Original Article

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Clinico-Pathologic Study of Exfoliative Dermatitis in Patients Visiting a Tertiary Care Centre in South India

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Abstract

Introduction: Exfoliative dermatitis is an extreme state of skin irritation resulting in extensive erythema and or scaling of the body. More than 90% of skin surface involvement is considered as a salient pre-requisite to make a clinical diagnosis of exfoliative dermatitis. Histopathology aids in the diagnosis of many cases of exfoliative dermatitis.

Purpose: Exfoliative dermatitis can be caused by a wide range of pre-existing dermatosis or can develop *de novo*. Our study aimed at studying the clinical and pathological correlation in exfoliative dermatitis.

Materials and Methods: 50 patients with clinical diagnosis of exfoliative dermatitis who presented to our skin department were taken up, evaluated with lab tests and skin biopsies. Skin biopsies were classified as conclusive, compatible, and undefined according to the biopsy reporting.

Results: Psoriasis was the most common cause of exfoliative dermatitis, followed by atopic in the pre-existing dermatosis group leading to exfoliative dermatitis. Drug-induced erythroderma was seen in 24%. 26% of exfoliative cases were idiopathic. A skin biopsy was able to yield a diagnosis in 60% (36% biopsy were conclusive, 24% were compatible with a diagnosis). The rest 40% biopsy reports were undefined or non-specific findings.

Conclusion: Thus, in our series of patients presenting with exfoliative dermatitis, the etiologic diagnosis was defined in 60.0% of patients with the skin biopsy. The biopsy could not establish a definitive diagnosis in the remaining 40.0% patients. We would like to emphasize the importance of biopsy in a case of exfoliative dermatitis. Furthermore, in the population with undefined biopsy report, we would suggest follow-up biopsies 3 months later or so.

Key words: Erythroderma, Exfoliative dermatitis, Skin biopsy

INTRODUCTION

Exfoliative dermatitis is an extreme state of skin irritation resulting in extensive erythema and or scaling of the body.[1] More than 90% of skin surface involvement is considered as a salient pre-requisite to make a clinical diagnosis of exfoliative dermatitis.[2] Pre-existing dermatoses is the single most common cause of adult exfoliative dermatitis followed by drugs, malignancies, and idiopathic cases.[3] Erythroderma can be fatal even when properly managed, primarily because of its metabolic burden and complications. Hence, it is mandatory to establish its etiopathology to facilitate precise management. The prognosis of erythroderma is determined by its underlying cause. The clinico-histopathological correlation in erythroderma is usually poor because specific cutaneous changes of dermatoses or a drug reaction are obscured by the non-specific changes of erythroderma. A skin biopsy is an essential investigation in the clinical evaluation and management of patients with erythroderma, especially in those patients with an undetermined cause. Skin biopsies

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were helpful in determining the etiology in 60.0% of the patients in the present series of cases of exfoliative dermatitis.

MATERIALS AND METHODS

A total 50 patients of exfoliative dermatitis presenting to the Outpatient Departments of KMC, Mangalore and Government Wenlock Hospital between August 2008 and August 2010 have been enrolled for the study. Patients presenting with erythema and scaling involving more than 90% of the body surface area were included for the study.

Written and informed consent was taken from the patients intended to be included in the study. Details of the presenting complaints were taken with regards to the site of onset and progression as well as the presence of symptoms of itching, oozing, scaling, fever, and malaise. A detailed history of all pre-existing skin disorders, drugs taken, precipitating and exacerbating factors and of symptoms pertaining to malignancy was taken.

All vital parameters were noted, and a detailed physical examination was done. Patients were examined in detail for cutaneous and systemic manifestations. Nails, the oral cavity, genitalia, the scalp were examined for any involvement, and a rectal examination was carried out in all patients. A detailed systemic examination was carried out to rule out systemic involvement.

A detailed examination of all the lymph node groups (cervical, axillary, infraclavicular, pectoral, inguinal, and femoral) was carried out with respect to their size, consistency, and distribution. Fine-needle aspiration cytology and lymph node biopsy were done if there was clinical suspicion of malignancy. Investigations carried out in all patients included full blood count, liver function tests (LFTs), renal function tests, fasting and postprandial blood glucose, serum electrolytes, urine analysis, serum immunoglobulin E (IgE), HIV enzyme-linked immunosorbent assay, chest X-ray, electrocardiogram, and fungal scrapings. Skin biopsies from the interscapular areas of the back and lesions were carried out on all patients, and the histopathological changes were noted.

