East African Medical Journal Vol. 84 No. 12 December 2007
EXFOLIATIVE ERYTHRODERMA AT KENYATTA NATIONAL HOSPITAL, NAIROBI
T.M. Munyao, MBChB, MMed, DDV, Senior Lecturer, N.A.O. Abinya, MBChB, MMed, Associate Professor, J. K Ndele, MBChB, MMed, Associate Professor, Department of Clinical Medicine and Therapeutics, College of Health Sciences, University of Nairobi, P.O. Box 19676-00202, Nairobi, Kenya, P.N. Kitili, MBChB, MMed, DDV, J.M. Maimba, MBChB, MSc. (Clin. Derm). E.N. Kamuri, MBChB, MSc.(Clin. Derm), H.W. Wanyika, MBChB, MSc.(Clin. Derm), Specialist Dermatologists, Dermatology Unit, Kenyatta National Hospital, P.O Box 20723-00202, Nairobi, Kenya

Request for reprints to: Dr. E.N. Kamuri, P.O. Box 20723-00202, Nairobi, Kenya

EXFOLIATIVE ERYTHRODERMA AT KENYATTA NATIONAL HOSPITAL, NAIROBI

T.M. MUNYAO, N.A.O. ABINYA, J.K. NDELE, P.N. KITILI, J.M. MAIMBA, E.N. KAMURI and H.W. WANYIKA

ABSTRACT

Background: **Exfoliative erythroderma (EE), (Synonyms: Exfoliative dermatitis, Red man syndrome) is a clinical syndrome characterised by generalised erythema and scale. It is an important cause of functional skin failure and associated high morbidity and variable mortality rates.**
Objectives: **To study demographics, aetiology, complications and clinical outcomes of exfoliative erythroderma (EE) on patients attending Kenyatta National Hospital (KNH).**
Design: **Cross- sectional descriptive study.**
Setting: **Kenyatta National Hospital, Dermatology Unit.**
Subjects: **All available medical records on inpatients seen by qualified dermatologists at KNH with generalised erythema and scale from 1996 to 2006.**
Main Outcome Measures: **Discharge or death.**
Results: **Incidence exfoliative erythroderma was documented in 146 out of all 123 admissions (13%) into the dermatology unit from 1996-2006. Demographic mean age was 47 years, M: F ratio was 3:2, 67% had no income and 53% and 30% were residents of Nairobi and adjacent districts respectively. Sixty three percent were due to skin diseases, 23% due to systemic diseases of which 20% were due to HIV / AIDS and 14% due to adverse cutaneous drug reactions. Ninety percent of patients were treated and discharged and 10% died; 50% of whom had dermatoses and 29% due to HIV associated antituberculous drugs.**
Conclusions: **Exfoliative erythroderma is an important cause of morbidity, admission and mortality in patients attending KNH. Dermatoses and HIV / AIDS were the most frequent causes. The mortality rate was relatively low and attributable to controllable diseases.**

INTRODUCTION

The normal human epidermis is a keratinised, regenerating, stratified squamous epithelium, being the product of the genetically programmed keratinisation process (1). Normal mean epidermal turnover time is 28 days and 0.5-1gm of Keratin is lost transepidermally daily (2). Exfoliative erythroderma (EE) is a clinical syndrome of diverse aetiologies (3-8) characterised histologically by generalised confluent cutaneous inflammation and clinically by generalised erythema, exudation, crusting and scale, and features of the aetiological factors (5).

The constant histological changes of EE (6) are not diagnostic and consist of variable spongiosis, acanthosis, hyperkeratosis, parakeratosis, vasodilatation and tortuosity of papillary dermal microvasculature and mixed inflammatory cell infiltrate. Features of aetiological factors are present in the majority of cases (9).

Aetiology: Diverse aetiological factors for exfoliative erythroderma are classifiable into four groups: dermatoses, systemic diseases, adverse cutaneous drug eruptions and idiopathic. Common examples include; dermatose (10,11), eczema, psoriasis and pemphigus, systemic diseases: HIV/AIDS (12), neoplastic diseases (13), adverse cutaneous drug eruptions: sulphonamides, penicillins and acetylsalicylic acid idiopathic exfoliative erythroderma (l4) (Red Man Syndrome) remains undiagnosed in spite of extensive pertinent workup. A proportion of these patients eventually develop mycosis fungoides and Sezary syndrome (15).

