Oral acitretin treatment in severe congenital ichthyosis of the neonate

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SUMMARY: Saraçoğlu ZN, Tekin N, Ürer SM, Sabuncu İ, Akşit A. Oral acitretin treatment in severe congenital ichthyosis of the neonate. Turk J Pediatr 2002; 44: 61-64.

Two newborn infants with ichthyosis, one with lamellar ichthyosis and one with nonbullous ichthyosis form erythroderma, who presented at birth with a collodion baby appearance, were treated with acitretin (1 mg/kg/day). Clinical improvement was achieved shortly after treatment. The second case received oral retinoid for 3.5 months and was followed for nine months. The result was excellent. The treatment resulted in a satisfactory improvement in the skin condition of the first case. The tolerance to the drug was good. Side effects were not observed. It was concluded that early management of severe ichthyosis cases could prevent life-threatening events such as hyperthermia, disturbance in electrolyte and fluid balance, and infection.

Key words: congenital ichthyosis, collodion baby, acitretin, retinoids.

Ichthyosis is regarded as a disorder of keratinization or cornification, and is due to abnormal epidermal differentiation or metabolism[1]. Infants with this disorder may die of complications such as sepsis, or protein and electrolyte loss in the first months of life. For this reason, temperature control, electrolyte and fluid balance, caloric intake, and the prevention of infection are very important in newborn infants affected with severe generalized ichthyosis[2,3]. Since beneficial effects of systemic retinoids have been shown in the treatment of many disorders of keratinization[1], we tried acitretin in two newborn infants, one with lamellar ichthyosis and the other with nonbullous ichthyosiform erthyroderma (NBIE). They presented at birth as collodion babies and were treated with acitretin beginning soon after birth in addition to supportive treatment. The efficacy of treatment and the course of the disease are discussed.

Case Reports

Case 1

A three-and-a-half-hour-old male infant was admitted with erythema and abnormal appearance of the face. He was born at term as the first child of a 23-year-old mother and 25-year-old father with first-degree consanguinity. On physical examination weight was 2600 g (25^{th} percentile), length 50 cm (50^{th} percentile), and head circumference 34 cm (50^{th} percentile). His skin was parchment-like, with a yellowish film stretched over it, ectropion and eclabium were present, and nasal passages were obstructed. He was born as a collodion baby (Fig. 1). After shedding of the collodion membrane, generalized erythroderma with fine, white scales was evident. Laboratory findings were as follows: Hb 19.5 g/dl, WBC count 22,160/mm^3, platelet count 261,000/mm^3. Biochemical values of urine and blood were within normal limits. He was diagnosed as lamellar ichthyosis. Acitretin (1 mg/kg/day) in addition to supportive treatment in a humidified incubator with vaseline ointments and a prophylactic regimen of antibiotics were started. One month of follow-up resulted in improvement in skin lesions and he was discharged from the hospital (Fig. 2).

Case 2

An hour-old female infant was admitted with collodion baby appearance. She was the second child of a 27-year-old mother and 29-year-old father with first-degree consanguinity. On

physical examination weight was 3,480 g (50th percentile), length 50 cm (50th percentile), and head circumference 34 cm (50th percentile). Plate-like lesions covered the whole body, and ectropion and eclabium were also present. Laboratory findings were as follows: Hb 19.03 g/dl, WBC count 19,900/mm^3, and platelet count 244,000/mm^3. Biochemical values of urine and blood were within normal limits. After shedding of the collodion membrane, generalized scaly erythroderma was apparent (Fig. 3). She was diagnosed as NBIE. She was placed in a humidified incubator and treated with a prophylactic regimen of antibiotics. Artificial tears were used because of ectropion. Ointments containing vaseline for moisturization were used to reduce scaling. Oral retinoid treatment with acitretin (1 mg/kg/day) was administered. She was discharged from the hospital at nine days of age with topical vaseline application and oral retinoid treatment. At one and a half months of age oral retinoid treatment was discontinued because only slight erythematous areas were left on the trunk. At two months of age she was admitted with an increase in lesions with lamellar scaling of the skin. Oral retinoid treatment was restarted. She was hospitalized twice: first for septic arthritis and then for pneumonia. Oral retinoid treatment was discontinued at four and a half months of age. To date liver function tests have been within normal levels, and radiological evaluation was normal. On her last visit she was eight months old. Her skin was smooth (Fig. 4). Her mother was using vaseline ointment over her body twice daily. She could sit up straight with no support. Her weight was 6,400 g, length 67 cm, and head circumference 43.2 cm.