The histopathologic diagnosis was defined according to the features described in the biopsy reports and classified as:

- Conclusive, when the pathology gave the diagnosis
- Compatible, when it was not conclusive but highly suggestive; or
- Undefined when the changes found by pathology were non-specific.

The definite etiologic diagnosis was determined in cases where the histopathologic diagnosis was conclusive or compatible and coincident with the clinical diagnosis. The etiologic diagnosis was considered as undefined is cases where the histopathologic diagnosis was non-specific or did not coincide with the clinical diagnosis.

RESULTS

The prospective study was conducted between August 2008 and August 2010. 50 patients with erythroderma were included for the study. The male:female ratio was 1.8:1. The mean age of onset was 55 years. Most of the patients belonged to the age group of 51-60 (24.0%), and the majority of the patients were above 50 years of age (56.0%). Most of the patients were farmers (32.0%) by occupation. Most of the female patients were housewives (24.0%) (Table 1).

A pre-existing skin disorder was the most common predisposing factors leading to erythroderma in 25/50 (50.0%) patients. Of the pre-existing skin disorders, psoriasis was the most common, present in 11/50 (22.0%) patients, followed by atopic dermatitis in 5/50 (10.0%) patients, other eczemas in 8/50 (16.0%) patients, and pityriasis rubra pilaris (PRP) in 1/50 (2.0%) patients.

A history of drug intake was present in 12/50 (24.0%) patients. History of intake of anticonvulsant drugs was present in 5/50 (10.0%) patients of which intake of phenytoin was the most common, present in 3/50 (6.0%) patients followed by carbamazepine in 2/50 (4.0%)

Table 1: Predisposing factors

Predisposing factors	Male (32)	Female (18)	Total (*n*=50)	Percentage
Pre-existing skin disorder				
Psoriasis	8	3	11	22.0
PRP	1	0	1	2.0
Atopic dermatitis	3	2	5	10.0-50.0
Other eczema	7	1	8	8.0
Drug intake				
Carbamazepine	1	1	2	4.0
Phenytoin	2	1	3	6.0
Nevirapine (ART)	1	0	1	2.0
ACE inhibitors	0	1	1	2.0-24.0
Clavix	0	1	1	2.0
NSAID	0	1	1	2.0
Dapsone	0	1	1	2.0
Ayurvedic medication	0	1	1	2.0
Details unknown	1	0	1	2.0
Malignancy	0	0	0	0.0
Idiopathic	8	5	13	26.0

ACE: Angiotensin-converting-enzyme, NSAID: Non-steroidal anti-inflammatory drugs, ART: Antiretroviral therapy, PRP: Pityriasis rubra pilaris

patients. History of intake of nevirapine, angiotensin-converting-enzyme inhibitors, clavix (clopidogrel and aspirin) , non-steroidal anti-inflammatory drugs, dapsone and ayurvedic medication was seen in 1/50 (2.0%) patient, respectively. The details of the drug intake in one patient were not known. Our study did not have any patients with a history of malignancy.

No cause for the erythroderma could be elicited in 13/50 (26.0%) patients, i.e., idiopathic.

The majority of the patients (27/50) had an acute presentation with a duration of illness of <3 months. A duration of illness between 3 months and 1 year was present in 14/50 (28.0%) patients. A duration of illness between 1 and 2 years was present in 2/50 (4.0%) patients and a duration of illness of more than 2 years was present in 7/50 (14.0%) patients.

On examination, erythema was present in 48/50 (96.0%) patients, followed by erosions in 46/50 (92.0%) patients, papules in 23/50 (46.0%) patients, plaques in 22/50 (44.0%) patients, pustule in 9/50 (18.0%) patients, vesicle in 3/50 (6.0%) patients, and petechiae in 3/50 (6.0%) patients.

Nail changes were seen in 27/50 (54.0%) patients. The most common change was discoloration in 20/50 (40.0%) patients, followed by ridges in 18/50 (36.0%) patients, dystrophy in 14/50 (28.0%) patients, pitting in 10/50 (20.0%) patients, onycholysis in 9/50 (18.0%) patients, shiny nails in 2/50 (4.0%) patients, and paronychia in 1/50 (2.0%) patients.

Lymph node involvement was present in 28/50 (56.0%) patients. Inguinal lymph nodes were involved in 23/50 (46.0%) patients, followed by femoral in 11/50 (22.0%) patients, axillary in 9/50 (18.0%) patients, cervical in 7/50 (14.0%) patients, infraclavicular in 5/50 (10.0%) patients, and pectoral in 2/50 (4.0%) patients.