Pathophysiology: Generalised erythema is attributable to increased cutaneous blood flow due to vascular response to mediators of inflammation and shunting at papillary capillary-venular junctions. Subsequently, heat loss, hypothermia and hyperdynamic cardiovascular function accrue. Accelerated epidermal turnover results in generalised scale and exfoliation in excess of 20-30 grammes daily (l4), hypoproteinaemia, oedema, anaemia and if protracted muscle wasting. Epidermal inflammation impairs the cornified layer barrier function resulting in increased transepidermal water loss (15) and dehydration with associated electrolyte aberrations, dessication and fissuring complicated by infections.

Clinical features: Exfoliative erythroderma is defined by generalised erythema exudation, crusting and scale. Features of functional skin failure include dehydration, transcutaneous infections, hypothermia, pedal oedema and anaemia, with variations depended on specific cause and duration of inflammation. Clinical criteria and signs attributable to the aetiology are derived from history and physical examination. Systemic complications include hypovolaemic and septic shock, prerenal acute renal failure and hyperdynamic cardiac failure.

Diagnosis: Exfoliative erythroderma is defined by generalised erythema exudation, crusting and scale. The aetiology and complications of EE are established on the basis of standard diagnostic criteria.

Differential diagnosis: Toxic epidermal necrolysis evolving form overlap Steven Johnson Syndrome.

Management: Effective management should include replacement therapy for functional skin failure. The patient must be kept warm, fluid and electrolytes, nutrition, emollients, infection control. Specific therapy should be directed at aetiological factors and systemic complications. Prognosis is variable and depended on aetiology, complications, prompt diagnosis and appropriate management.

MATERIALS AND METHODS

Objectives: To study demographics, aetiology, complications and clinical outcomes in EE patients attending KNH.

Study design: Medical records based cross- sectional descriptive study. Patients seen by qualified dermatologists in KNH with generalised erythema and scale were included. Subjects with unverified diagnoses and inadequate data were excluded.

Ethical considerations: Work on this proposal was approved by the KNH Institutional Scientific and Ethical review Committee. Data on medical records was kept confidential.

RESULTS

Incidence rate: One hundred and forty six patients with ED seen by qualified dermatologists out of a total of 1,123 (13%) were admitted into the dermatology ward from 1996-2006.

Table 1
Demography

Parameter	N	μ	±1SD	M (%)	Fem (%)	Nil (%)	Low	Mid	High	Residence (%) NBI	Nbi-l00	>100km
Age	134	47	23	-	-	-	-	-	-	-	-	-
Gender	146	-	-	60	40	-	-	-	-	-		-
Income	134	-	-	-	-	67	21	12	0	-	-	-
Residence	109	-	-	-	-	-	-	-	-	53	30	17

N=Sample size, μ=Mean: years, SD=Standard deviation: years, M=Male, Fem=Female, Mid=Middle, Nbi=Nairobi

Table 2
Previous ailments

Parameter	No.	Der. (%)	Med. dis.(%)	Hosp. (%)	GP. (%)	Derm	Herb.
Diagnosis	62	45	55	-	-	-	-
Place of Tx	55	-	-	82	13	2	3

No.=Sample size, Der=Dermatoses, Med. dis=Medical diseases, Hosp=Hospital, GP= General Practitioner, Derm= Dermatologist, Herb=Herbalist Tx=Treatment.

Table 3
Aetiology

			Dermatoses			Syst. Dis.		ACDRs			
Parameter	No.	(%)	Ec(%)	Pso(%)	Pf%	HIV(%)	Neo(%).	Te	Atb	Pe	Oth
Dermatoses	123	63	83	15	2	-	-	-	-	-	
Syst. Dis.	44	23	-	-	-	89	11	-	-	-	
ACDRs	27	14	-	-	-	-	-	40	29	11	20
Total	194	100		63		23			14		

ACDRs=Adverse cutaneous drug reactions: Carbamazepine=40%, Atb=Antituberculous drugs EHRZ =29%, Te=Carbamazepine =40%, Pe=Penicillin=11 %, Oth=Others=20% Syst.Dis=Systemic diseases, Ec=Eczema, Pso=Psoriasis, Pf=Pemphigus foliaceous, HIV=HIV / AIDS Neo=Neoplasms: Prostatic carcinoma=3, Multiple myeloma=l, NH Lymphoma=1,CL Leukaemia=l

Table 4
Laboratory investigations

Parameter	No.	Low (%)	Normal (%)	High (%)
Haemoglobin	103	64	36	0
WBC Count	135	8	64	28
Neutrophils	59	15	33	42
Lymphocytes	54	22	65	13
Serum Sodium Na^+	78	23	67	10
Serum Potassium K^+	77	7	83	10
Blood Urea Nitrogen	90	-	-	15
Serum Creatinine	86	-	-	13
Total Serum Proteins	89	15	68	17
Serum Albumin	87	66	31	3

Microbiology: One out of two Ziehl Nielsen smears for acid fast bacilli was positive. Five out of eight pus swabs from patients with otitis media grew *St. aureus* sensitive to amikacin and gentamycin, vancomycin and minocin, amoxyl, erythromycin, meronem, ciproxacin and cefotaxime, gentamycin and vancomycin, amikacin and meronem respectively. Three out of eight were due to *E.coli, pseudomonas* and proteus species sensitive to cefotaxime, meronem, timentin and gentamycin, minocin, meronem and ciproxacin respectively.

