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Original Article

Frequency of various etiological factors associated with erythroderma

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Abstract

Objectives To identify the relative frequency of various etiological factors associated with erythroderma.

Patients and methods This descriptive study, using non-probability convenience sampling, was carried out in the Dermatology Department of Military Hospital, Rawalpindi, from 1st August, 2007 to 31st July, 2008. The study group comprised of 50 patients of clinically diagnosed erythroderma. The relevant laboratory evaluation including skin biopsy was carried out in all cases. The results were statistically analyzed through computer software SPSS 10.

Results Among the total 50 patients, 33 (66%) had some pre-existing dermatoses. This was proved by history and supported by histopathology. In this group, eczema was found in 19 (38%), followed by psoriasis in 8 (16%) patients. Contribution from other diseases e.g. pemphigus foliaceus, ichthyosis, scabies, bullous and non-bullous ichthyosiform erythroderma was not very significant. After this group the second commonest cause of erythroderma was drug reaction, which contributed 6 (12%) patients. In 2 (4%) patients, erythroderma was due to cutaneous T cell lymphoma, and no underlying cause was found in 9 (18%) patients which were labeled as idiopathic.

Conclusion Pre-existing dermatoses were a common cause of erythroderma in our population and drugs and malignancy were a much less frequent cause. Skin biopsy was a useful investigation in confirming the cause of erythroderma, as specific histological characteristics were recognizable in majority of these cases.

Key words
Erythroderma, exfoliative dermatitis, eczema, psoriasis, Norwegian scabies, pityriasis rubra pilaris, bullous ichthyosiform erythroderma, drug reaction.

Introduction

Erythroderma is the term applied to any inflammatory skin disease which affects more than 90% of the body surface.[1] In most cases there is continuous exfoliation of the scale, and the term exfoliative dermatitis (ED) is sometimes used synonymously. It is a rare skin condition with an overall incidence of 35 per 100,000 dermatological patients.[2]

The causative factors may be previous dermatoses, drug reactions, malignancies, systemic diseases, infections and idiopathic disorders. The four common causes of idiopathic erythroderma are atopic dermatitis of the elderly, intake of drugs overlooked by the patient, pre-lymphomatous eruptions and occult malignancies.[1,3] Laboratory findings are typically unhelpful in establishing the etiology of ED.[4] Skin biopsy is the only relevant investigation, as the histopathological features of

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the underlying disorder are recognizable in more than half of the cases.[5,6]

Since ED is a serious disease, due to its various complications, optimal therapy depends upon the establishment of the cause.[7] This study was planned to evaluate the frequency of various etiological conditions leading to erythroderma in our setting and to determine how valuable skin biopsy is in the diagnosis.

Patient and methods

The study was a descriptive, cross-sectional study conducted from 1st August 2007 to 31st July 2008 at the Dermatology Department of Military Hospital, Rawalpindi. A total of 50 patients of either sex with clinical diagnosis of erythroderma, were included in the study. Patients unwilling to undergo investigations or those with bleeding disorders, in whom skin biopsy was contraindicated, were excluded from the study.

Clinical diagnosis of erythroderma was made on the basis of erythema and/or scaling covering more than 90% of body surface area. A detailed history and complete physical examination was carried out in all patients.

In addition to the routine laboratory investigations e.g. blood complete picture, urine routine examination, liver and renal function tests, chest X-ray and direct microscopy for fungus and scabies mites; skin biopsy was performed in all cases and histopathological findings were recorded.

Disease specific investigations such as ultrasonography of abdomen, lymph node and bone marrow biopsies and work up for occult malignancy were carried out only in those who were diagnosed as cutaneous lymphoma on skin biopsy.

The data was analyzed by using SPSS version 10. Descriptive statistics were used to calculate mean and standard deviation for age of onset of erythroderma. Frequency (%) was calculated for presenting complaints (pruritus), clinical findings (pallor, pedal edema, lymphadenopathy, hepatosplenomegaly), dermatological findings (erythema, scaling, alopecia, nail and mucosal involvement) and causative factors (preexisting dermatoses, drugs, malignancy and idiopathic).

