

ORIGINAL ARTICLE

Neonatal and infantile erythroderma: A clinical and follow-up study of 42 cases

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Erythroderma in neonates and infants is a frequently encountered problem in the daily practice of pediatric dermatology. The objective of this study was to determine the frequency of various causes of this clinical entity, as well as which clinical and laboratory findings are useful in the differentiation of these causes, and to assess the evolution of this disease in this age group. Forty-two patients with erythroderma under 1 year of age were included in this study. A follow-up period of 3–5 years was completed. The study was performed in the Department of Dermatology, Al-Sadr and Alhakeem teaching hospitals and a private section in Najaf governorate, Iraq during the period 1998–2006. The diagnosis was made at an average of 3 months after the onset of the disease. The underlying causes included seborrheic dermatitis in 21.4%, atopic dermatitis in 14.3%, different types of *Ichthyoses* in 31.5%, psoriasis in 4.7%, pityriasis rubra pilaris in 2.4%, Staphylococcal scalded skin syndrome in 7.14%, Netherton syndrome in 4.7%, immune deficiency syndromes in 4.8% and undetermined erythroderma in 9.5% of the patients. Of 29 cases, histopathological examination of skin biopsy showed non-specific features in 58.7% and could confirm the diagnosis in 41.3% cases. The prognosis was poor with a mortality rate of 26.2% and severe dermatoses persisted in 60% of the survivors. It is difficult to make the etiological diagnosis of neonatal erythroderma from the first examination. Associated immune deficiency should be suspected if the condition associated with skin indurations, severe alopecia, failure to thrive and/or have infectious complications. The prognosis is poor especially in those with immune deficiency or a chronic persistent course.

Key words: clinical, follow up, histopathology, neonatal and infantile erythroderma.

INTRODUCTION

Erythroderma is defined as an inflammatory skin disorder affecting more than 90% of the body surface. It represents an extreme state of skin irritation resulting in extensive erythema with variable degrees of scaling of the body.^{1,2} Although numerous underlying causes of neonatal and infantile erythroderma have been reported in the published work,^{3–11} the etiological diagnosis is frequently difficult and usually delayed due to similar clinical and even histopathological features of the disease.^{10–13} The disease represents a problem in its diagnosis and treatment, especially in the neonatal period.

Erythroderma in adult age group patients has been reported by various authors,^{14–17} but there are few studies discussing this problem in neonates or infants. Most of these studies were retrospective or represent isolated conditions as case reports.^{5–11,18–22} The objective of the present study was to do a prospective study to assess the etiology, clinical features, some laboratory parameters and patient evolution in this condition in our environment.

PATIENTS AND METHODS

The study was done in Al-Sadr teaching hospital, Al-Hakeem teaching hospital and private section in

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Najaf governorate, Iraq during the period from January 1998 to January 2006. Neonates and infants presented with erythroderma were enrolled in this study. Forty-two patients (23 boys and 19 girls) who completed the follow up for at least 3 years were included. A detailed history was elicited in each case including personal data, onset of the disease (acute or chronic), duration, previous attacks of erythroderma, drug history and family history of a similar condition or atopy. Clinical data during the episode, such as scaling, pruritus, hair and nail involvement, mucosal involvement, pedal edema, state of hydration, lymphadenopathy and hepatosplenomegaly, were also assessed. The patients were seen at different intervals for follow up. The mean follow-up period was 61 months.

Laboratory investigations, including complete blood picture, erythrocyte sedimentation rate, serum protein levels, liver and renal function tests, serum electrolytes and general urine examination, were performed in all patients.

A skin biopsy specimen was obtained from 29 patients during the erythrodermic stage. The hematoxylin–eosin (HE) stained sections were examined to assess the presence of relevant features of the final aetiological diagnosis.

RESULTS

In the 8-year study period, 42 cases of neonatal and infantile erythroderma were included. Twenty-three (54.8%) patients were male and nineteen (54.2%) were female, with a male : female ratio of 1.21:1. Final diagnosis was the result of evaluation of the clinical, biochemical and histological findings and of the evolution of erythroderma in each individual patient. The diagnosis was made at an average of 3 months after the onset of the disease. The underlying diseases are listed in Table 1. The underlying cause could not be determined in four cases in spite of detailed history, examination and investigations with a follow-up period of 3–5 years. The mean age of onset was 7 weeks, congenital erythroderma was observed in 13 (30.9%) patients, and were all of *Ichthyosis* except for one case with immune deficiency syndrome. Five cases of *Ichthyosis* were presented as collodion baby before they developed the final pattern. The disease occurred relatively early, in

Table 1. Underlying causes and congenital onset in 42 cases of erythroderma

Underlying disease	No. (%)	Congenital onset
Seborrheic dermatitis	9 (21.4)	0/9
Atopic dermatitis	6 (14.3)	0/9
Psoriasis	2 (4.8)	0/2
<i>Ichthyosis</i>	13 (31)	10/13
Netherton's syndrome	2 (4.8)	2/2
Pityriasis rubra pilaris	1 (2.4)	0/1
Staphylococcal scalded skin syndrome	3 (7.14)	0/2
Severe combined immune deficiency syndrome	2 (4.8)	1/3
Undetermined	4 (9.5)	0/4

cases that were not congenital, before the age of 13 weeks. Family history of erythroderma was found in nine (21.4%) cases, seven (77.8%) of them with *Ichthyosis*. Family history of atopy was found in 13 (31%) cases including four (66.7%) of six cases with atopic dermatitis, seven (53.6%) of 13 cases with *Ichthyosis* and in one case of a patient with seborrheic dermatitis and an undetermined group for each of them.

