Study of the Incidence, Clinical Features, and Management of Adult Exfoliative Dermatitis in Sakon Nakhon Hospital, Thailand

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ABSTRACT:

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Background: Exfoliative dermatitis is the clinical finding of generalized erythema and scaling of the skin affecting more than 90% of the total body surface area. Prospective studies of exfoliative dermatitis are few in the literature. The aim of this study was to analyze the incidence, clinical features, and management of exfoliative dermatitis patients.

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Materials and Methods: This prospective study was performed at Sakon Nakhon Hospital, Thailand, and included 32 patients who were diagnosed with exfoliative dermatitis in January-December 2019. Then the patients were followed up for 12 months. The incidence, clinical features, laboratory investigations, treatments, and outcomes were collected.

Results: Hospital incidence in 1 year of exfoliative dermatitis was 160 cases/100,000 dermatological outpatients or 32 cases/year. The mean age was 50 years old. Psoriasis was the most frequent etiology of exfoliative dermatitis. All patients had pruritus and erythematous plaques with scales. Other common clinical features were nail alterations and fever. Abnormal laboratory investigations were anemia, leukocytosis, eosinophilia, and high erythrocyte sedimentation rate. Combinations of systemic drugs (systemic steroids, methotrexate, cyclosporine, acitretin) and topical drugs were the main treatments. The comparison between psoriasis and eczema groups in exfoliative dermatitis showed that the eczema group had higher ages, higher eosinophilia, lower serum total protein, shorter durations of treatments, lower percentages of last body surface area, and higher numbers of complete clearance patients than the psoriasis group.

Conclusion: This study had high hospital incidence of exfoliative dermatitis in Thailand. Exfoliative dermatitis usually presented generalized scaly erythema of the skin. Multiple skin disorders could cause exfoliative dermatitis. Complete physical examinations and investigations should be performed in each patient.

Key words: Exfoliative dermatitis, incidence, clinical features, management, outcome

Introduction

Exfoliative dermatitis(ED) or erythroderma, is characterized by generalized scaly erythema of the skin, affecting more than 90% of our total body surface area(BSA). The incidence of ED varies between 0.9 cases per 100,000 persons in the Netherlands and 1-2 cases per 100,000 persons in Finland[1,2]. In Thailand, hospital incidences of ED are 4.9 cases/year per 100,000 dermatological outpatients and 9 cases/year[3,4].

Exacerbation of previous skin disorders (e.g. psoriasis, eczema, atopic dermatitis, pityriasis rubra pilaris, pemphigus vulgaris (PV), pemphigus foliaceus), drug eruption, and cutaneous T cell lymphoma (CTCL) can cause ED[5,6]. Although generalized scaly erythema of the skin is the main symptom in ED, patients may present other symptoms (e.g. fever, arthritis, nail change, conjunctivitis, lymphadenopathy)[6,7]. Abnormal investigations are anemia, leukocytosis, eosinophilia, and high erythrocyte sedimentation

rate (ESR)[6,7]. Thus, complete physical examinations and investigations should be performed in each ED patient. Treatments include systemic drugs, topical drugs, phototherapy, and supportive treatment. However, the treatments are different due to the etiology of individual patients. Currently, prospective studies of ED are rare in the literature. The aim of this study was to analyze the incidence, clinical features, and management of ED patients.

Methods

This prospective study was performed at the Division of Dermatology, Department of Medicine, Sakon Nakhon Hospital, Thailand. A total of 32 new patients who were diagnosed with ED in January-December 2020 were included in this study. Then all the patients were followed up for 12 months. The inclusion criteria for the patients in this study were as follows: (1) was at least 18 years old, (2) had generalized scaly erythema skin in at least 90% of BSA, (3) was diagnosed with ED by a dermatologist, (4) gave permission to record demographic data, clinical features, investigations, treatments, and outcomes. The only exclusion criterion was that the patient did not allow the recording of data. The data collected from the patients included demographic data (e.g. sex, age, underlying disease), clinical features (e.g. pruritus, pain, burning, skin sign, arthritis, nail alterations, fever, lymphadenopathy, hepatitis), laboratory investigations (e.g. blood count, blood chemistry, ESR), treatments (systemic drugs, topical drugs, durations of treatments, and outcome (percentages of last BSA, complete clearance). Finally, all data of the 32 patients were analyzed in the study due to complete follow up records for 12 months. No missing data were detected.