Results

A total of 50 patients were seen during the study period. Thirty five (70%) were males and fifteen (30%) were females. The males outnumbered females in a proportion of 2.33:1. The ages of patients ranged from 5 to 70 years (mean age 47.8 years, SD ± 17.57 years). Forty nine (98%) patients had erythema, all had some degree of scaling (100%), and 48 (96%) had pruritus. Onychopathy was seen in 20 (40%), diffuse alopecia in 4 (8%), and mucosal involvement in 1 (2%) patient. As far as the systemic features are concerned; 15 (30%) presented with fever (> 38ºC), 5 (10%) had pallor, 5 (10%) had lymphadenopathy, 2 (4%) had hepatomegaly, and in 7 (14%) patients there was significant pedal edema.

The initial site of involvement was head and neck in 12 (24%), upper or lower limbs in 9 (18%), extensor surfaces in 8 (16%), trunk in 5 (10%), flexural regions in 3 (6%), and genitalia in 1 (2%) patient. Lymph node biopsy in the five patients having lymphadenopathy showed evidence of dermatopathic lymphadenopathy. Skin biopsy was performed in all cases and histological diagnosis matched with the clinical

Table 1 Various factors associated with erythroderma (n=50).

Causative factors	*N (%)*
Preexisting dermatoses	*33 (66)*
Chronic actinic dermatitis	10 (20)
Airborne dermatitis	3 (6)
Irritant contact dermatitis	5 (10)
Seborrheic dermatitis	1 (2)
Psoriasis	8 (16)
Pemphigus foliaceus	2 (4)
Nonbullous ichthyosiform erythroderma	1 (2)
Bullous ichthyosiform erythroderma	1 (2)
Pityriasis rubra pilaris	1 (2)
Norwegian scabies	1 (2)
Drugs	*6 (12)*
Carbamazepine	3 (6)
Cotrimoxazole	1 (2)
Phenytoin	1 (2)
Penicillin	1 (2)
Malignancies	*2 (4)*
Cutaneous T-cell lymphoma	2 (4)
Idiopathic	*9 (18)*

diagnosis in 30 (60%) patients. Final diagnosis was the result of the evaluation of the clinical, biochemical and histological findings.

The patients were divided into four etiological groups (**Table 1**). The first group comprised of 33 (66%) patients, who had a history of some previous dermatoses, and were later on confirmed by skin biopsy. Various forms of eczema were seen in 19 (38%) patients [chronic actinic dermatitis 10 (20%), irritant contact dermatitis 5 (10%), airborne dermatitis 3 (6%), seborrheic dermatitis 1 (2%) patient]. Psoriasis was seen in 8 (16%), pemphigus foliaceus in 2 (4%), Norwegian scabies in 1 (2%), nonbullous ichthyosiform erythroderma in 1 (2%), bullous ichthyosiform erythroderma in 1 (2%) and pityriasis rubra pilaris in 1 (2%) patient.

The second group, which comprised of drug-induced erythroderma, had 6 (12%) patients. This was confirmed by a specific history of drug ingestion and histological evidence of eosinophil rich perivascular infiltrate. Carbamazepine was the etiological agent in 3, cotrimoxazole, phenytoin and penicillin in 1 patient each. The third group comprised of malignancy-associated erythroderma. It included 2 (4%) patients who were both suffering from cutaneous T-cell lymphoma and there was no case of any other systemic malignancy. The last group was idiopathic, which comprised of 9 (18%) patients, with no specific history, associated factor or a specific histology (**Table 1**).

Discussion

Erythroderma results from many different causes. There are several publications on this subject, largely from England, USA and the Scandinavian countries reporting different incidences of each etiologic factor. This study was conducted primarily to determine the main etiological agents in erythroderma in our population belonging to northern Punjab and eastern NWFP, and the value of skin biopsy in the diagnosis in such patients. There have been two similar studies on the subject from Lahore.[5,8]

The approach to patients with erythroderma depends on their previous dermatologic history. Patients with long-standing dermatologic disorders e.g. eczema and psoriasis may develop erythroderma during a flare up. In such cases, the etiologic diagnosis or the associated factors are easy to determine, otherwise, erythroderma remains a diagnostic challenge. The clinical features of erythroderma are non-specific and certain clues such as scaling or pruritus cannot be related to any specific cause, as these are present in nearly all patients. Erythroderma of longer duration can cause hair loss, or nail dystrophy regardless of its origin, but these changes again are not suggestive of any specific disease.