Peripheral blood eosinophilia was present in 8/50 (16.0%) patients with drug-induced exfoliation. Deranged LFTs were seen in 6/50 (12.0%) patients with drug-induced exfoliation (Table 2).

An abnormal ultrasonography abdomen was seen in 3/50 (6.0%) female patients (altered echotexture of the liver in two patients and ascites in one patient) and 3/50 (6.0%) male patients (fatty hepatomegaly).The serum IgE levels were raised in 38/50 (76.0%) of the patients.

Classification of Skin Biopsies

Skin biopsies were classified as conclusive when the pathology gave the diagnosis, compatible when it was not conclusive but highly suggestive of the diagnosis; or undefined when the changes found by pathology are non-specific.

Based on the histological features, skin biopsies were conclusive of the diagnosis in 18/50 (36.0%) patients, compatible in 12/50 (24.0%) patients, and undefined in 20/50 (40.0%) patients (Table 3).

The conclusive skin biopsies included psoriasis in 6/50 (12.0%) patients, PRP in 1/50 (2.0%) patients, drug induced in 5/50 (10.0%) patients, and eczema in 6/50 (12.0%) patients (Table 4).

The compatible skin biopsies included, drug induced in 4/50 (8.0%) patients, eczema in 7/50 (14.0%) patients, and psoriasis in 1/50 (2.0%) patient (Table 5).

Table 2: Histopathological change

Histopathological changes	Males (32)	Females (18)	Total (*n*=50)	Percentage
Hyperkeratoses	9	3	12	24.0
Acanthosis	15	10	25	50.0
Parakeratosis	10	5	15	30.0
Spongiosis	13	5	18	36.0
Elongated rete ridges	5	2	7	14.0
Perivascular lymphocytic infiltrate	18	7	25	50.0
Apoptotic keratinocytes	2	1	3	6.0
Eosinophilic infiltrate	2	4	6	12.0
Vascular change	2	3	5	10.0
Pigment incontinence	5	3	8	16.0

Table 3: Skin biopsies

Biopsy reports	Males (32)	Females (18)	Total (*n*=50)	Percentage
Conclusive	12	6	18	36.0
Compatible	8	4	12	24.0
Undefined	12	8	20	40.0

Table 4: Conclusive skin biopsies

Histopathologic Diagnosis	Male (32)	Female (18)	Total (*n*=50)	Percentage
Psoriasis	4	2	6	12.0
PRP	1	0	1	2.0
Drug induced	2	3	5	10.0
Eczema	5	1	6	12.0

PRP: Pityriasis rubra pilaris

Table 5: Compatible skin biopsies

Histopathologic Diagnosis	Males (32)	Females (18)	Total (*n*=50)	Percentage
Drug induced	2	2	4	8.0
Psoriasis	1	0	1	2.0
Eczema	5	2	7	14.0

Of the 11 patients who presented with a history of psoriasis, a conclusive skin biopsy was obtained in 6/50 (12.0%) patients, compatible in 1/50 (2.0%) patient, and undefined in 4/50 (8.0%) patients. A conclusive skin biopsy of platelet-rich plasma (PRP) was obtained in 1/50 (2.0%) patient, who on history and clinical examination had features suggestive of PRP. Of the 12/50 (24.0%) patients who had presented with a history of drug-induced exfoliation, a conclusive skin biopsy was obtained in 5/50 (10.0%) patients, compatible in 4/50 (8.0%) patients, and undefined in 3/50 (6.0%) patients. Of the 26/50 (52.0%) patients who on history and clinical examination had features suggestive of eczema, a conclusive skin biopsy was obtained in 6/50 (12.0%) patients, compatible in 7/50 (14.0%) patients, and undefined in 13/50 (26.0%) patients (Table 6).

DISCUSSION

The male:female ratio in our study was 1.8:1, this is comparable to the study by Akhyani *et al.*[4] In our series, the mean age of onset was in the fifth decade, which is comparable to studies by Kondo *et al.*[5] and Rym *et al.*[6] The majority of the males were farmers (32%), and the majority of the females were housewives (24.0%).

Predisposing Factors

Pre-existing skin disorder

A pre-existing skin disorder was the most common predisposing factor leading to erythroderma, seen in 25/50 (50%) patients. This is comparable with most of the other studies.[3,5,7-9] However, in studies by King *et al.*,[10] drug reactions were the most common predisposing factor leading to erythroderma.

