

Exfoliative dermatitis: A 7-year retrospective study in Ramathibodi Hospital

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ABSTRACT:

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Background: Exfoliative dermatitis or erythroderma is an inflammatory skin disorder that may be caused by various diseases and medications.

Objectives: To determine the cause, clinicopathological features and prognosis of these patients in Ramathibodi Hospital.

Materials and Methods: We reviewed the clinical, laboratory, biopsy materials and follow-up data of 38 patients diagnosed with exfoliative dermatitis in Ramathibodi hospital over 7-year periods (2004 through 2010).

Results: The male to female ratio was 3:1. The mean age at diagnosis was 65 years. The two most common etiologies were drug eruption (47.3%), followed by pre-existing dermatosis (36.8%). Cutaneous T-cell lymphoma was found in one case. The cause of the erythroderma could not be determined in 13% of the cases. The onset of the disease was usually insidious except in drug-induced exfoliative dermatitis. In the drug-induced group, anti-tuberculosis drug was the most offending drug (27.8%). In the pre-existing dermatosis group, psoriasis is the most common etiology (64%). Scaling, erythema and pruritus were found in all patients. Nail involvement was found mostly in cases with pre-existing dermatosis. Eosinophilia and hypoalbuminemia were common findings, which presented in more than 50% of the patients.

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Abnormal liver function tests occurred more commonly in the drug-induced group. Histopathology was mostly unrewarding. A clinicopathologic correlation was present only in psoriasis, eczema and cutaneous T-cell lymphoma. Follow-up data was obtained in 26 patients. Most of the patients improved after treatment (69%). Small group of the patients were still unchanged (15%) and 4 patients died from another causes unrelated to the erythroderma.

Conclusion: This study outlines the underlying etiology of exfoliative dermatitis, which had a high percentage of drugs and pre-existing dermatosis. Histopathology were non-specific in most of the cases. The prognosis of most patients is relatively good.

Key word: exfoliative dermatitis, erythroderma, clinicopathological, prognosis

บทคัดย่อ:

วิภาดา พันธุ์ฉวี พลอยทราย รัตนเขมากร การศึกษาย้อนหลัง 7 ปีในผู้ป่วยผิวหนังแดงลอกในโรงพยาบาลรามธิบดี วารสารโรคผิวหนัง 2013; 29: 151-158.

หน่วยโรคผิวหนัง ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามธิบดี มหาวิทยาลัยมหิดล

โรคผิวหนังแดงลอกเป็นการอักเสบของผิวหนังซึ่งเกิดจากหลายสาเหตุทั้งโรคภายใน, โรคผิวหนังหรือยา

วัตถุประสงค์: เพื่อหาสาเหตุ ลักษณะทางคลินิก ลักษณะทางพยาธิวิทยา และการพยากรณ์โรคในผู้ป่วยผิวหนังแดงลอกที่ได้รับการตัดชิ้นเนื้อในโรงพยาบาลรามธิบดี

วิธีการศึกษา: เป็นการศึกษาย้อนหลังโดยรวบรวมข้อมูลลักษณะทางคลินิก ผลการตรวจทางห้องปฏิบัติการ ลักษณะทางพยาธิวิทยา และการติดตามผลการรักษาจากเวชระเบียนของผู้ป่วยโรคผิวหนังแดงลอกที่ได้รับการตัดชิ้นเนื้อ 38 รายในแผนกผิวหนังโรงพยาบาลรามธิบดีในช่วงเวลา 7 ปี (พ.ศ.2547-2553)