All the patients had erythema and some degree of scaling covered most areas of the body, 17 (40.5%) patients had no other specific skin manifestations. Pruritus was observed in 18 (42.8%) cases. It was more prominent in cases of atopic dermatitis. The associated dermatological findings, like skin infiltration, hair and nail involvement, are summarized in Table 2. Alopecia was observed in 19 (45.2%) patients. Pedal edema, palmoplantar hyperkeratosis and mucosal involvement was found in six (14.2%), three (7.1%) and one (2.4%) patient, respectively. Fifteen (35.7%) patients had fever ($\geq 38^{\circ}\text{C}$) during the episode and lymphadenopathy was found in nine (21.4%) patients. The other systemic findings are shown in Table 3.

Hematological investigations revealed mild anemia (hematocrit value, 35–38%) in 22 (52.4%) patients, six (14.2%) patients had a hematocrit level less than 35% and one patient (2.4%) had severe anemia with a hematocrit value of less than 30%. Elevated erythrocyte sedimentation rate (ESR) was found in 15 (35.7%) and eosinophilia ($>0.5 \times 10^9/\text{L}$) in 23 (57.1%) patients (Table 3). Low serum proteins were observed in 12 (28.5%) and with major hypoalbuminemia ($<30 \text{ gm/L}$) in two (4.4%) patients.

Table 2. Dermatological findings 42 cases of erythroderma

Underlying disease	Skin induration	Scalp involvement	Nail involvement
Seborrheic dermatitis	0	5/9	4/9
Atopic dermatitis	1/3	2/6	1/6
Psoriasis	1/2	0	1/2
<i>Ichthyosis</i>	3/13	7/13	6/13
Netherton's syndrome	0	2/2	1/2
Pityriasis rubra pilaris	1/1	0	0
Staphylococcal scalded skin syndrome	0	0	0
Severe combined immune deficiency syndrome	1/2	0	0
Undetermined	4/4	3/4	4/4
Total %	11/26.2	19/45.2	17/40.5

Table 3. Systemic findings and complications in 42 cases of erythroderma

Underlying disease	Severe dehydration (sodium, >160 mmol/L)	Eosinophils count ($>0.5 \times 10^9/L$)	Failure to thrive	Death
Seborrheic dermatitis	0	5/9	1/9	0
Atopic dermatitis	0	4/6	1/6	0
Psoriasis	0	2/2	0	0
<i>Ichthyosis</i>	2/13	4/13	6/13	5/13
Netherton's syndrome	1/2	2/2	2/2	1/2
Pityriasis rubra pilaris	0	0	0	0
Staphylococcal scalded skin syndrome	1/3	2/3	0	1/3
Severe combined immune deficiency syndrome	1/2	1/2	1/2	2/2
Undetermined	1/4	3/4	1/4	2/4
Total%	6/14.3	23/54.8	12/28.6	11/26.2

Skin biopsy specimen examinations ($n = 29$) showed non specific histopathological findings in 17 (58.7%) specimens, and showed regular acanthosis with parakeratosis, dilatation of capillaries of the superficial dermis and variable perivascular inflammatory infiltrate. Histological examination that led to the diagnosis of *Ichthyosis* in seven (53.9%) of 13 cases demonstrated significant orthokeratosis, hyperkeratosis arranged in laminated and compact pattern, prominent hypergranulosis and acanthosis with no or scanty inflammatory infiltrate. Two cases of bullous *Ichthyosiform* erythroderma showed the characteristic epidermolytic hyperkeratosis on histopathological examination (Fig. 1) while changes typical of pityriasis rubra pilaris, psoriasis and staphylococcal scalded skin syndrome were demonstrated in one specimen for each of these cases.

The mortality rate in this series at the end of the follow-up period was 26.2% (11 patients). These patients died of direct or indirect causes (i.e. complications related to erythroderma) at a mean age of 8 months. The skin prognosis in the remaining patients

was poor at the end of the follow-up period in 26 (61.9%) patients, with seven (16.3%) of them having persistent erythroderma, 13 (31%) chronic generalized dermatoses and six (14.3%) with persistent localized lesions. Five patients (11.9%) recovered (three with seborrheic dermatitis, one with atopic dermatitis and one from the undetermined group).