Of the pre-existing skin disorders, psoriasis was the most commonly implicated in this study (22.0%), which is comparable to most of the other studies.[3,6,8] A history of atopic dermatitis predisposing to erythroderma was seen in 5/50 (10.0%) patients. In other studies,[5,8] the percentage of patients with atopic erythroderma has been reported to vary from 4.76% to 23.9%. A history of non-atopic eczema was seen in 8/50 (16.0%) patients in this study. In other studies,[3,6-9] the percentage of patients with non-atopic eczema has been reported to vary from 5.12% to 25.3%. The high number of patients with non-atopic eczema in this study is explained by the presence of a greater number of manual laborers, who would be more occupationally exposed to dust and plant allergens.

Table 6: Distribution of cases according to the etiologic classification of skin biopsies

Histopathologic Diagnosis	Conclusive	Compatible	Undefined
Psoriasis	6	1	4
PRP	1	0	0
Drug induced	5	4	3
Eczema	6	7	13

PRP: Pityriasis rubra pilaris

A history of PRP was seen in 1/50 (2.0%) patient. In different studies,[3,9] the percentage of patients with PRP has been reported to vary from 1.25% to 8.2%.

Drug Reactions

A history of a drug reaction leading to erythroderma was present in 12/50 (24.0%) patients in this study, which is comparable to studies by Seghal and Srivastava[11] (24.7%). The most commonly implicated drugs in this study were anti-epileptic medications in 5/50 (10.0%) patients, comparable to studies Akhyani *et al.*[4] and Chaudary and Gupte.[12] A higher percentage was reported by King *et al.*[10] (34.0%). Both these studies had included a higher number of patients (135 and 82 respectively).

Malignancy

None of the patients in this study had a history of malignancy. This is comparable to the study by Kondo *et al.*[5]

Idiopathic

No cause of the erythroderma could be elicited in 13/50 (26.0%) patients, i.e., idiopathic, which is comparable to several other studies.[5,4,6,8] In different studies, the number of idiopathic cases has been reported to vary from 6.51% to 36.0%.[6,8,9]

Skin Biopsy

Skin biopsies were able to yield a diagnosis in 30/50 (60.0%) patients, comparable to the study by Vasconcellos *et al.*[13] In other studies,[3-6,8] the percentage of diagnostic skin biopsies have been reported to vary between 27.7% and 83.3%.

Skin biopsies diagnostic of psoriasis were obtained in 7/50 (14.0%) patients comparable to the study by Nigam *et al.*[14] In the study by Chaudary and Gupte,[12] diagnostic skin biopsies of psoriasis were obtained in all the patients with clinical features suggestive of psoriasis. In other studies,[3,9] the percentage of skin biopsies diagnostic of psoriasis has been reported to vary from 5.35% to 40.0%. However, a smaller number of skin biopsies were carried out in these studies.

Skin biopsy diagnostic of PRP was obtained in 1/50 (2.0%) patients, comparable to the study by Jain *et al.*,[15] in which 1/25 (4.0%) patient had a diagnostic skin biopsy of PRP. In other studies,[3,5] the percentage of skin biopsies diagnostic of PRP have been reported to vary from 1.25% to 3.57%.

Skin biopsies diagnostic of drug-induced erythroderma was obtained in 9/50 (18.0%) patients, which is higher than that obtained by Chiratikarnwong.

Thus, in the series of patients presenting with erythroderma, the etiologic diagnosis was defined in 60.0% of patients and undefined in 40.0% patients.

CONCLUSION

Erythroderma, which may be referred to as exfoliative dermatitis, is an inflammatory disorder in which erythema and scaling occur in more or less generalized distribution.

The onset of the disease in the majority of the patients was acute, in contrast to most other studies. In accordance with other studies, a pre-existing skin disorder was the most common predisposing factor leading to erythroderma (psoriasis was the most common, atopic dermatitis, PRP) followed by drug-induced erythroderma. Among the drug reactions, anti-epileptics were most commonly implicated. There were no patients with malignancy in this study.

The clinico-histopathological correlation in erythroderma is usually poor because specific cutaneous changes of dermatoses or a drug reaction are obscured by the non-specific changes of erythroderma.

The skin biopsy is an essential investigation in the clinical evaluation and management of patients with erythroderma, especially in those patients with an undetermined cause. Skin biopsies were helpful in determining the etiology in 60.0% of the patients in the present series of cases of exfoliative dermatitis.

Close follow-up of erythroderma of unknown cause, by repeating cutaneous biopsies in time, will allow us to identify patients in the latter group for early diagnosis.

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