Statistical analyses were performed with SPSS version 25. Categorical variables were described as frequency and percentages, while continuous variables were expressed as mean, standard deviation (SD), and median, depending on the distribution of the data. Differences between groups were tested by Fisher's exact test, Student t-test, and Mann-Whitney test. A two-sided p-value of <0.05 was considered statistically significant.

The study was approved by the local ethics committee and followed the principles of the Declaration of Helsinki. Consent forms of all the participants were obtained.

Results

All 32 patients had a complete follow up for 12 months. There were 18 males and 14 females, with a male-to-female ratio of 1.3. The mean age was 50 years, and 23 (72%) patients had previous skin disorders (15 psoriasis, 6 eczema, 1 atopic dermatitis, 1 PV). The most frequent etiology associated with ED was psoriasis (17 patients, 53%), followed by eczema (10 patients, 31%), drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, PV, lupus

erythematous/dermatomyositis (LE/DM) overlap, and extensive dermatophytosis with seborrheic dermatitis with autosensitization (Table 1). There was no evidence of idiopathic or malignancy-associated ED in this study.

As shown in Table 1, all patients had pruritic scaly erythematous plaques, while 1 patient had erosion, 5 patients had pain and a burning rash, and 3 patients had a pustular rash. Other common clinical features were nail alterations (26 patients) and fever (10 patients). Hepatitis, edema, generalized lymphadenopathy, arthritis, conjunctivitis, and oral mucositis were found in some patients.

Laboratory abnormalities are also summarized in Table 1, including anemia, leukocytosis, eosinophilia (high percentages of eosinophil, high eosinophil count), and high ESR. Skin biopsies were performed in 19 patients. Results of the skin biopsies were psoriasis, eczema, LE/DM, and drug eruption. There were no reports of CTCL from histopathology.

Table 1 The demographic data, clinical features, and laboratory investigations in exfoliative dermatitis patients

Number of patients	32 patients
Male: Female	18:14 (ratio 1.3:1)
Ages (mean±SD)	50±17.7 years
Cause of exfoliative dermatitis	
Psoriasis	17 (53.1%)
Eczema	10 (31.3%)
DRESS syndrome	2 (6.3%)
Pemphigus vulgaris	1 (3.1%)
LE/DM overlap	1 (3.1%)
Extensive dermatophytosis with seborrheic dermatitis with autosensitization	1 (3.1%)
Previous skin disorders	**23 patients (71.9%)**
- Psoriasis	15 (46.9%)
- Eczema	7 (21.9%)
- Pemphigus vulgaris	1 (3.1%)

Table 1 The demographic data, clinical features, and laboratory investigations in exfoliative dermatitis patients (continue)

Number of patients	32 patients
Main Symptoms	
Pruritic erythema rash with scale	32 (100%)
Pain/burning rash	5 (15.6%)
Pustular rash	3 (9.4%)
Erosion	1 (3.1%)
Other symptoms	
Nail alterations	26 (81.3%)
Fever	10 (31.3%)
Hepatitis	5 (15.6%)
Edema	4 (12.5%)
Conjunctivitis	4 (12.5%)
Generalized lymphadenopathy	3 (9.4%)
Arthritis	3 (9.4%)
Oral mucositis	1 (3.1%)
Investigation	
Hb (mean±SD)	11.9±2.5 g/dL
WBC (mean±SD)	11,140.3±3,128.3 /mm^3
Eosinophil %, median (min-max)	6.5 (0-37) %
Eosinophil count, median (min-max)	562.8 (0-4,935.8) /mm^3
Albumin (mean±SD)	3.5±0.6 g/dL
Total protein (mean±SD)	7.2±0.7 g/dL
ESR, median (min-max)	36.5 (7-119) mm/h
Skin biopsy	**19 patients (59.4%)**
Eczema	10 (31.3%)
Psoriasis	7 (21.9%)
Interface dermatitis (LE/DM)	1 (3.1%)
Drug eruption	1 (3.1%)

SD, standard deviation; DRESS, drug reaction with eosinophilia and systemic symptoms; LE, lupus erythematosus; DM, dermatomyositis; Hb, hemoglobin; WBC, white blood cell; ESR, erythrocyte sedimentation rate

Table 2 The demographic data, clinical features, laboratory investigations, treatments, and outcomes of 32 patients with exfoliative dermatitis according to etiology