DISCUSSION

Although we consider various published studies on erythroderma, most of them dealt with the adult age group,^{14,17} and few studies have only included patients with neonatal or infantile erythroderma.^{10,11} They were retrospective and most of them concentrated on isolated case reports.^{5-9,14-17}

The most frequent underlying causes in this study were *Ichthyosis*, seborrheic dermatitis (Fig. 2) and atopic dermatitis in addition to other diseases shown in Table 1. These figures were more or less similar to findings in other studies.^{10,11} The drugs that were on the top of causes in some studies in older children

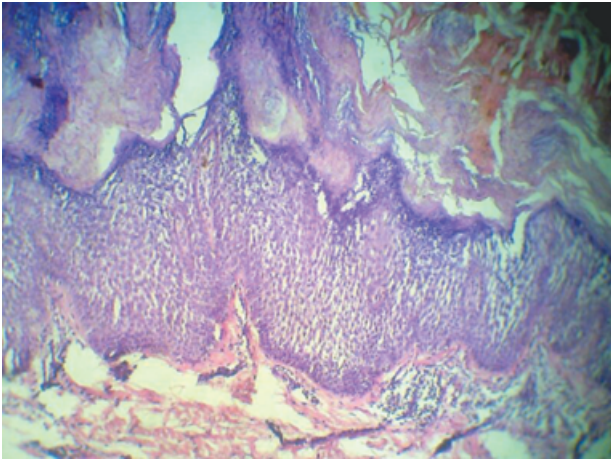


Figure 1. Histopathological specimen from a patient with ichthyosiform erythroderma showing typical changes of epidermolytic hyperkeratosis (HE stain, original magnification $\times 40$).



Figure 2. A 40-day-old infant with erythrodermic seborrheic dermatitis.

and adults^{11,14–17} were not detected as a primary cause in this age group. This is probably related to more consciousness in describing the drugs in this age group, or certain variation in the metabolism of drugs in them.

The congenital onset of erythroderma (30.9%) is probably more suggestive of *Ichthyosis* or immunodeficiency syndromes than other dermatoses. The diagnosis of *Ichthyosis* is easy in classical cases with thick scales and massive and compact orthokeratosis or when presented with harlequin or collodion baby



Figure 3. A 5-day-old baby with collodion baby-like presentation of non-bullous ichthyosiform erythroderma.

(Fig. 3). The presence of other findings with *Ichthyosis* may make diagnosis difficult, such as presence of neurological, ocular or hair abnormalities. The diagnosis of complex *Ichthyosis*, such as seen in Netherton's syndrome, is difficult and delayed by a few months; the characteristic hair involvement (i.e. Trichorrhexis invaginata) visible upon light microscopic examination of the hair from the scalp, or sometimes from the eyebrows or the eyelashes, appeared as late as 7 months in one case. Repeated light microscopic examination of the hair is therefore necessary in suspected cases of Netherton's syndrome to confirm the diagnosis.

Erythrodermic psoriasis and congenital *Ichthyosiform* erythroderma are often indistinguishable during the first months of life. Appearance of typical psoriatic lesions a few months later and the characteristic histopathological features differentiate these conditions at a later time.

Erythroderma that is associated with diarrhea and profound failure to thrive may suggest presence of immune deficiency syndromes, as these associated features are not present in atopic or seborrheic dermatitis. Alopecia was observed in (45.2%). It may be a complication of any severe type of erythroderma.

The eosinophil count is increased in allergic or mostly drug-induced cases of erythroderma in adult cases.^{14–17} In this series, there was no relationship between the eosinophil count and clinical severity or the etiological diagnosis of erythroderma. The elevated count in our cases, with the absence of this cause,

may be explained by the increased tendency toward eosinophilic inflammatory response in neonates.²³ The presence of anemia and elevated ESR were also observed in other published studies.¹¹

The main complications noticed in this study were hypernatremic dehydration, infections and failure to thrive (Table 3). Hypernatremia, which was reported primarily in Netherton's syndrome in some published works,^{3,6,10,17} was observed in one half of the cases with this syndrome in this study.

Cutaneous infections caused by staphylococcal, streptococcal or rarely by Gram-negative bacilli were common and resulted in septicemic infection in 17 (40.5%) cases. Repeated bacteriological examinations and prophylactic topical antiseptic treatment may reduce such a high incidence of septicemia.

Failure to thrive affected 12 (28.6%) patients, most of them belonging to the *Ichthyosis* group, especially those with Netherton's syndrome, and this is similar to previous published reports.¹⁴ It is also noticed in those with immunodeficiency syndromes and is probably multifactorial in origin.

The mortality rate is probably now well explained in this potentially life-threatening condition for infants with the risk of septicemic infection, hypernatremic dehydration, hypoalbuminemia and hyperpyrexia.

Clinicopathological correlation is usually poor, because the specific cutaneous changes of dermatoses are obscured by the non-specific changes induced by the inflammatory reaction of erythroderma.¹² This was shown in this study also where the histological findings confirmed the underlying dermatological condition in only 41.3% of the cases. The histological picture in remaining specimens shows either subacute or chronic dermatitis or psoriasiform reaction and this is in agreement with other studies in adult erythroderma.^{12,13,15}

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