Radiology: Three chest radiographs were done. One showed pneumonia and two reticulonodular pattern.

HIV serology by Elisa was positive in thirty one out of sixty six (47%) of patients.

General management: Out of one hundred and forty six patients, One hundred and eighteen, (81%) were nursed in a heated room. Twelve (17.5%) received intravenous fluids. Sixty five (45%) received systemic steroids and ninety three (64%) received antihistamines. Specific management was administered as indicated. Out of forty three patients, eleven (26%) received methotrexate for psoriasis, five (12%) received non steroidal anti-inflammatory, four (9%) received ethambutol, isoniazid, rifampicin and pyrazinamide for pulmonary tuberculosis, three (7%) each received lamotrigine, ketoconazole, enalapril and nifedipine and insulin for seizures, oral candidiasis, systemic arterial hypertension and diabetes respectively. Two (4%) received imuran dapsone in combination for immunobullous disorders and one each (2%) received blood transfusion, melphalan/chlorambucil, salbutamol,

valtrex, diflucan and haloperidol for severe anaemia, chronic lymphocytic leukemia, asthma, HIV / AIDS, oropharyngeal candidiasis and affective disorder respectively.

Clinical outcome: One hundred and thirty two out of one hundred and forty six (90%) of patients were treated and discharged and fourteen out of one hundred and forty six (10%) died.

Mortality Data: Demography,ten out of the fourteen of the deceased had been unemployed. Only two had been employed, one was an electrician and the other was a small scale businessman. Occupational data was unavailable for the other two.

Ten had been either residents of Nairobi or adjacent districts. Two had been residents of districts beyond 100 km from Nairobi. Residential data was unavailable for the other two.

dermatoses and HIV / AIDS account for 63% and 20% respectively of all causes of exfoliative erythroderma. ACDRs and malignant neoplasms account for 14% and 3% respectively. Noteworthy is carbamazepine 40% and antituberculous drugs in HIV / AIDS patients 29%, and the relative paucity of malignant neoplasms.

Eczema and psoriasis account for 83% and 15% of the dermatoses group. This reflects the universal trend attributable to lack of or delayed expert care; only one out of one hundred and forty six patients (0.7%) had been seen by a dermatologist, and use of popular potentially irritant and sensitising skin and care products such as medicated and herbal toiletries by vulnerable subjects.

Inclusion criteria were documented in all patients. However, other systemic examination findings were recorded in only six patients: four with leg oedema and one each with shiny fingernails and

Table 5
Mortality data- demography

Parameter	No.	(%)	μ	Ra. yr	M:F	S	M	W	Ch
Rate	14	10	-	-	-	-	-	-	-
Age	14	-	45 y	. 14-83	7:2	-	-	-	-
Mar. sta.	14	-	-	-	-	2	8	2	2
Adm-dth	14	-	16 d	-	-	-	-	-	-

μ=mean, Ra. yr=Range in years, M:F=Male: Female, S= Single, M=Married W=Widowed, Ch=Child, y=years, d=days, Mar. sta. = Marital status. Adm-dth= Admission to death.

Table 6
Mortality data- general

Parameter	No.	D	Sy dis	Hv+ Atb	Rf	An	L	C11	Ne
Cause of death	11	6	-	4	-	-	-	-	1
Prev dis.	10	5	5	-	-	-	-	-	-
HIV Serology	8	-	-	-	-	-	-	-	-
U/E	10	-	-	-	1	-	-	-	-
CBC	-	-	-	-	-	1	5	1	-

D=Dermatoses, Sy dis = Systemic diseases, Hv+Atb= HIV AIDS patients on antituberculous drugs SHRZ., Rf=Renal failure, An=Anaemia L=Leukocytosis, Cll=Chronic lymphocytic leukaemia, Ne=Neoplasm. Prev dis. = Previous diseases., UIE=Urea and electrolytes, CBC=Complete blood counts.