Fig. 1. Collodion membrane with eclabium, ectropion and obstructed nasal passages (Case 1).

Fig. 2. Generalized scaly erythroderma at one month of age (Case 1).

Fig. 3. Generalized scaly erythroderma most prominent on the trunk (Case 2).

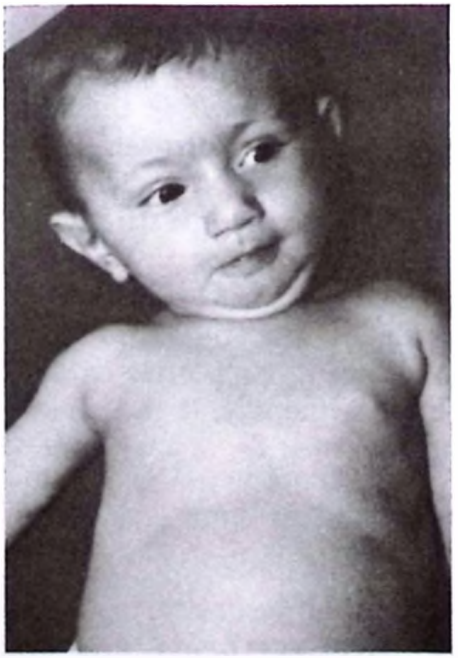

Fig. 4. After the treatment (at eight months of age) (Case 2).

Discussion

Severe generalized ichthyosis seen at birth is a life-threatening condition. Mortality is high due to complications such as marked temperature instability, skin irritation, water loss via the epidermis predisposing to hypernatremic dehydration, pyoderma, septicemia and pneumonia secondary to aspiration of squamous material in the amniotic fluid[4]. Cutaneous infections are common problems. Larreque et al.[5,6] reported a mortality rate as high as 33% in 267 collodion babies in 1976 and as 11% in 1984. Öztürk et al.[3], in their patient group of 16 collodion babies, reported a mortality rate of 25% and major complications were hypernatremia, cutaneous infection and sepsis.

These two infants were born as collodion babies. After shedding of the membranes in the second case, scaling affected the whole skin surface. Ectropion and eclabium were noted as severe as in the first infant. In the first case, after shedding of the collodion membrane, generalized scaly erythroderma was apparent and affected all areas including scalp, ears, face, flexures, palms and soles.

In severe congenital ichthyosis cases, general principles of treatment are maintainance of electrolyte and fluid balance, control of body temperature, and prevention of infection with a prophylactic regimen of intravenous antibiotics[1-3]. Management of ichthyosis primarily consists of daily hydration and lubrication of the skin. Erdem[7] reported five successfully treated cases with a topical preparation containing 5% lactic acid. Use of 12% ammonium lactate lotion, or a lactic, citric or ureic ointment base were also recommended[4]. Both patients presented here were placed in a humidified incubator. Daily sponge baths and application of emollients containing vaseline were introduced.

Systemic retinoids are effective in many disorders of keratinization, and have been shown to be helpful in reducing scaling, pruritus and erythema in most patients with severe congenital ichthyosis[1]. Oral retinoid treatment with isotretinoin, etretinate, or acitretin may be required for some patients. El-Ramly et al.[8] presented eight cases of ichthyosis treated with retinoids; the results were responses in five lamellar ichthyosis cases, while none of the patients with nonbullous or bullous congenital ichthyosiform erythroderma gave more than a slight response. On the other hand it was reported that aromatic retinoid treatment resulted in a satisfactory improvement in the skin conditioning of three patients with nonbullous congenital erythroderma[9]. Tamayo et al.[10] also recommended oral retinoid treatment after their experience in eight children with lamellar ichthyosis. In our two cases clinical course was impressive. After induction of oral retinoid in the early neonatal period, collodion membranes detached completely in a few days.