	Psoriasis	Eczema	DRESS syndrome	LE/DM overlap	PV	Extensive dermatophytosis
Number of patients	17	10	2	1	1	1
Ages, years	44	58.8	57	61	27	63
Other diagnosis	PSA	AI, sepsis	ARF	-	-	AI
Hb, g/dL	12.1	11.7	8.6	10.6	13.5	15.2
WBC, /mm^3	10,875.9	11,465	8,650	9,380	13,160	17,110
Eo, %	3	12	6.5	13	1	2
Eo count, /mm^3	368.1	961.4	562.8	1,219.4	131.6	342.2
TP, g/dL	7.4	6.7	6	8	7.8	7.9
ESR, mm/h	38	20.5	70	90	32	73
Anemia/ patients	7	7	2	1	-	-
Leukocytosis/ patients	10	7	-	-	1	1
Eosinophilia/ patients	7	8	2	1	-	-
Low TP/ patients	-	4	2	-	-	-
High ESR/ patients	12	7	2	1	1	1
Systemic Tx	MTX Acitretin CsA	MTX Pred	Dexa IV Pred	Pred AZA HCQ	Pred AZA	Itraconazole Pred
Durations of Tx,months	12	9.3	3.25	12	12	2
% of last BSA,(min-max)	40 (5-100)	0 (0-35)	0	30	20	0
Complete clearance, patients	-	6	2	-	-	1

DRESS, drug reaction with eosinophilia and systemic symptoms; LE, lupus erythematosus; DM, dermatomyositis; PV, pemphigus vulgaris; PSA, psoriatic arthritis; AI, adrenal insufficiency; ARF, acute renal failure; Hb, hemoglobin; WBC, white blood cell; Eo, eosinophil; TP, total protein; ESR, erythrocyte sedimentation rate; Tx, treatments; MTX, methotrexate; CsA, cyclosporine A; pred, prednisolone; dexa, dexamethasone; IV, intraveneous; AZA, azathioprine; HCQ, hydroxychloroquine; BSA, body surface area

As shown in Table 2, psoriasis was the predominant etiology of ED. The mean age of psoriasis patients was 44 years. This group had plaque type psoriasis (15 patients) and pustular

psoriasis (2 patients). Nail alterations were the most common among other clinical features: pitting nail, onycholysis, chronic paronychia, subungual hyperkeratosis, nail dystrophy, onychomadesis, oil spot, and beau line. Abnormal investigations were anemia, leukocytosis, and high ESR. Treatments of psoriasis included methotrexate (7.5-15 mg/week, 10 patients), acitretin (10-25 mg/day, 10 patients), cyclosporine (100-250 mg/day, 4 patients), topical steroid, topical vitamin D analogue, topical tar, emollient, and antihistamine. The mean duration of treatments was 12 months. The median BSA of the last following episode was 40% (min-max: 5-100%) and no complete clearance (0% BSA) at the 12th month.

Table 3 The comparison of demographic data, laboratory investigations, treatments, and outcomes between the psoriasis and eczema groups in exfoliative dermatitis patients

	Psoriasis (17 patients)	**Eczema (10 patients)**	**P-value**
Ages, years	44	58.8	0.036 (95%CI: -28.6 - -1.0)[1]
Percentages of eosinophil, %	3	12	0.027[2]
Eosinophil count, /mm^3	368.1	961.4	0.018[2]
Total protein, g/dL	7.4	6.7	0.02 (95%CI: 0.3-1.2)[1]
Low total protein, patients	0	4	0.012[3]
Durations of treatments, months	12	9.3	0.037 (95%CI: 0.2-5.2)[1]
Percentages of last BSA, %	40	0	0.001[2]
Complete clearance, patients	0	6	0.001[3]

1, Student t-test, 2 Mann-Whitney test, 3 Fisher's exact test

The eczema group had 10 patients (9 eczema, 1 atopic dermatitis, no evidence of contact dermatitis). The mean age was 58.8 years. Nail alterations were the most common among other clinical features (8 chronic paronychia, 1 onychomadesis). One patient had generalized lymphadenopathy (histopathology of the lymph node was reactive hyperplasia). Abnormal investigations included anemia, leukocytosis, eosinophilia, and high ESR. One patient had *Staphylococcus aureus* septicemia. Treatments of eczema were methotrexate (7.5-12.5 mg/week, 6 patients), prednisolone (20 mg/day, 3 patients), topical steroid, emollient, and antihistamine. The mean duration of treatments was 9.3 months. The median BSA of the last following episode was 0%

(min-max: 0-35%) and 6 patients had complete clearance during the treatments (Table 2).

