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Original Research Article

Erythroderma: a clinico etiological study of 77 patients in a tertiary care centre in Kerala

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ABSTRACT

Background: Erythroderma is defined as generalized erythema and scaling of the skin affecting more than 90% of body surface area. Identification of the underlying disease process represents one of the most complex challenges in proper patient care.
Methods: A retrospective study was done in Department of Dermatology in a Tertiary Care Centre. History, clinical findings and investigations of erythroderma patients were recorded and clinic-histopathological correlation was analyzed by kappa coefficient (K).
Results: Erythroderma was more prevalent in elderly males with a mean age of 64.56 years and a male to female ratio of 3:1. A clinical evidence of pre-existing dermatoses was found in 65 patients, commonest being eczema (41.3%) followed by psoriasis (40.3%). Evidence of a trigger was seen in 54.54% patients, commonest being the use of ayurvedic medications (42.8%). Clinico-histopathological correlation was seen in 53.9% cases.
Conclusions: Although the clinical presentation of erythroderma is similar, etiological factors are varied and it depends largely on the population studied. Most commonly, erythroderma is due to generalization of pre-existing dermatoses as seen in our study. Hence careful evaluation of clinical clues and histopathological correlation plays a pivotal role in diagnosis of the primary cause and the effective management of erythroderma.

Keywords: Erythroderma, Histopathology, Psoriasis, Eczema

INTRODUCTION

The term erythroderma was coined by Hebra and it is defined as generalised erythema and scaling involving more than 90% of body surface area.[1] It can result in hemodynamic, systemic and biochemical changes in the body. Erythroderma is mostly due to generalization of pre-existing dermatoses such as psoriasis or eczema, drug reactions or due to an internal disease.[1] Identification of the underlying disease process and the possible triggering agents is vital for the proper management of the condition. Careful clinico-pathologic correlation is important to the identify specific underlying causes of erythroderma.[2]

This study was conducted to assess the clinical and investigational profile of erythroderma patients retrospectively and to analyze clinical- histopathological correlation to understand the commonest etiologies and triggers in our patients.

METHODS

The study was conducted in the Department of Dermatology of a Tertiary Care Hospital in Kerala. The clinical history, examination findings and relevant investigations were retrospectively recorded from case records of patients admitted with a provisional diagnosis of erythroderma. For better monitoring and identification of the possible systemic complications and to investigate the cause in each case, they were always treated as inpatients. Following data were recorded: personal data, past medical history (including history of skin diseases), drug consumption history, previous episodes of erythroderma, onset and evolution of erythroderma, symptoms, and physical examination. Laboratory investigations including complete hemogram, serum electrolytes, blood sugar, liver and kidney function tests and urine microscopy, serum markers for viral hepatitis B and C, HIV antibody testing, electrocardiogram and skin biopsy were performed as part of the routine investigation for all erythrodermic patients in our dermatology ward. Biopsy was avoided in patients where the cause was clinically obvious like pre-existing skin diseases and drugs. Microscopy for scabies mite and fungus, stool examination for occult blood, chest radiography, abdominal ultrasound was done whenever necessary. Clinico-histopathological correlation was analysed by kappa coefficient (K).

RESULTS

The age group of patients in the study varied from 1year to 88 years with a mean age of 64.67 years. Males were predominant with a male to female ratio of 3:1. The duration of disease ranged from 2 days to 54 weeks with an average of 6.5 weeks. The clinical features of erythroderma were almost identical regardless of the etiology. Erythema appeared first followed by scaling over a period of 3-5 days (Figure 1).

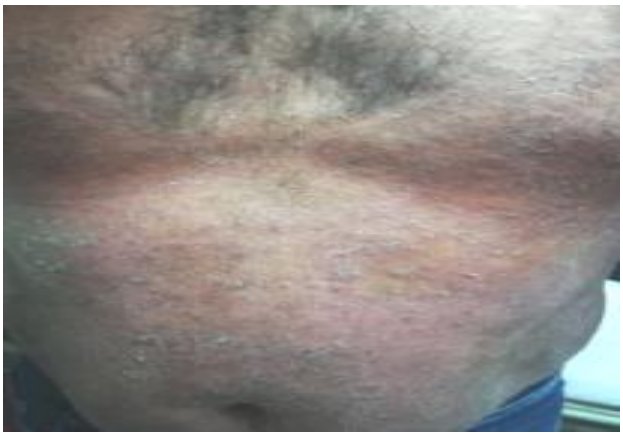

Figure 1: Generalized erythema and scaling in psoriatic erythroderma.

