Erythroderma in Thai Patients

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Abstract

Erythroderma is a clinical manifestation of dermatoses from different causes. Our objective was to determine its incidence, causes and clinicopathological features. Clinical, laboratory, and biopsy materials of 49 patients diagnosed as having erythroderma were reviewed. They were treated in our department over a 10-year period (1985 through 1994). The male-female ratio was 2:1. The mean age at diagnosis was 51.7 years. The most common causative factors were drugs (38.77%) and preexisting dermatoses (26.5%). Hepatomegaly, jaundice and abnormal liver function tests were found more commonly in the drug allergy group, while in cases with preexisting dermatoses nail involvement was a common finding. Clinicopathologic correlation in our study did not inform the etiology because it showed chronic nonspecific dermatitis or psoriasiform dermatitis, without any clue as to its origin. Drug-induced-erythroderma had an acute onset and a good prognosis with rapid resolution when the causative drug was withdrawn, while histopathology and laboratory findings were largely unrewarding.

Key word : Erythroderma, Clinicopathologic Study, Drug

Erythroderma or exfoliative dermatitis is a clinical manifestation of dermatoses from different causes. It is characterized by generalized or nearly generalized erythema of the skin accompanied by a variable degree of scaling.

Data from dermatology textbooks are mainly based on three large retrospective studies, all from Western countries[1-3]. More recently, six additional studies have been published, from Finland, India, Netherlands, United states, Spain[4-8] and Singapore[9].

To study the causes, incidence and clinicopathological features of erythroderma, patient records at Siriraj Hospital, Thailand between 1985 and 1994 (10 years) were reviewed. Our data are discussed and compared with those of earlier series.

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MATERIAL AND METHOD

Patients

From 1985 to 1994, 49 patients over the age of 12 were admitted to Siriraj Hospital with the diagnosis of generalized exfoliative dermatitis or erythroderma. The information was collected from the patients' records and included clinical, laboratory, histopathologic, and follow-up data.

Patients were classified into five groups depending on the cause of the erythroderma: (1) exacerbation of a preexisting dermatosis, (2) systemic drug reactions, (3) cutaneous T cell lymphoma, (4) paraneoplastic, (5) idiopathic.

RESULTS

Clinical data and etiology

In the 10-year study period, erythroderma was diagnosed in 49 patients. Men outnumbered women in a proportion of 2:1. The mean age at diagnosis was 51.7 ± 19.7 (SD) years (range, 16-83 years). The mean follow-up period was 6.5 months (range, 1 month to 3 years). Fig. 1 shows patient distribution according to age when erythroderma was first diagnosed. Clinical data are shown in Table 1.

The 49 patients were divided into five etiologic groups: (1) previous dermatoses: psoriasis 8; atopic dermatitis 1, pityriasis rubra pilaris 3, pemphigus foliaceous 1 (total: 13, 26.5%) (2) drug reactions (total: 19, 38.77%) (3) cutaneous T cell lymphoma (total: 0, 0%) (4) malignancies: cervical carcinoma, 1 (total: 1, 2.04%) (5) undetermined (total: 16, 32.65%). Among our patients, drug allergy was the most common cause of the erythroderma. Because there is no accurate test to determine drug hypersensitivity, the diagnosis was established by history. The causal relationship between a drug and erythroderma was established from the antecedent of intake of the drug in days preceding the onset of erythroderma, and clearing of the latter on withdrawal of the drug. If the reaction showed signs of regression during continued administration of the drug, any causal relationship was judged to be unlikely[10]. The most common agents were antibiotics (10 cases), anticonvulsants (3 cases), antituberculous drug (1 case), allopurinol (1 case), and others (4 cases) (Table 2).

