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Erythroderma: A clinical, etiological and histopathological study at a tertiary care hospital in Karnataka

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Introduction

Erythroderma was described by Hebra in 1868 as a generalised redness of skin.(1) It manifests as extensive erythema and scaling over the body, classically >90% of body surface area.(2) The incidence was estimated by Hasan and Jansen as 1-2 per 100,000 patients.(3) Sehgal and Strivasta reported the incidence from India as 35 per 100,000 dermatologic outpatients. It may be due to a pre-existing dermatosis, drug induced reaction, malignancy and miscellaneous or idiopathic disorder. Among malignancies, lymphomas, including T-cell lymphomas like mycosis fungoides and sezary syndrome are commonly implicated.(4) Skin biopsy is one of the cornerstones of the diagnostic investigations. However, in the setting of erythroderma, the histopathological changes are more subtle and hence difficult to interpret.(5)

Materials and Method

The study is a retrospective analysis of the clinical and laboratory parameters of all cases diagnosed as erythroderma and treated at K.S. Hegde Charitable Hospital attached to K.S. Hegde Medical Academy over the past 5 years. The study was initiated following ethical clearance. The following data were collected from patient files from the medical records department: personal information, onset and evolution of erythroderma, past medical history, drug intake, aggravating factors, past episodes of erythroderma, physical examination of skin, mucosae, hair, nails and other systems. Laboratory investigations such as complete blood count, erythrocyte sedimentation rate (ESR), blood sugar, liver and renal function tests, serum electrolytes were noted. Results of skin biopsies, Chest X-ray, ECG and ultrasound and patch test were collected and analysed. A biopsy was not done in cases where the diagnosis was clear clinically or when the patients were seriously ill. Data was analysed using standard statistical methods and SPSS 20.

Results

The retrospective analyses of all the erythroderma cases admitted to the dermatology department during the last 5 years were included in the study. Forty eight cases of erythroderma were admitted during the past 5 years. There was a predominance of male patients with a male: female ratio of 3.8:1. The age range was 17-81 years, mean age was 54.4 years.

Patient distribution according to age and gender is shown in Fig. 1.

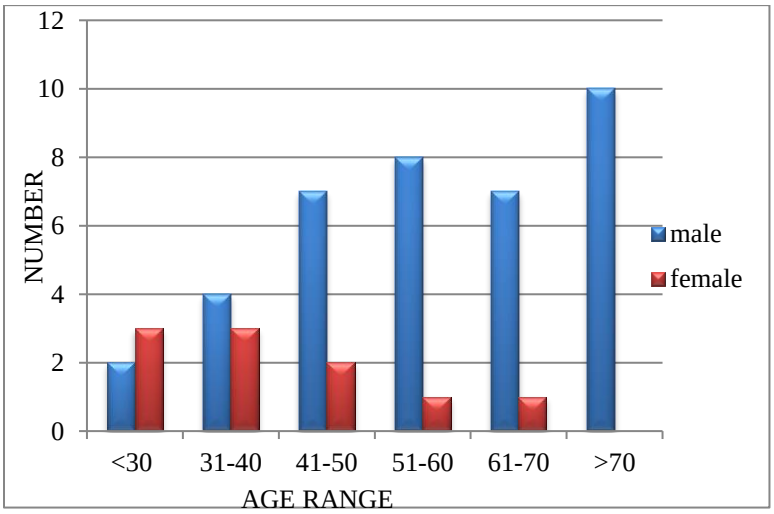

Fig. 1: Age and gender wise distribution of erythroderma

Sudden onset was seen in 7 cases, notably in drug reactions (100%).

Gradual onset was seen in 41 cases.

The most common clinical features and their incidence can be seen in Table 1. Erythema and scaling existed in all the patients. Pruritus was recorded in

91.7% of the patients, fever in 15 (31.3%), and pedal edema in 22 (45.8%). Palmoplantar keratoderma (PPK) was found in 16 patients (33.3%), majority of these were psoriasis patients. Nail changes were seen in 52.1% which included beau's lines, nail pitting, longitudinal ridging, discolouration, onycholysis, subungal hyperkeratosis and onychodystrophy. Lymphnode involvement was detected in 26 (54.1%) by palpation or imaging techniques. The various etiologies of the cases of erythroderma are represented in Fig. 2 and Table 1.