The scales were larger in acute cases and smaller in chronic cases. The onset of erythroderma was insidious, except in the drug-induced cases, where it was acute in onset. The predominant clinical symptom apart from the classical presentation of erythema and scaling was shivering and feverish feeling in 28.6% of erythroderma patients. Decreased urine output was seen in 6.5% of patients. Lymph node enlargement was seen in 57.1% of which 36.45% had generalised lymphadenopathy. There was significant dependent oedema in 50.6% of patients. Nail changes were seen in 38 patients (49.4%) and the most common finding was longitudinal ridging. From the clinical assessment of etiology, 84.4% of patients had a history of pre-existing dermatosis and 6% had drug allergy. Eczema (32 patients) was the most prevalent dermatosis followed by psoriasis (31 patients). Asteatotic eczema was the most prevalent type of eczema (n=13).

Histopathological evaluation in 51 patients showed features of eczema in 39.2%, psoriasis in 23.5%, drug allergy in 5.9% and evidence of cutaneous T cell lymphoma (CTCL) in 2% of patients. Changes often resemble that of non-specific subacute or chronic spongiotic dermatitis (Figure 2).

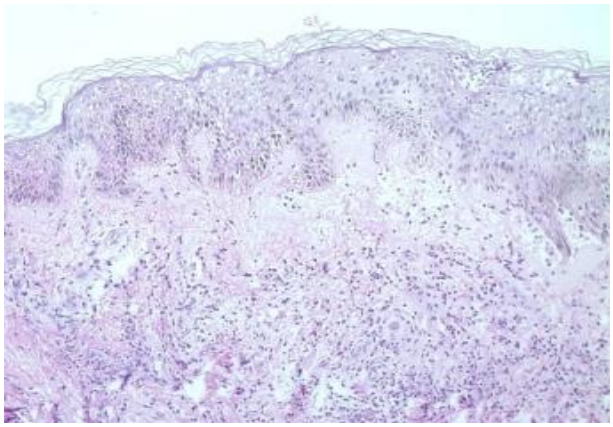

Figure 2: Erythroderma secondary to eczema showing hyperkeratosis, acanthosis, focal dermal edema with perivascular lymphocytic infiltrate and focal lymphocytic exocytosis (H and E, x10).

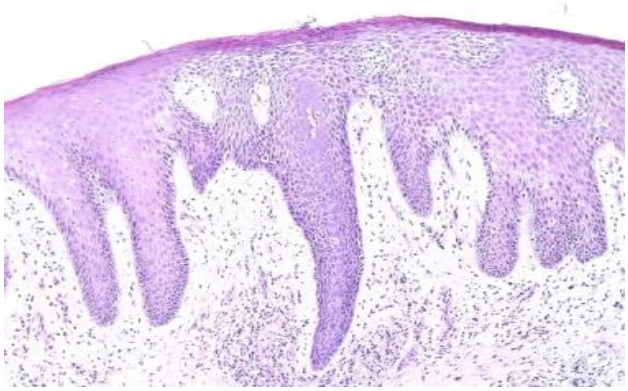

Figure 3: Psoriatic erythroderma showing psoriasiform hyperplasia, focal parakeratosis, mild spongiosis with focal intraepidermal lymphocytes and dilated capillaries in papillary dermis (H and E, x10).

Presence of mounds of parakeratosis with few neutrophils, epidermal hyperplasia and blood vessel dilatation in upper dermis along with mild spongiosis was seen in psoriatic cases (Figure 3). Presence of perivascular lymphocytic infiltrate with eosinophils was in favour of drug induced erythroderma. Atypical cells with cerebriform nuclei along with eosinophils in the infiltrate were suggestive of CTCL. The overall clinico-pathological correlation was 53.9% with Kappa value of 0.362 indicating a fair agreement.