Drug-induced erythrodermas in this series had a more acute onset than erythroderma due to

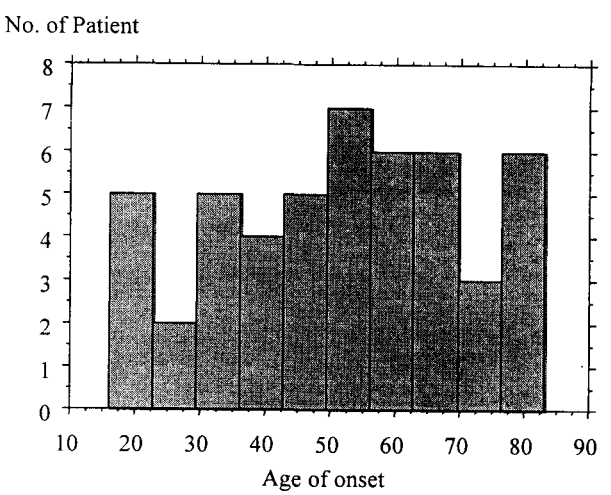

Fig. 1. Histogram shows age distribution of 49 patients.

Table 1. Clinical findings in patients with erythroderma.

Clinical findings	No. of Patient	Per cent
Keratosis of palms and soles	22	44.9
Nail involvement	17	34.7
Scalp involvement	26	53
Mucous membrane involvement	7	14.3
Photosensitivity	1	2
Fever	17	34.7
Lymph node enlargement	14	28.6
Hepatomegaly	5	10.2
Splenomegaly	0	0
Jaundice	7	14.3

Table 2. Culpable drugs in 49 patients.

	No. of patients	%
Antibiotics	10	52.6
Penicillin	4	21.1
Sulfonamides	4	21.1
Tetracycline	2	10.5
Anticonvulsants	3	15.8
Phenytoin	2	10.5
Phenobarbital	1	5.3
Antituberculous drugs	1	5.3
Thiacetazone	1	5.3
Allopurinol	1	5.3
Colchicine	1	5.3
Phenylbutazone	1	5.3
Other	2	10.5

other causes (p = 0.0239 : Logrank (Mantel-Cox)) (Fig. 2). The resolution time for the drug-induced erythrodermas after the drug was withdrawn was quite long (mean: 5.94 ± 5.41 weeks) when compared with the other drug eruptions such as Steven-Johnson's Syndrome. However, the resolution in the drug-induced group was significantly shorter than the other groups (p = 0.0239 : Logrank (Mantel-Cox)) (Fig. 3).

Five of forty nine patients had hepatomegaly; 4 of them (80%) were caused by drugs. In contrast, in 44 patients with no hepatomegaly, 15

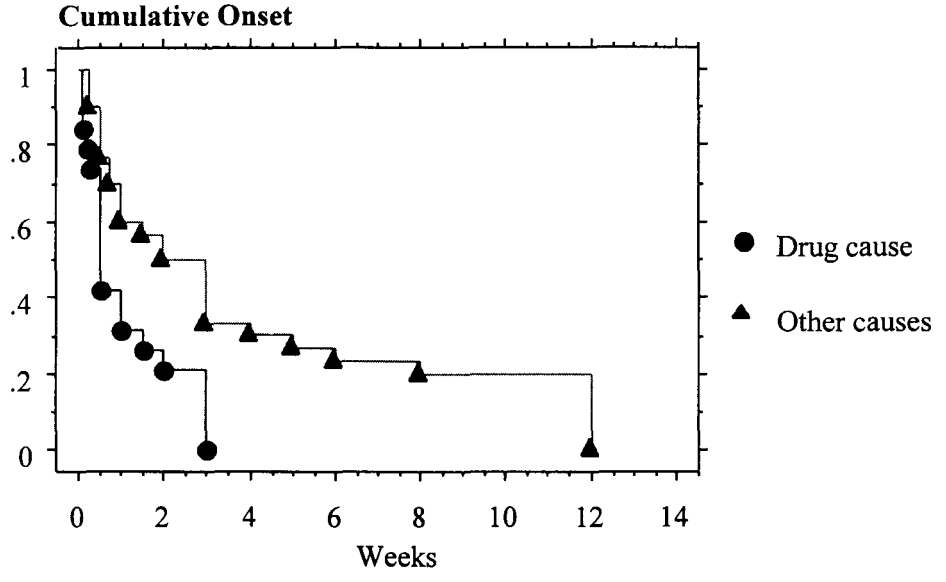

Fig. 2. Onset time of drug-induced erythroderma *versus* the other groups (p = 0.0021 : Logrank (Mantel-Cox)).