DISCUSSION

The demographics and health service utilisation pattern is similar to the general patient population characteristics attending the hospital. The prevalent diseases in the general dermatology population;

alopecia. All pus swabs taken grew variable virulent pathogens underlining failure of cutaneous barrier function to microbial invasion. Microbiological studies are indispensable since overwhelming sepsis is inevitable and often fatal, and indiscriminate antibiotic use is discouraged due to the risk of adverse

reactions and possible ineffectiveness. Other manifestations of functional skin failure: dehydration, negative nitrogen balance, hypothermia and heart failure were not documented and may have been prevented by timely appropriate management. However one patient developed acute renal failure leading to death.

High HIV seroprevalence rate of 47% is consistent with the selected hospital patient population. The mortality rate of 10% is relatively low in comparison with 20-40% from international data(2,15). This is attributable to the epidemiology of EE in the study population being due to dermatoses, and relatively minimal degenerative and malignant diseases prevalent in developed world patient populations.

In conclusion exfoliative erythroderma is an important cause of morbidity and mortality in patients attending KNH. Dermatoses and HIV / AIDS were the most frequent causes. The mortality rate was relatively low and attributable to controllable diseases.

We recommend measures to improve compliance with treatment guidelines amongst dermatology patients should be instituted to reduce the complication of exfoliative erythroderma and associated morbidity and mortality.

REFERENCES

1. Bannister, H. L., Berry, M. M., Collins, P. *et al.* Churchill Livingstone. Microstructure of the skin. *Grays Anatomy*. 1995: **5:** 381-388.
2. Freedberg, I. M. Exfoliative dermatitis. In: Fitzpatrick, T.B., Eisen, A.Z., Wolff, K., Austen, K.F. Dermatology in general medicine. 5th ed. New York: McGraw-Hili, 1999: 527-531.
3. Botella-Estrada, R., Sanmartin, O., Oliver, V., Febrer, I. and Aliaga, A. Erythroderma. A Clinicopathological study of 56 cases. *Arch. Dermatol.* 1994; **130:**1503-507.
4. Walsh, N. M., Prokopetz, R., Tron, V.A., *et al.* Histopathology in erythroderma: review of a series of cases by multiple observers. *J. Cutan. Pathol.* 1994; **21:** 419-523.
5. Nicolis, G. E. and Helwig, E. B. Exfoliative dermatitis: a clinicopathologic study of 135 cases. *Arch. Dermatol.* 1973; **108:**788-797.
6. Dermatitis (Eczema): Generalised exfoliative dermatitis or generalised erythroderma histopathology of the skin th edition 1990; **7:** 111-112 Lever, W.F., Schaumberg-Lever (editors).
7. Sarkar, R., Sharma, R. C., Koranne, R.V. and Sardana, K. Erythroderma in children: a clinico-etiological study. *J. Dermatol.* 1999; **26:**507-511.
8. Chiratikarnwong, K. Erythroderma: 14 years study at Songklanagarind Hospital. *Songkla Med. J.* 2000; **18:**31-36.
9. Zip, C., Murray, S. and Walsh, N. M. The specificity of histopathology in erythroderma. *J. Cutan. Pathol.* 1993; **20:**393-398.
10. Rogerio, N. K., Airton, dos Santos, G. L., Minelli, Mauro, F. M. and Rubens, P. Exfoliative dermatitis: clinical and etiologic study of 58 cases. *An. Bras. Dermatol.* 2006; **81:**233-237.
11. Vasconcellos, C., Domingues, P.P., Aoki, V., *et al* Erythroderma: analysis of 247 cases. *Rev. Saude. Publica.* 1995; **29:**177 -182.
12. Morar, N., Dlova, N., Gupta, A. K., *et al.* Erythroderma: a comparison between HIV positive and negative patients. *Int. J. Dermatol.* 1999; **38:** 895-900.
13. Hitoshi, K., Yoshio, S., Kazutoshi, D., *et al.* Gallbladder carcinoma presenting as exfoliative dermatitis (erythroderma). *Inter. J. Gastro. Cancer.* 2005; **35:** 153-155.
14. Botella-Estrada, R., Sanmartin, O., Oliver, V. *et al.* Erythroderma. A Clinicopathological study of 56 cases. *Arch. Dermatol.* 1994; **130:**1503-1507.
15. Hasan, T. and Jansen, C.T. Erythroderma: a follow-up of fifty cases. *J. Am. Acad. Dermatol.* 1983; **8:** 836-840.
16. Sanusi, H. U. and Kelly, A. P. Erythroderma (Generalized Exfoliative Dermatitis) *WebMD.com. eMedicine* Specialties> Dermatology> PAPULOSQUAMOUS DISEASES September 23, 2007.