ผลการศึกษา: พบผู้ป่วยชายมากกว่าผู้ป่วยหญิง 3 เท่า โดยมีอายุเฉลี่ย 65 ปี การดำเนินโรคมักจะค่อยเป็นค่อยไป ยกเว้นในกลุ่มที่มีสาเหตุจากยา สาเหตุที่พบบ่อยที่สุดเกิดจากยา (47.3%) รองลงมาคือโรคผิวหนังเดิมของผู้ป่วย (36.8%) โดยผู้ป่วยหนึ่งรายเป็น cutaneous T-cell lymphoma และไม่ทราบสาเหตุ (13%) ยาที่พบบ่อยที่สุดในกลุ่มที่เกิดจากยา ได้แก่ ยาต้านวัณโรค (27.8%) และโรคสะเก็ดเงินเป็นสาเหตุที่พบบ่อยที่สุดในกลุ่มที่เกิดจากโรคผิวหนังเดิมของผู้ป่วย (64%) ลักษณะผื่นแดง คันและลอกเป็นขุยพบในผู้ป่วยทุกราย ความผิดปกติของเลือดมักพบในผู้ป่วยที่มีโรคผิวหนังอยู่เดิม Eosinophilia และ Hypoalbuminemia พบได้บ่อยโดยพบบ่อยกว่าครึ่งหนึ่งของผู้ป่วย การทำงานของตับที่ผิดปกติส่วนใหญ่เกิดในกลุ่มที่มีสาเหตุจากยา ลักษณะทางพยาธิวิทยาโดยส่วนใหญ่ไม่ได้ช่วยในการวินิจฉัยโรคนอกจากในกลุ่มที่มีสาเหตุจากโรคผิวหนัง เช่น โรคสะเก็ดเงิน โรคผื่นผิวหนังอักเสบและ cutaneous T-cell lymphoma ข้อมูลการติดตามผลการรักษาในผู้ป่วย 26 รายพบว่าผู้ป่วยส่วนใหญ่ดีขึ้นหลังการรักษา (69%) อาการคงที่ (15%) และผู้ป่วย 4 รายเสียชีวิตจากสาเหตุอื่นที่ไม่เกี่ยวข้องกับการโรคผิวหนังแดงลอก

สรุป: การศึกษานี้แสดงถึงสาเหตุของโรคผิวหนังแดงลอกในโรงพยาบาลรามธิบดีซึ่งพบว่าส่วนใหญ่เกิดจากยา และโรคผิวหนังเดิมของผู้ป่วย ผลทางพยาธิวิทยาส่วนใหญ่ ไม่เฉพาะเจาะจงและการพยากรณ์โรคในผู้ป่วยส่วนใหญ่ ก่อนข้างดี

คำสำคัญ: โรคผิวหนังแดงลอก, ลักษณะทางคลินิก, ลักษณะทางพยาธิวิทยา, การพยากรณ์โรค

Exfoliative dermatitis or erythroderma is defined clinically as generalized redness and scaling of the skin involving more than 90% of the body surface area. It was first described by Hebra in 1868. It is a symptom complex that may caused by a variety of diseases and medications. The most common cause are exacerbations of an underlying skin disease, drug reactions and malignancies, primarily cutaneous T-cell lymphoma (CTCL). The histopathology is often non-specific.

In this study, we aim to determine the cause, clinicopathological features and prognosis of the patients diagnosed with erythroderma in Ramathibodi Hospital between 2004-2010 (7 years) and compare this study with the previous published studies.

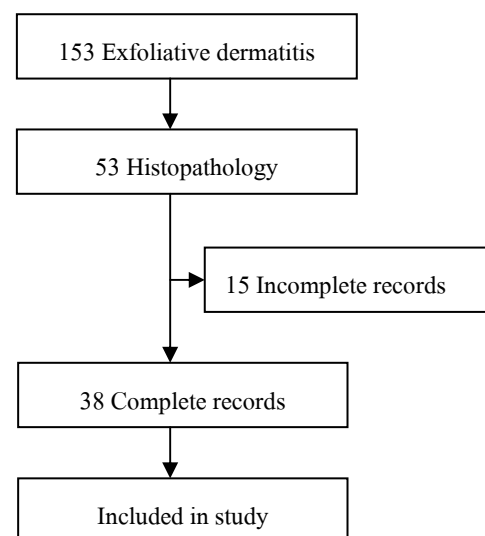
Patients and materials

This study included all patients diagnosed with erythroderma who had undergone skin biopsy by the dermatologist in dermatology unit, Ramathibodi Hospital, during the period from Jan 2004 to Dec 2010. All the patients diagnosed with erythroderma had erythema involving more than 90% of the body surface area. The data was obtained from the patients' medical records including the onset and duration of the erythroderma, previous skin diseases or drugs intake history, clinical, laboratory, histopathologic and follow-

up data.

Results

153 patients diagnosed with exfoliative dermatitis during 7-year period (2004-2010). Skin biopsy were done in fifty-three patients. Fifteen charts were missing. Thirty-eight patients were included in this study. (Figure 1)



The male to female ratio was 3:1. The mean age at diagnosis was 65 years. The onset of the disease was usually insidious, usually more than two weeks, except in drug-induced group.

Etiology

This study categorized patients into four groups based on their etiology. The most common etiology was drug eruption (47.3%), followed by pre-existing dermatosis (36.8%). Cutaneous T-cell lymphoma was found in one case (2.6%). The cause of the erythroderma could not be determined in 13% of the cases. (Table 1)

Table 1 Etiology

Etiology	Number of patients	%
Drug eruptions	18	47.3
Pre-existing dermatosis	14	36.8
Idiopathic	5	13.1
Malignancy (CTCL)	1	2.6

In the drug-induced exfoliative dermatitis group including 18 patients, anti-tuberculosis drug was the most offending drug (27.8%), followed by antibiotics (16.6%) and lipid-lowering agent (16.6%), antihypertensive drug (11.1%) and herb (11.1%). NSAIDS, fluconazole, laxatives were recorded as the etiology in only one case for each drug. The culprit drugs are shown in Table 2.