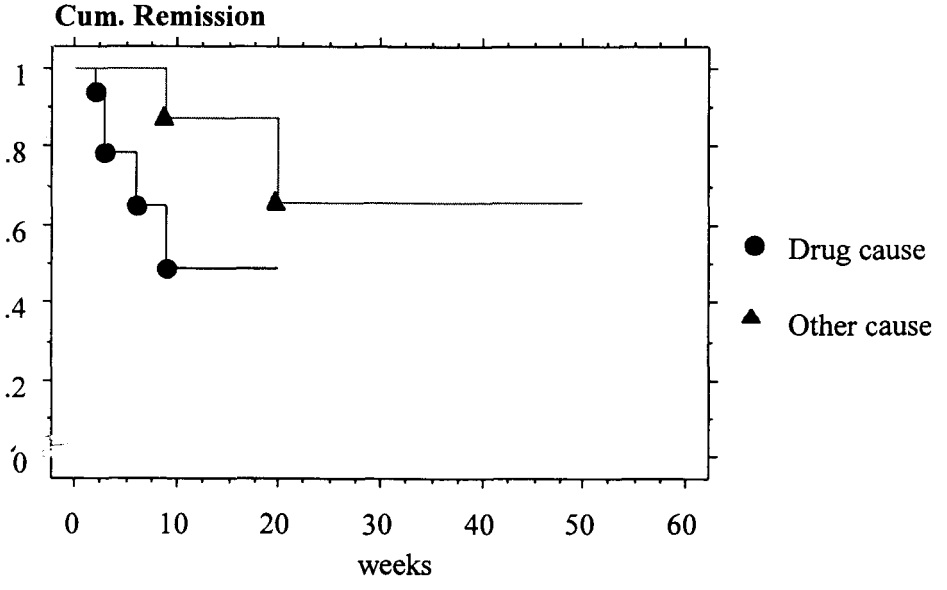

Fig. 3. Cumulative remission time of drug-induced erythroderma and the other groups (p = 0.0239 : Logrank (Mantel-Cox)).

were caused by drugs (34%). The relationship between drug cause and hepatomegaly was significant (p=0.046). Seven of the 49 patients had jaundice; 6 of them (86%) were caused by drugs. Only 1 in 30 patients without jaundice was caused by drugs (3.3%). Thus, the relationship between drug cause and jaundice was highly significant (p=0.0059).

Nail changes in the form of pitting, ridging, subungual hyperkeratoses, onycholysis were found in 17 patients. The nail change was found in seven of eight patients with psoriasis, all three cases with pityriasis rubra pilaris, and one patient with pemphigus foliaceus. However, only two of nineteen patients with drug reaction and four of sixteen patients with idiopathic erythroderma had nail involvement. Thus, the relationship between the nail change and erythroderma caused by previous dermatoses was significant (p=0.0001).

Alopecia occurred in 3 patients (6%). It was a diffuse pattern. Twenty six patients (53%) developed scalp lesions similar to their skin lesions. Erosion of the mucous membrane was found in 7 patients (14.3%); 4 of them were caused by drugs and the other three were idiopathic erythroderma. The relationship between drug cause and mucous membrane involvement was not significant (p= 0.2295).

Laboratory findings

The main laboratory abnormalities are summarized in Table 3. Eosinophilia of the blood was present in 25 of 47 patients. Eight of these were considered to have a drug allergy. Ten of 22 patients without eosinophilia also had a drug allergy. There was no significant relationship between drug allergy and eosinophilia (p=0.3437).

Abnormal liver function test (LFT) was defined by high bilirubin (total >1.5 mg/dl, or direct > 0.3 mg/dl) or elevated liver enzyme (SGOT > 40 U/L or SGPT > 40 U/L) (Table 3). Thirteen of forty six patients had abnormal LFT; 9 of them (69%) were caused by drugs. In contrast, in 33 patients with normal LFT, 8 were caused by drugs (24%). The relationship between drug cause and hepatomegaly was significant (p=0.0044). Unfortunately, Sézary cell count was not done and idiopathic cases may be pre- Sézary Syndrome.