Long-term therapy with oral retinoids has provoked anxiety regarding the adverse effects on bone mineralization. In humans, the most commonly reported effect is the production of osteophytes and the calcification of ligaments. Other studies in humans have reported decreases in the radiologic appearance of bone[11,12]. Paige et al.[13] observed no evidence of skeletal toxicity in 42 children treated over an 11-year period. Usage of aromatic retinoid for more than two years in three lamellar ichthyosis cases resulted in a satisfactory improvement without any major side effects. Cheilitis, mild dryness of mucous membranes, slight hair loss, and pruritus are other side effects which were not detected in our cases[12]. In this report the result was satisfactory in the first case and excellent in the second case. Although some severe congenital ichthyosis cases heal completely in time, mortality due to the complications is high in the neonatal period. Because of its efficacy, good tolerance and easy administration, the oral retinoid acitretin is a treatment of choice for severe congenital ichthyosis forms.

REFERENCES

1. Griffiths WA, Judge MR, Leigh IM. Disorders of keratinization. In: Champion RH, Burton JL, Burns DA, Breatnach SM (eds). Textbook of Dermatology (6th ed) Vol II. London: Blackwell Science Co; 1998: 1483-1529.
2. Akiyama M. Severe congenital ichthyosis of the neonate. Int J Dermatol 1998; 37: 722-728.
3. Öztürk A, Çaksen H, Çetin N, Kurtoğlu S. A retrospective study on 16 collodion babies. Turk J Pediatr 1997; 39: 55-59.
4. Margileth AM. Dermatologic conditions. In: Avery GB, Fletcher MA, Macdonald MG (eds). Neonatology, Pathophysiology and Management of the Newborn (5th ed). Philadelphia: J.B. Lippincott Co; 1999: 1323-1360.
5. Larreque M, Bressieux JM, Fournet JP. Collodion baby. Mod Probl Paediatr 1976; 20: 40-49.
6. Larreque M, Ottavy N, Bressieux JM, Lorette J. Collodion baby: 32 new case reports. Ann Dermatol Venereol 1986; 113: 773-785.

7. Erdem G. Treatment of collodion babies with a topical preparation containing lactic acid. Turk J Pediatr 1982; 24: 97-101.

8. El-Ramly M, Zachariae H. Long-term oral treatment of two pronounced ichthyotic conditions: lamellar ichthyosis and epidermolytic hyperkeratosis with aromatic retinoid, Tigason (Ro 10-9359). Acta Derm Venereol 1983; 63: 452-456.

9. Frenk E. Oral treatment of lamellar icthyhyosis (non-bullous congenital ichthyosiform erythroderma) with an aromatic retinoid. Dermatologica 1981; 162: 91-103.

10. Tamayo L, Ruiz-Maldonado R. Oral retinoid (Ro 10-9359) in children with lamellar ichthyosis, epidermolytic hyperkeratosis and symmetrical progressive erythrokeratoderma. Dermatologica 1980; 161: 305-314.

11. Margolis DJ, Attie M, Leyden JJ. Effects of isotretinoin on bone mineralization during routine therapy with isotretinoin for acne vulgaris. Arch Dermatol 1996; 132: 769-774.

12. DiGiovanna JJ, Sollitto RB, Abangan DL, Steinberg SM, Reynolds JC. Osteoporosis is a toxic effect of long-term etretinate therapy. Arch Dermatol 1995; 131: 1263-1267.

13. Paige DG, Judge MR, Shaw DG, Atherton DJ, Harper JI. Bone changes and their significance in children with ichthyosis on long-term etretinate therapy. Br J Dermatol 1992; 124: 387-391.