In the pre-existing dermatosis group including 14 patients, psoriasis was the most common etiology (64%). The remaining cause was eczema accounting for 36% of the cases.

Table 2 The culprit drugs (n = 18)

Drug	Number of patient	%
Anti-tuberculosis drug	5	27.8
IRZE	1	5.6
IEOS	1	5.6
Ethambutol	3	16.6
Antibiotics	3	16.6
Amoxycillin	1	5.6
Levofloxacin	1	5.6
Ampicillin/Sulbactam	1	5.6
Lipid-lowering agent	3	16.6
Simvastatin	2	11.1
Atorvastatin	1	5.6
Antihypertensive drug	3	16.6
Amlodipine	2	11.1
Losartan/HCTZ	1	5.6
Herb	1	5.6
NSAIDS (Diclofenac)	1	5.6
Fluconazole	1	5.6
Laxatives	1	5.6

I = Isoniazid; R= Rifampicin; Z = Pyrazinamide; E= Ethambutol;
O = Ofloxacin; S= Streptomycin; HCTZ = Hydrochlorothiazide

Malignancy was found in only one case. Cutaneous T-cell lymphoma was diagnosed from the fourth biopsy.

Clinical presentation

Scaling, erythema and pruritus were found in all patients. Scalp involvement was recorded in 31% of the cases. Nail changes were found in 8 cases (21%). Nail abnormalities included pitting nails, onycholysis,

subungual hyperkeratosis, dystrophic nails and Beau's line were significantly found in pre-existing dermatosis group than other group ($P=0.002$). In this group, nail involvement was found mostly in psoriasis (62%). Keratosis of palms and soles were recorded in 7 cases (18%). Mucosal involvement was not found in our study.

Table 3 Clinical presentations of patients with erythroderma

Clinical presentations	Number of patients	%
Scalp involvement	12	31.5
Nail involvement	8	21
Keratosis of palms and soles	7	18.4
Mucous membrane lesion	0	0
Fever	5	13.1
Lymphadenopathy	5	13.1
Hepatosplenomegaly	1	2.6
Edema	3	7.8

Systemic symptoms included fever (13%), lymphadenopathy (13%), edema (8%), and hepatomegaly (2.6%). Fever and lymphadenopathy were present in all groups. Hepatosplenomegaly occurred only in the case of cutaneous T-cell lymphoma. (Table 3)

Table 4 Lab abnormalities in all erythrodermic patients and drug-induced subgroup.

Lab findings	Total	Drug-induced	P-value
Anemia Hct < 40% (male) Hct < 34% (female)	50%	42.1%	-
Leukocytosis (WBC > 11,000/ μ l)	42.1%	37.5%	-
Eosinophilia (Eosinophil > 450/ μ l)	57.8%	54.5%	0.5
Elevated creatinine level (Cr > 1.3 mg/dl)	28.9%	45.4%	-
Hypoalbuminemia (Albumin < 34 g/L)	60.5%	34.7%	-
Abnormal LFT TB > 1, DB > 0.3 or SGOT > 40 or SGPT > 40	31.5%	58.3%	0.06

Laboratory investigations

Eosinophilia and hypoalbuminemia were two common findings which presented in more than 50% of the patients. Eosinophilia was found mostly in drug-induced group but was not significant difference from patients in other groups ($P=0.5$). Elevated liver function test including SGOT (15.7%), SGPT (23.6%), bilirubin (10.5%) occurred more frequent in the drug-induced group ($P=0.06$). Elevated creatinine level (28.9%), anemia (50%), leukocytosis (42%) were other laboratory investigations in our study. (Table 4)

Clinicopathologic correlation was shown in Table 5. Only biopsy specimen from psoriasis, eczema and

cutaneous T-cell lymphoma patients which showed a clue for diagnosis. In idiopathic cases, non-specific skin biopsy was reported.

Prognosis

Follow-up data was obtained for 26 patients. Most of the patients improved after treatment (69%). Small

group of the patients still unchanged (15%) and 4 patients died from other causes unrelated to the erythroderma. Erythroderma from psoriasis, cutaneous T-cell lymphoma and idiopathic showed protractible course.