Histopathologic examination

Histopathologic examination was performed in 36 (73%) of the 49 patients. The biopsy was usually performed on the first day after admission to the hospital. A skin biopsy was not performed in the rest of the cases because the cause of erythroderma was clear from the start (previous dermatoses or treatment with some drug in the days before the appearance of erythroderma).

Histologic diagnosis and its clinical correlation are shown in Table 4 (final diagnosis was the result of the evaluation of the clinical, biochemical, and histologic findings and of the evaluation of the erythroderma in each individual patient).

Table 3. Laboratory findings in patients with erythroderma.

Laboratory findings	Drug	Other causes
Anemia: males (Hct. < 40%) females (Hct. < 37%)	61.1%	56.7%
Leucocytosis (wbc > $10x10^9$/L)	77.8%	66.7%
Eosinophilia (>$500x10^6$/L)	44.4%	58.6%
Elevated creatinine level (>1.5 mg/dl)	22.2%	13.8%
Hypoalbuminemia (<4 mg/dl)	76.5%	71.4%
Abnormal Liver Function Test	52.9%	13.8%
• Bilirubin : total >1.5 mg/dl, or direct > 0.3 mg/dl		
• or SGOT > 40 U/L		
• or SGPT > 40 U/L		

DISCUSSION

The clinical features of erythroderma are nonspecific, with few cause-orienting clues. Some conclusions may be drawn from the mode of onset of erythroderma. In about 60 per cent of cases related to drugs, the onset was acute, i.e., erythroderma was established in 3 days or less after appearance of rash. Certain clinical features such as the degree of desquamation, fever, lymphadenopathy, photosensitivity, involvement of scalp, palms, soles, or mucous membrane could not be related to any specific cause. However, nail involvement was found more in cases related to previous dermatosis such as psoriasis and pityriasis rubra pilaris. Hepatomegaly, jaundice and abnormal LFTs were seen more in cases caused by drug hypersensitivity.

Laboratory examinations were not informative in our study as well as in others[3,4]. Anemia, leukocytosis, eosinophilia and hypoalbuminemia were the common abnormalities found in this condition regardless of causes. It seemed that the leucocytosis and eosinophilia was a reaction to the erythroderma and had no other significance. Eosino-

Table 4. Histopathologic diagnosis and its clinical correlation.

Histologic diagnosis	no. of patients	Final diagnosis	no. of patients
Chronic nonspecific dermatitis	22	Psoriasis	2
		Drug reactions	8
		Idiopathic erythroderma	12
Psoriasiform dermatitis	4	Psoriasis	1
		Drug reactions	2
		Idiopathic erythroderma	1
Psoriasis	4	Psoriasis	4
Drug reactions	2	Drug eruption	2
Pityriasis rubra pilaris	3	Pityriasis rubra pilaris	3
Pemphigus foliaceous	1	Pemphigus foliaceous	1

Table 5. Causes of erythroderma in previous publications compared with the present series.

Authors(s) (year)	No. of patients	Preexisting dermatoses (%)	Systemic drug reaction (%)	CTCL (%)	Paraneo plastic (%)	Idiopathic (%)
Wilson[2] (1954)	50	46	8	4	4	38
Abrahams et al[1] (1963)	101	35	11	2	6	46
Nicolis and Helwig[3] (1973)	135	27.5	40	8	12.5	12
Hasan and Jansen[5] (1983)	50	54	10	4	0	32
King et al[6] (1986)	82	32	34	18	0	16
Sehgal and Srivastava[8] (1986)	80	57.5	20	0	0	22.5
Botella-Estrada et al[4] (1994)	56	66	12.5	12.5	0	9
Sigurdsson et al[7] (1996)	102	53	5	13	3	26
Present series	49	26	39	0	2	33

CTCL, Cutaneous T-cell lymphoma

philia was a common finding in our study (53%) similar to other studies (20 to 48 %)[3,5,7,8]. However, there was no significant relationship between drug allergy and eosinophilia (p=0.3437).