Associated clinical parameters did not show significant correlation to any etiology except for nail changes. Subungual hyperkeratosis showed a statistically significant correlation with psoriatic erythroderma (p=0.02). The most common triggering factor responsible for flaring up the pre-existing disease was ayurvedic medications (31%) followed by allopathic drugs (12%). No significant correlation was noted between the erythroderma etiology and co-morbidity parameters. Assessment of the investigations of patients revealed anaemia in 33.8%, hypoalbuminemia in 33.8% with albumin globulin reversal in 31.2% of patients. Eosinophilia was seen in 40.3% patients. Total leucocyte counts were raised in 24.7% of patients. But no significant correlation was found between the etiology and these investigation results. Final etiological diagnosis was made after considering clinical, biochemical and histological findings in each patient.

DISCUSSION

Erythroderma was first described by Hebra in 1868 as a reaction pattern characterized by generalized erythema with scaling affecting more than 90% body surface. It may be associated with systemic manifestations and metabolic changes. In erythroderma there is increase in the epidermal turnover rate. The transit of the cells through the epidermis is shortened and this results in an overall greater loss of epidermal material, which is manifested clinically as severe scaling and shedding.[3] The amount of protein loss is so large that the systemic metabolism is affected.[4] The extensive skin involvement in erythroderma may lead to systemic complications and may threaten the life of patients, especially in the elderly.

The diagnostic approach of patients with erythroderma depends on their previous dermatological history. Patients with pre-existing dermatological conditions may develop erythroderma during a flare up of the dermatosis. The etiological diagnosis is relatively straightforward in such cases. In other situations, etiological diagnosis of erythroderma is challenging.[2] In such cases the histological examination shows either a subacute or chronic dermatitis and psoriasiform pattern.[5] Rarely patients with idiopathic erythroderma may progress to CTCL. So, each case of undetermined etiology requires thorough histologic examination with multiple repeated biopsies to rule out lymphoma.[5]

We had collected data of 77 patients with erythroderma over a three years period and did clinico-histopathological correlation using Kappa coefficient. The task of establishing the etiology of erythroderma is challenging as it itself masks the clinical and histological clues of its cause. When erythroderma results from flare of underlying dermatoses subsequent to triggers like drugs including indigenous medications, stress or environmental allergens, the etiological diagnosis is easy. But in most cases the final etiological diagnosis is a result of the evaluation of the clinical, biochemical, histological findings and the evolution of the erythroderma.[2]

Almost all studies record a higher incidence in 5th-6th decade with a definite male preponderance as in this study.[6,7] Like many other series, the majority of clinical features were non-specific. Most common cause of erythroderma in our study was a pre-existing dermatosis followed by drug induced erythroderma. Generalisation of a pre-existing dermatitis was the most common etiology of erythroderma in previous studies (Table 1). Eczema was the most common pre-existing dermatosis which had flared up to an erythroderma followed by psoriasis in our study. In studies on erythroderma patients by Rym et al and Hulmani et al psoriasis was the most common pre-existing dermatosis.[6,7] The study done by Miyashiro et al showed the predominant etiology of erythroderma as eczema.[8] On assessing the associated clinical symptoms and examination findings, we could not find much correlation with the etiology of erythroderma.

Table 1: Etiology of erythroderma.

Study	Total no. of patients	Predominant etiology	Eczema (%)	Psoriasis (%)	Drug induced (%)	Malignancy (%)	Idiopathic (%)
Khalid et al[9]	82	Preexisting dermatoses	11	32	22	5	26
Akhyani et al[5]	97	Preexisting dermatoses	19.6	27.8	21.6	11.3	7.2
Hulmani et al[7]	30	Preexisting dermatoses	20	33.3	16.6	3.3	16.6
Present study	77	Preexisting dermatoses	41.6	40.3	7.8	2.6	5.2

The only statistically significant correlation was found with subungual hyperkeratosis of nails and psoriatic erythroderma. In a study done in 309 patients in Brazil, significant nail alterations were more frequent in patients with psoriatic erythroderma (83.3%) and subungual hyperkeratosis was the predominant nail change (44.4%).[8] In the study by Khaled et al acute onset of symptoms and fever correlated with the drug induced etiology.[9]