The medical records of the patients showed various aggravating factors such as winter season in 13 (27%), parthenium exposure in 7 (14.5%), stress in 2 patients and indigenous medication in 3 patients. Pre-existing skin disorders present in patients were as follows- Twelve patients had previous known history of psoriasis and 1 patient had psoriatic arthritis, 8 patients had history of atopic dermatitis and 5 patients had a history of contact dermatitis (2 nickel, 1 wood dust and 2 hair dye). Eight patients had previous episodes of erythroderma (5 of psoriasis, 2 atopic dermatitis and 1 idiopathic). Diabetes mellitus was seen in 10 patients, hypertension in 8 patients, dyslipidemia in 4 patients, deep vein thrombosis in 2 patients acute kidney injury, pulmonary edema and carcinoma lung in one patient each. One patient had epilepsy and another had gout, both of which were diagnosed as drug induced erythrodermas and the drugs implicated were phenytoin and allopurinol respectively. The most commonly observed laboratory abnormalities are presented in Table 1. Anaemia was seen in 58.3%, raised ESR in 35.4%, leucocytosis in 31.3%, hypoprotenemia in 27.1% and eosinophilia in 25%. Laboratory findings were not contributory to the underlying diagnosis.

Table 1: Epidemiological, clinical and lab features of 48 patients according to etiology

Etiology	Psoriasis N= 17	Atopic dermatitis N=7	Contact dermatitis N=8	Seborrheic dermatitis N=1	PRP N=2	Scabies N=2	Drug N=2	CTCL N=1	Idiopathic N=8	Total N=48
Age Mean	49.8	56	51.5	70	40	80	52	45	62.6	54.4
Male: Female ratio	3.25:1	6:1	7:1	0:1	0:2	2:0	1:1	1:0	8:0	3.8:1
Sudden /gradual onset	2/15	1/6	2/6	0/1	0/2	0/2	2/0	0/1	0/8	7/41
Clinical findings	N	N	N	N	N	N	N	N	N	N
Pruritus	14	7	8	1	2	2	2	1	7	44
Fever	7	1	1	0	0	0	2	1	0	15
PPK	6	1	3	0	2	0	0	0	4	16
Tachycardia	1	0	2	0	0	0	0	0	0	3
Edema	7	4	3	1	0	2	2	0	3	22
Nail changes	11	2	5	1	1	0	0	1	4	25
Nose sign	4	2	2	0	0	0	0	0	2	10
Lab parameters										
Anaemia	10	4	6	1	0	2	2	0	3	28
Leukocytosis	6	2	2	1	0	0	2	0	2	15
Eosinophils	0	5	2	0	0	2	0	0	3	12
Raised ESR	4	1	2	1	0	2	2	1	4	17
hypoprotenimia	6	2	2	0	0	1	1	0	1	13

CTCL= Cutaneous T Cell Lymphoma, PRP= Pityriasis Rubra Pilaris

Skin biopsy was performed in 33 (68.75%) patients. In the remaining patients a biopsy was not done as the diagnosis was clear or as the patient was moribund. Histopathology contributed to a diagnosis in 18 cases (54.5%), including psoriasis (n=8), pustular psoriasis (n=2), pityriasis rubra pilaris (n=2), atopic dermatitis (n=4), contact dermatitis (n=1) and CTCL (n=1). Non-specific features were observed in 5 patients. (Table 2)

Table 2: Comparison of clinical and histopathologic diagnosis

Clinical diagnosis	No: biopsies done-33	Histopathological diagnosis
Psoriasis	10 cases	8 cases – psoriasis 2- non specific dermatitis
Pustular psoriasis	2 cases	2-pustular psoriasis
PRP	2 cases	2-PRP
Atopic dermatitis	5 cases	3-acute spongiotic dermatitis 1- chronic spongiotic dermatitis 1-non specific dermatitis
Contact dermatitis	5 cases	1-spongiotic dermatitis 4- non specific dermatitis
CTCL	3 cases	1-CTCL

		2- non specific dermatitis
Idiopathic	6 cases	3- non specific dermatitis 2-chronic spongiotic dermatitis 1-lichenoid dermatitis

Among the 17 patients diagnosed with erythroderma secondary to psoriasis, 10 patients had a previous history of chronic plaque psoriasis and few of the patients gave history of scaly lesions over scalp and other typical body sites. Typical nail changes of psoriasis were seen in 64.7% and psoriatic arthritis was seen in a single patient. The previously diagnosed cases of psoriasis had a mean duration of 7.9 years. Ten cases were biopsied and 2 cases showed a histopathology of non-specific dermatitis. The rest of the patients showed typical changes of psoriasis such as parakeratoses, munro's microabscess and suprapapillary thinning. Disease exacerbation was attributed to sudden stopping of medication and stress.