Clinicopathologic correlation in our study did not inform the etiology which was similar to other studies[3,4]. Frequently, the histopathologic diagnosis was chronic nonspecific dermatitis or psoriasiform dermatitis, without any clue as to its origin. In this series histologic diagnosis was helpful in establishing a final diagnosis in 9 (25%) of the 36 patients in whom cutaneous biopsies were performed. The best clinicohistologic correlation was found in psoriasis, pityriasis rubra pilaris and pemphigus foliaceous-related erythroderma. Nevertheless, our data concerning pemphigus foliaceous were small since only one patient with this disease was included in this article.

Comparison of the etiologic groups among the previous series and our own is given in Table 5. The main cause of the erythroderma in our series was drug reactions. The culprit drugs found in our series were similar to that found in our series of Stevens-Johnson syndrome[11]. The exacerbation of a preexisting dermatosis was the second most important cause in our series which was found to be the main cause in most of the previous studies. Although our department is in the tropical region, all patients denied any influence of sun exposure on their disease so no phototesting with UV light was performed.

The group of patients with idiopathic erythroderma deserves special mention. The clinical characteristics of this subset were not different from those of the general group. The most common histologic finding was chronic nonspecific dermatitis (12 in 13 patients). In most cases, the onset of erythroderma was insidious (13 in 16 patients).

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โรคผิวหนังแดงในผู้ป่วยไทย

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โรคผิวหนังแดงเป็นอาการแสดงทางผิวหนังที่มีอาการแดงทั่วตัวซึ่งเกิดขึ้นได้จากหลายสาเหตุ วัตถุประสงค์ของการศึกษานี้ได้แก่ การหาอุบัติการ, สาเหตุ และลักษณะทางคลินิก ร่วมกับลักษณะทางพยาธิของผู้ป่วยดังกล่าว เราได้ทำการศึกษาลักษณะทางคลินิก. ผลทางห้องปฏิบัติการ และผลชิ้นเนื้อของผู้ป่วยจำนวน 49 รายที่ได้รับการวินิจฉัยว่าเป็นโรคผิวหนังแดง ซึ่งได้รับการรักษาในภาควิชาตจวิทยา โรงพยาบาลศิริราชในช่วง 10 ปีที่ผ่านมา (พ.ศ. 2528 ถึง 2537) จำนวนผู้ป่วยหญิง : ผู้ป่วยชาย เป็น 2 : 1 ค่าอายุเฉลี่ยเมื่อได้รับการวินิจฉัยคือ 51.7 ปี สาเหตุที่พบได้บ่อยที่สุดคืออาการแพ้ยา (38.77%) รองลงมาคือ โรคผิวหนังอื่น ๆ (26.5%) ในกลุ่มผู้ป่วยแพ้ยาจะพบอาการตับโต ตัวเหลือง และความผิดปกติของผลทางห้องปฏิบัติการทางตับได้สูงกว่ากลุ่มอื่น ขณะที่ความผิดปกติที่เล็บพบได้บ่อยในผู้ป่วยที่เกิดจากโรคผิวหนังอื่น ๆ ในการศึกษานี้เราพบว่าลักษณะทางคลินิกและลักษณะทางพยาธิไม่สามารถบอกถึงสาเหตุของโรคได้ เพราะลักษณะทางพยาธิที่พบบ่อยได้แก่ chronic nonspecific dermatitis และ psoriasiform dermatitis ซึ่งไม่สามารถบอกถึงสาเหตุของโรคได้ เราพบโรคผิวหนังแดง ที่เกิดจากยามักจะมีการกระจายของโรคเร็วและมีการดำเนินของโรคที่ดีและหายได้เร็วกว่าเมื่อหยุดยา ขณะที่ลักษณะทางพยาธิและผลการตรวจทางห้องปฏิบัติการมักจะไม่ช่วยการวินิจฉัยหรือการหาสาเหตุ

คำสำคัญ : โรคผิวหนังแดง, การศึกษาลักษณะทางคลินิกร่วมกับลักษณะทางพยาธิ, การแพ้ยา

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