The age variation and gender distribution in this study was similar to the prevalence reported in previous studies.[3,8-11] Diffuse scaling and pruritus were found in almost all of our patients, however, systemic features like lymphadenopathy, visceral enlargement, edema and mucosal involvement were seen in a few patients in our study compared with the study by Pal *et al*.[8] In contrast to other studies,[3,9,10] drugs were a less frequent cause in our patients. Carbamazepine was the drug which most frequently caused erythroderma in our set-up. Similar association was reported by Akhyani *et al*.[9] However in past this drug had been mentioned as a less frequent cause.[3] The drugs more commonly implicated in other studies are pyrazolone derivatives, hydantoin derivatives, cimetidine, lithium salts and gold salts.[9,12,13]

This study had a high percentage of erythroderma secondary to preexisting dermatoses that are recognized as the most common causes of adult erythroderma in majority of studies.[1,3,8,9,12,14] The commonest dermatoses causing erythroderma in our patients' sample were different forms of eczema (38% patients). In studies on erythroderma from Pakistan by Pal *et al*.[8], from India by Sehgal *et al*.[12] and Sudho *et al*.[15] psoriasis was the most common underlying cause of erythroderma. Only 1 (2%) patient of pityriasis rubra pilaris presented in erythroderma, which is similar to other studies,[3,9] however in a study from Iran by Akhyani *et al*.[9] pityriasis rubra pilaris was reported as a frequent cause (8%) of erythroderma.

Onset of erythroderma was insidious except in drug-induced cases, where it was abrupt and florid. This finding was similar to other studies.[2,3,9] Among various categories of erythroderma in this study, the best prognosis was noted in drug-induced erythroderma, as it resolved as soon as the causative agent was withdrawn. Similar findings have been shown by Sehgal *et al*.[12]

The percentage of cases in which no underlying disease is demonstrable diminishes with the thoroughness of investigation and the duration of observation. The reviewed literature on erythroderma showed that idiopathic group constituted 10% or more of the patient population[3,8] compared with 18% in this study.

In erythrodermic patients, skin biopsy is one of the important investigation and an essential diagnostic procedure. In this study histopathology was done in all cases and the histological findings in each case were compared with the clinical diagnosis. Thirty (60%) biopsy sections were rewarding in reaching a definitive diagnosis. Similar findings have been reported previously.[5,10] Zip *et al*.[16] reported that, despite of the uniformity of the clinical expression of erythroderma, diagnostic histopathologic features of the underlying disease are retained in the majority of the patients.

Skin biopsy holds great importance in helping the clinician to reach a diagnosis in patients without history of dermatologic diseases and who deny recent intake of any medicine. Even if there is no definitive diagnosis, the histological picture of subacute or chronic dermatitis or psoriasiform reaction indicates that there is nothing sinister in such a patient. Nevertheless, some cases of erythroderma which are resistant to treatment may require multiple skin biopsies and if indicated a lymph node biopsy to rule out underlying lymphoma or malignancy.

During the study period, no death was recorded due to erythroderma. In initial documented studies, the death rate due to erythroderma

varied from 18 to 64%.[12] Our findings support Hassan *et al*.[17] view that erythroderma does not pose a significant risk to the patient's life. This could be due to smaller sample size and lower frequency of malignancy associated erythroderma. Therefore a larger sample and longer follow up of these patients may be required to evaluate mortality related to erythroderma.

Conclusion

Pre-existing dermatoses were the commonest cause of erythroderma and in this group of patients various forms of eczema were the most common underlying pathology. Drugs and malignancy were a less frequent cause of erythroderma. The clinical features of erythroderma were identical irrespective of the etiology. Skin biopsy was a useful investigation in cases of erythroderma since the histopathological characteristics of the underlying disorder were recognizable in more than half the cases.

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