In the present study a fair to substantial correlation between clinical and histopathological diagnosis was noted in those who were biopsied (n=51). Kappa coefficient in our study was 0.362 with 53.9% positive clinico-histopathologic correlation. In the study done by Khaled et al had an overall 77% clinico-histopathological correlation with a kappa value of 0.753 was recorded.[8] In a study done in 370 erythroderma patients from Kerala, a positive clinico-histopathological correlation was noted in 57.15% of cases.[10] In this study the best correlation was noted in case of erythrodermic mycosis fungoides. In our study also higher correlation was noted in patient with etiology of cutaneous T cell lymphoma (kappa value-0.652 indicating a substantial agreement). In view of the possibility of underlying malignancy in erythroderma, careful evaluation for the same is mandatory even in patients with previous history of existing dermatoses whose clinico pathologic features are inconclusive. This may call for long term follow up with repeated skin biopsies, especially in elderly.[5]

The clinco-pathological correlation indicates that skin biopsy definitely has a role in evaluating the cause of erythroderma and thereby its effective management. They are particularly important in patients without a pre-existing dermatological diseases and those who do not have history any drug intake.[2] The higher percentage of idiopathic erythroderma in a study by Khaled et al was explained by the lack of adequate skin biopsies.[9] According to Hulmani et al, histopathology helped in correlating and confirming the etiology of erythroderma in 80% of cases.[7] Histopathological correlation was found in 74% of patients in a study by Rym et al, in 52% of cases by Bandyopadhyay et al, and 72.54% in a study by Kondo et al.[6,11,12]

No significant correlation was found between the etiology and other investigation results. This finding was similarly reported by Haroon and Pal.[13] There was no HIV-infected patient in our study. Erythroerma is reported more frequently in HIV-positive patients due to various dermatoses or due to adverse drug reactions.[3] In one series reported by Morar et al, a large proportion of erythrodermic patients were HIV-positive but they were no significant increase in the number of episodes of erythroderma. It was concluded that in the young black patient's erythroderma may be a marker for HIV infection.[14]

The most common triggering agent which caused the aggravation of the pre-existing dermatosis into erythroderma was Ayurvedic medications in our study (Table 2). Topicals including herbal medication triggering 42.11% of psoriatic erythroderma was noted by Bharathiya et al from Pune.[15] Ayurvedic or herbal medications aggravated erythroderma in 16.6% cases in a study by Hulmani et al from Mangalore.[7] Traditional medicines was implicated in 20.8% of erythroderma patients by Tan et al from Singapore.[16] Injudicious use of oral or topical herbal and household remedies and ill-formulated over the counter topical creams may be responsible for generalization of localized dermatoses. Incorrect method of preparation, dosages and timing of therapy may be a probable cause of exacerbrations.[17] Self-medication and indiscriminate use of any drugs by patients should be avoided. As our study was a retrospective survey, we were not able to verify the diagnosis ourselves. Small sample size was yet another limitation of our study. True incidence of erythroderma in our population could not be determined as this was a cross-sectional study and no defined population group was available. Also, cases of erythroderma secondary to the cutaneous lymphoma may have been missed due to lack of further follow up.

Table 2: Triggering factors for erythroderma.

Clinical etiology	Triggering factors								
	Ayurvedic	Homeo	Indigenous	Allopathic drugs	Stoppage of drugs	Infections	Stress	Sun exposure	Irritants
Eczema	12	2	2	1	1	1	0	2	1
Psoriasis	11	3	1	4	3	0	1	1	0
Drug	0	0	0	5	0	0	0	0	0
Malignancy	0	0	0	0	0	1	0	0	0
Idiopathic	1	0	1	0	0	0	0	1	0
Total	24	5	4	10	4	2	1	4	1

CONCLUSION

The etiological factors of erythroderma are varied and it depends largely on the study population, commonest factor being generalization of pre-existing eczema. Clinico-histopathological correlation improves diagnosis, helping a prompt and specific therapy at earliest. The role of alternative medicines in precipitating this life-threatening disease should always be kept in mind. In cases were no underlying cause is found, close follow-up is recommended.

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