The group of patients diagnosed with eczemas comprised of contact dermatitis (n=8), atopic dermatitis (n=7) and seborrheic dermatitis (n=1). A history of previous contact allergy was obtained in 5 patients. Patch test was done in 5 out of the 8 cases of contact dermatitis after the erythroderma resolved: nickel-2, paraphenylenediamine-2, mercapto mix-1. A history of allergic rhinitis, bronchial asthma was present in 8 patients. Few of the patients also gave a history of flexural localization of lesions before progressing to erythroderma. Histopathology showed characteristic findings in 67% of the biopsied cases showing spongiosis, eosinophils and dermal infiltration. Five cases showed non specific dermatitis.

A single case of CTCL was diagnosed with help of biopsy findings such as band like inflammatory infiltrate comprising of atypical lymphocytes and Pautrier's microabscess.

The histopathology did not yield any specific findings in the 8 idiopathic cases of erythroderma. Six cases showed non-specific dermatitis and 2 showed spongiotic dermatitis. Acanthosis, parakeratosis, spongiosis were seen in 50% of the cases. Majority (75%) of the cases showed a perivascular infiltrate comprising lymphocytic infiltrate (25%), eosinophils (12.5%) and mixed infiltrate containing histiocytes, plasma cells and neutrophils in 62.5%.

Table 3: Comparison of various studies with regard to etiology

Author, Year, Country	Pre-existing dermatoses		Drug reactions	Malignancies	Idiopathic	Others	Total
	N (%)	Total	Total	Total	Total	Total	
Present study	Psoriasis: 17 (35.42%) Eczema: 16 (33.33%) Pityriasis rubra pilaris: 2 (4.2%) Scabies: 2 (4.2%)	37 (77.1%)	2 (4.2%)	1 (2.08%)	8 (16.6%)		48
Cesar et al., 2016, Portugal[7]	Psoriasis: 46 (44.7) Eczema: 17 (16.5) Subacute cutaneous lupus: 1 (1%) Pemphigus foliaceous: 1 (1%) Scabies:1 (1%)	67 (65%)	19 (18.4%)	13 (12.6%)	4 (3.9%)		103
Shirazi et al., 2015., India[8]	Eczema: 16 (27.4%) Psoriasis:10 (17.2%) Lichen planus: 2 (3.4) Pityriasis rubra pilaris: 2 (3.4%) Sarcoidosis: 1 (1.7%)	31 (53.1%)	19 (32.7%)	2 (3.4%)	6 (10.3%)		58
Banerjee et al., 2015, India[1]	Psoriasis: 11 (34.37%) Eczema: 9 (28.12%)	20 (62.25%)	4 (12.5%)	0 (0%)	8 (25%)		32
Hulmani M et al., 2014., India[9]	Psoriasis: 10 (33.3%) Eczema: 8 (26.6%) Pityriasis rubra pilaris: 1 (3.3%)	19 (63.6%)	5 (16.6%)	1 (3.3%)	5 (16.6%)		30
Li J et al., 2012, China[10]	Psoriasis: 143 (55%) Eczema: 32(12.3%) Bullous pemphigoid: 2 (0.8%) Pemphigus foliaceous: 2 (0.8%) Pityriasis rubra pilaris: 1 (0.4%) Dermatomyositis: 1 (0.4%)	181 (69.6)	33 (12.7%)	6 (2.3%)	37 (14.2%)	3 (1.2%)	260
Khaled, 2010, Tunisia[11]	Psoriasis: 27 (32.9%) Eczema: 9 (11%)	36 (43.9%)	18 (21.9%)	4 (4.9%)	21 (25.6%)	3 (3.7%)	82
Rym BM et al., 2005,	Psoriasis: 41 (51.3%) Eczema:6 (7.5%) Pemphigus foliaceus: 5(6.3%)	58 (72.5%)	9 (11.3%)	7 (8.8%)	6 (7.5%)		80

Tunisia[12]	Dermatophytosis: 3 (3.8%) Pityriasis rubra pilaris: 1(1.3%) Lichen planus:1 (1.3%) Scabies: 1 (1.3%)						

