha pattern while Baden and Goldsmith showed either normal or alpha pattern[8,9]. Dale et al concluded that the harlequin fetus was a genetically heterogenous group of disorders with altered lamellar granules, intercellular lipids and variation in expression of structural protein markers of normal epidermal keratinization[10]. Many investigators have considered that the harlequin fetus is the most severe form of autosomal recessive non-bullous congenital ichthyosiform erythroderma / lamellar ichthyosis. Certainly the large number of affected siblings, reported of parental consanguinity and absence of affected people in successive generations would support an autosomal recessive pattern[5,10,11].

Prenatal diagnosis of the harlequin fetus by fetal skin biopsy is possible. In 1980, Elias et al reported the successful prenatal diagnosis at 20 weeks' gestation and showed premature marked hyperkeratosis[12]. Now ultrasonography is a good method in prenatal diagnosis of a harlequin fetus[13,14].

In the past, most harlequin fetuses died in infancy as a result of prematurity, abnormal temperature control, sepsis from deep skin fissuring and respiratory and feeding difficulties[6].

Nowadays, there are many reports on better survival[15,16]. At present the report of the longest survival of a harlequin baby is 7 years[17]. The management includes good intensive care of the skin and the eyes, appropriate fluid and calorie intake, parenteral antibiotics and retinoid therapy [18-21]. Lawlor and Pieris was the first to use etretinate to treat a harlequin fetus in 1985[18]. Etretinate is a synthetic retinoid derived from vitamin A. The mode of action is unknown but retinoids have been shown to control differentiation and proliferation of keratinizing and non-keratinizing epithelium[22]. Lawlor gave etretinate to a patient on the 2nd day after birth and the skin was markedly improved[18]. The main systemic side effects are liver toxicity, bone hyperostoses and teratogenicity, so long term side effects should be monitored regularly[22].

Our patient had a clinical picture very similar to other case reports of harlequin fetus. Etretinate was given on the 7th day, the thickness of the skin and ectropion were much improved at 1 month of age. We plan to treat the patient with etretinate using the lowest dose as long as she can tolerate it. We intend to withdraw etretinate in several months to assess the continuing requirement for the drug and monitor the side effects of oral retinoids regularly. So far there is no sign of etretinate toxicity.

Although our patient survived, she had much delay in growth and development. Now she has developed into congenital ichthyosiform erythroderma with generalized fine scales and diffuse erythema all over the body like the other case reports of harlequin fetuses[23].

SUMMARY

The case of a harlequin baby is reported. A 4 day-old-girl was presented at birth with generalized large thick rigid scales all over the body and severe ectropion. She was treated with good intensive care of the skin and the eyes, appropriate fluid and calorie intake and parenteral antibiotics. Oral etretinate in the dose of 0.5-1 mg/kg was given, without side effects, from day 7 after birth up to the present time. The patient survived and now she is over 3 years old. The skin lesions developed into congenital ichthyosiform erythroderma. Unfortunately she has delayed growth and development.

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เด็กดักแด้: รายงานผู้ป่วย 1 ราย

ศรีศุภลักษณ์ สิงคาลวณิช, พ.บ., วราภรณ์ แสงทวีสิน, พ.บ.**, สุนทร ฮ้อเผ่าพันธ์, พ.บ.**, วิไล ราตรีสวัสดิ์, พ.บ.***

โรค harlequin baby หรือเด็กดักแด้ เป็นโรคผิวหนังที่ถ่ายทอดทางกรรมพันธุ์ซึ่งพบได้ไม่บ่อย แรกเกิดผิวหนังจะหนาเป็นเกล็ดทั้งตัวร่วมกับปากปลิ้นและตาปลิ้น ส่วนใหญ่ของทารกที่เป็นโรคนี้จะเสียชีวิตภายในไม่กี่สัปดาห์หลังคลอดจากการติดเชื้อแทรกซ้อนและหายใจลำบาก รายงานผู้ป่วย ทารกเพศหญิง 1 รายซึ่งรับไว้ในโรงพยาบาลเด็กและอาการทางคลินิกเข้าได้กับเด็กดักแด้ ผู้ป่วยได้รับการดูแลรักษาโดยรับไว้ในตู้อบ, ให้ยาปฏิชีวนะทางเส้นเลือด, ทายาเพื่อให้ความชุ่มชื่นแก่ผิวหนังและให้อาหารอย่างเพียงพอ ร่วมกับการให้ยาอนุพันธ์ของวิตามินเอ ตั้งแต่วันที่ 4 หลังคลอดจนถึงปัจจุบัน ขณะนี้ผู้ป่วยอายุ 3 ปีและยังมีชีวิตอยู่แต่มีน้ำหนักน้อยและพัฒนาการช้ากว่าเด็กปกติ ลักษณะผิวหนังเป็นสะเก็ดแดงทั้งตัว (Congenital ichthyosiform erythroderma) นับเป็นรายงานผู้ป่วย harlequin baby รายแรกของประเทศไทยที่มีชีวิตรอดอยู่นานเกิน 1 ปี

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