Table 5 Clinicopathologic correlations (n = 38)

Histologic findings	Number of patients (%)	Final diagnosis
Superficial perivascular dermatitis	3 (7.9%)	Drug eruption Idiopathic Paraneoplastic
Psoriasiform dermatitis	6 (15.8%)	Drug eruption Idiopathic Psoriasis
Lichenoid dermatitis	5 (13.2%)	Drug eruption Idiopathic
Spongiotic dermatitis	16 (42.1%)	Drug eruption Idiopathic Eczema
Psoriasis	7 (18.4%)	Psoriasis
Cutaneous T-cell lymphoma	1 (2.6%)	Cutaneous T-cell lymphoma

Table 6 Prognosis (n=26)

Etiology	Cleared	Improved	Unchanged	Dead
Drug eruptions (n=12)	5	4	2	1
Pre-existing dermatosis (n=8)	0	6	0	2
Idiopathic (n=5)	1	2	1	1
Cutaneous T-cell lymphoma (n=1)	0	0	1	0

Table 7 Comparison of etiology with previous studies

Authors (years)	Number of patients	Drugs (%)	Pre-existing dermatosis (%)	CTCL (%)	Idiopathic (%)
Abrahams et al ¹ (1963)	101	11	35	2	46
Nicolis and Helwig ² (1973)	135	40	27.5	8	12
Hasan and Jansen ³ (1983)	50	10	54	4	32
King et al ⁴ (1986)	82	34	32	18	16
Botella-Estrada et al ⁵ (1994)	56	21.5	66	12.5	9
Leenutaphong et al ⁶ (1999)	49	39	26	0	33
Akhyani et al ⁷ (2005)	97	21.6	57.9	10.3	7.2
Xiao-Ying YUAN et al ⁸ (2010)	82	17	72	2.4	6.1
Present studies (2012)	38	47.3	36.8	2.6	13.1

Discussion

Erythroderma is not a common skin condition. Establishing the etiology of erythroderma can be challenging because it can be caused by a variety of cutaneous and systemic diseases. Subgroup comparison based on etiology from various studies was showed in Table 7. In our study, the most common cause of erythroderma was drug-induced which is similar to previous studies including study from Siriraj Hospital, Thailand.^{2,4,6} Drug as an etiology of erythroderma varied among studies. Anti-tuberculosis drug were main causative agents in our study while antibiotics^{4,6}, sulfonamides² were the cause of erythroderma from other studies. Cutaneous T-cell lymphoma induced erythroderma showed low incidence in compare with other studies.^{2,4 5,7} The onset of exfoliative dermatitis was usually insidious, gradually develop in more than

two weeks, except in drug-induced group.

Clinical features were mostly not indicative of the underlying etiology. In our study, certain clinical features such as the degree of erythema, scaling, itching, scalp and palmoplantar involvements could not be related to a specific cause. Nail involvement was the only feature that was significantly found in pre-existing dermatosis group especially in psoriatic patients. Systemic symptoms such as fever and lymphadenopathy were present in all groups but hepatosplenomegaly occurred only in the case of cutaneous T-cell lymphoma.

Laboratory investigations were not informative in our study as well as in other studies.^{2,5} Anemia, leukocytosis, eosinophilia and hypoalbuminemia common abnormalities found in our study.

Eosinophilia and abnormal liver function test found

more frequent in drug-induced exfoliative dermatitis group but was not statistically significance difference when compared to the other groups. Histopathology was mostly unrewarding. Most of the biopsy specimens were non-specific. Spongiotic dermatitis was found more frequent in our study. A clinicopathologic correlation was present only in psoriasis, eczema and cutaneous T-cell lymphoma.

Follow-up data was obtained for 26 patients. Most of the patients symptoms improved after treatment (69%). Small group of the patients were still unchanged (15%) and 4 patients had died from another causes unrelated to the erythroderma. In the persistence group, CTCL was diagnosed from the fourth biopsy. This patient also developed lymphadenopathy and hepatosplenomegaly at the time of diagnosis (3 years after onset of exfoliative dermatitis).

Idiopathic erythrodermic group showed non-specific dermatitis from skin biopsy and the cause could not be determined. There is a possibility that these patients represent a pre-malignant phase. A regular follow-up with repeated skin biopsy may lead to final diagnosis.

In conclusion, this study outlined the underlying etiology of exfoliative dermatitis, which showed high percentage of drug-induced and pre-existing dermatosis. Histopathology was non-specific in most of the cases. The prognosis of most patient is relatively good. Protracted clinical course is a clinical clues to investigate for malignancy. Close follow up with total body physical examination and repeated skin biopsy are crucial in persistent cases.

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