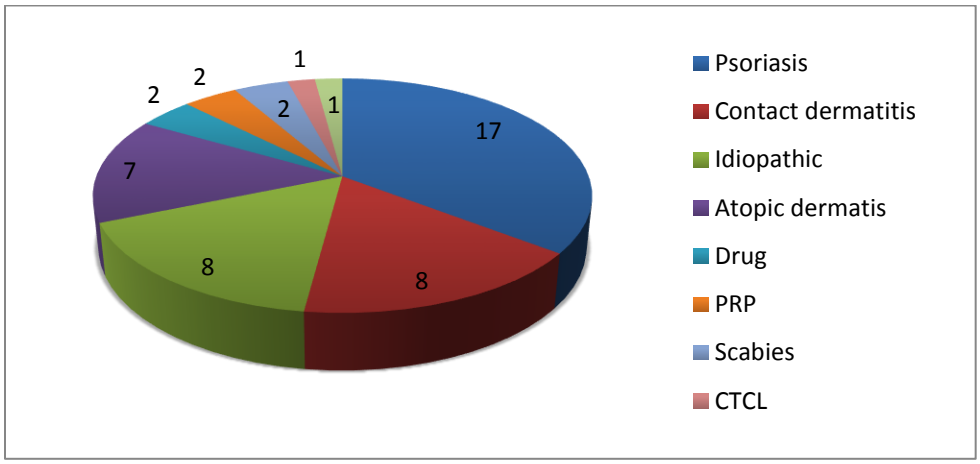

Fig 2: Etiologies of erythroderma

Discussion

Over the 5 years of our retrospective study we found an incidence of 9.6 cases /year. A survey of erythroderma by all the dermatologists in Netherlands showed an annual incidence of 0.9 cases/100000 inhabitants and a series from Tunisia reported a hospital incidence of 6.3 cases/year.[6]

We found that erythroderma predominantly occurred in the fifth to sixth decade and this correlates with the findings of several other studies.[1,7,9,11,13] A male predominance was seen in our study population similar to various other studies.[1,3,7,9,12-15] The onset of erythroderma was gradual in majority of cases with the exception of drug reaction erythrodermas.

Most of the patients presented with non-specific clinical features, the commonest of which was erythema and scaling (100%) followed by pruritus in 91.7%.

Khaled et al and Rym et al reported a significant association of nail changes and palmoplantar keratoderma.[11,12] The percentage of lymphadenopathy in our study was 54.2 which is comparable with other studies.[7,9] Fernandes NC et al reported that lymphadenopathy was associated with CTCL, drug reactions and psoriasis.[16] Our study did not show a significant association of lymphadenopathy with any specific etiology. The incidence of raised ESR was 35.4%. Eosinophilia was seen in 25% cases, predominantly in atopic dermatitis. A similar incidence of eosinophilia among erythroderma was reported by Rym et al that was significantly associated with psoriasis, eczema and cutaneous T-cell lymphoma.[12]

In the present study skin biopsy was useful in establishing a diagnosis in 18 (54.5%) out of the 33 (68.75%) patients for whom a biopsy was done. Various other studies show that biopsies were useful for a specific diagnosis ranging from 35%-74%.[1,7,11-13,15] These results suggest that skin biopsies, though not always diagnostic, are valuable.

Among the etiological groups majority of the patients belonged to the group of pre-existing dermatoses (Table 3). Psoriasis constituted the majority in this group (35.42%) followed by eczema (33.33%); corroborating with previous studies.[1,7,9-12] In the drug induced group, the drugs responsible were allopurinol and phenytoin. Both of these drugs are very common causative agents of drug induced erythroderma as per recent studies.[7,9,10] The incidence of malignancy as a cause for erythroderma in our study was low as in the case of few previous studies.[9,10,13]

Following all the standard investigations to identify the etiology, it could not be confirmed in 8 patients, who were classified as idiopathic erythroderma. A similar incidence was reported by Hulmani et al.[9] All the 8 patients had a long duration of disease and belonged to the elderly age group. Since studies have demonstrated a possibility of idiopathic erythrodermas to progress to cutaneous T cell lymphomas a close follow up and serial biopsies are recommended.[17]

Conclusion

Erythroderma is a condition characterised by erythema, scaling and several other non-specific clinical features. There are multiple lab abnormalities that are detected however none of which are diagnostic. Skin biopsies nevertheless provided a specific diagnosis in more than 50% of the cases. Most of the cases were attributed to pre-existing dermatoses. Other causes were drug induced and due to malignancies. In cases with no underlying cause, a close follow up is recommended considering the risk of developing cutaneous T cell lymphoma.

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