Two patients had DRESS syndrome. The culprit drugs were allopurinol and rifampin. Other clinical features were fever, conjunctivitis, oral mucositis, hepatitis, generalized lymphadenopathy, and acute renal failure. The treatment was high dose systemic steroids and tapered off within 3 months. One patient had PV presented with generalized scaly erythema skin (100% BSA) with multiple erosions (30% BSA). The other 2 patients were cases of LE/DM overlap, and extensive dermatophytosis (Table 2).

As shown in Table 3, the comparison between the psoriasis and eczema groups showed that the mean age was higher in the eczema group (P=0.036, 95%CI: -28.6 - -1.0). High percentages of eosinophil (P=0.027), high eosinophil count (P=0.018), low serum total protein level (P=0.02), and number of low serum total protein patients (P=0.012) were statistically significant in the eczema group. The eczema group had shorter durations of treatments (P=0.037), lower percentages of last BSA (P=0.001), and higher numbers of complete clearance patients (P=0.001) than the psoriasis group.

Discussion

In two previous studies in Thailand by Leenutaphong et al. and Sakuntaphai et al. it was shown that the hospital incidences of ED were 4.9 cases/year in 100,000 dermatological outpatients[3] and 9 cases/year[4], respectively. For a period of 1 year in Sakon Nakhon, the hospital incidence of ED was 160 cases/100,000 dermatological patients or 32 cases/year. The higher incidence of ED in this study may be explained by the fact that (i) the hospital did not have a full-time position for a dermatologist before, thus patients might receive inadequate treatments that could cause the exacerbation of previous skin disorders, and (ii) some patients were referred from other hospitals due to lack of dermatologists in their hospitals. Males predominated in this study, and this finding was similar to the previous reports[4,8,9]. The mean age was 50 years. This result was similar to two studies in Thailand[3,4] and Banerjee et al[8]. Similar to the findings of previous studies[6,8,10], the most frequent etiology associated with ED in this study was psoriasis.

Nail alterations and fever were most frequent symptoms in this study. Five patients had hepatitis. During treatments, the liver function test of 4 patients became normal. This finding may be explained by the subsiding of the inflammation process. One patient had a persistently high level of AST and ALT caused by alcohol dependence. 3 patients had generalized lymphadenopathy DRESS syndrome, eczema, and extensive dermatophytosis). During the follow up, the enlarged lymph nodes of DRESS syndrome and extensive dermatophytosis patients became

normal in size. This may be because the drug allergy and infection had improved.

Abnormal investigations (Table 1) included anemia, leukocytosis, eosinophilia, and high ESR, similar to previous reports[4,5,6,10,11]. Eleven in 32 patients had hypoalbuminemia, similar to Miyashiro et al.[5] and Kondo et al.[12], but the mean of albumin was normal (3.5 g/dL). However this result was nearly hypoalbuminemia. The hypoalbuminemia occurs probably due to extensive protein loss caused by a high epidermal turnover rate[13,14].

In the comparison between the psoriasis and eczema groups, we found that the mean age was higher in the eczema group, similar to Miyashiro et al.[5] However, another study, Cesar et al., showed the mean age for eczema lower than the psoriasis group[15]. Thus, long-term prospective studies are needed in the future. High percentages of eosinophil, high eosinophil count, low serum total protein, and number of low serum total protein patients were statistically significant in the eczema group. Eosinophilia usually occurs in eczema, because eosinophilia has generally been considered to be a hallmark of allergic diseases (especially eczema group or asthma)[16]. Low serum total proteins are known to be due to protein leakage through severe skin lesions and may be combined with a low diet intake in elderly patients. The eczema group had shorter durations of treatments, lower percentages of last BSA, and higher numbers of complete clearance patients than the psoriasis group, similar to Miyashiro et al.[5] This finding showed ED from eczema has a better prognosis than ED from psoriasis. The absence of relapse or death in this study may be due to the short durations of the study and lack of malignancy-associated ED. The limitation of the study was the short duration of time that was given to carry out the research. A long-term prospective study is needed in future research.

Conclusion

This is a prospective study of exfoliative dermatitis conducted over 1 year. Psoriasis was the most frequent etiology of exfoliative dermatitis. Pruritic erythematous plaques with scales were the main symptoms. Anemia, leukocytosis, eosinophilia, and high ESR were found in most patients. The exfoliative dermatitis from the eczema group had a better prognosis than for the psoriasis group.

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