

Original Research Article

Dermatological manifestations of acquired immunodeficiency syndrome: an observational study among HAART naïve patients from an ART centre of excellence

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ABSTRACT

Background: Dermatological manifestations can be a window to the clinical and immunological status of patients with HIV infection. Introduction of HAART has dramatically shifted the pattern of HIV associated dermatoses. The present study has been carried out to find out the same among HIV infected patients not started on HAART therapy.

Methods: Two hundred (200) HIV-positive, HAART-naïve patients attending ART centre of excellence were examined between November 2005 to July 2007, for the presence of mucocutaneous manifestations, correlation with CD4 count and analyzed using SPSS software.

Results: Out of the 200 patients examined, 64.5% (n=129) were found to have mucocutaneous manifestations. Out of those 129 patients 70 (54.3%) were male and 59 (45.7%) were females. Age of the patients ranged from 5 to 62 years with a mean±S.D of 32.08±11.48 yrs. Fungal infections (n=67, 51.9%) were the most common infectious dermatoses, followed by viral infections (n=35, 27.1%), scabies infestations (n=17, 13.2%) and bacterial infections (n=2, 1.6%). Of all the fungal infections, candidiasis (43.28%) was the commonest. Majority (64.5%) of the mucocutaneous manifestations were seen in patients with CD4 count <200 cells/mm³ and difference in CD4 count was significantly associated with cutaneous penicilliosis and oral hairy leukoplakia (p<0.044).

Conclusions: Infectious dermatoses remain as the far most common skin manifestations in HAART naïve patients. Lower the CD4 higher will be the incidence. Rare endemic infections like penicilliosis should be considered in differentials of umbilicated lesions in this part of the country.

Keywords: HIV, HAART naïve, Penicilliosis, CD4 count, Norwegian scabies

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) was first reported with published medical literature in 1981 and henceforth, recognized as a novel disease. Kaposi's sarcoma in a young homosexual man was the first dermatological condition that made AIDS a visible disease.¹ AIDS currently dominates as most dreaded sexually transmitted infection around the world,

especially in developing countries including India. Manipur, the state where the current study has been carried out, has shown highest estimated adult HIV prevalence with 1.15% compared to national prevalence of just 0.26%.² There were at least 26,225 HIV positive people, as per the sero-surveillance and sentinel surveillance reports during the study period. The seropositivity among different high-risk groups under surveillance was highest in injecting drug users with a

percentage of 45.22, followed by heterosexually promiscuous with a percentage of 27.4.³

The hallmark of HIV infection is a progressive, qualitative and quantitative deficiency of helper CD4 T lymphocyte which is needed for foreign antigen presentation and phagocytosis. When the number of CD4 cells declines below a certain level, opportunistic conditions including unusual infections and neoplasms set in. With the advent of antiretroviral therapy (ART), many of the skin disorders associated with HIV disease (e.g. Kaposi sarcoma) as well as serious opportunistic infections are observed less frequently than in the past. However, with longer survival, medical problems that previously were less common have emerged (e.g. anal intraepithelial neoplasia), and ART itself has created new dermatologic challenges, including drug reactions, lipodystrophy and immune reconstitution inflammatory syndrome (IRIS). The pattern of dermatoses has entirely changed in post HAART (Highly Active Anti-Retroviral Therapy) era. The present study has been carried out to find out the same among HIV infected patients not started on HAART therapy.

Objectives

To study the pattern of mucocutaneous manifestations in HIV/AIDS in HAART naïve patients in North East India and to correlate the different mucocutaneous findings with the CD4/CD8 counts.

METHODS

Two hundred (200) HIV-positive, HAART-naïve patients of both sexes attending ART centre of excellence in Manipur state, were examined at random regardless of age or duration of HIV positivity, for the presence of mucocutaneous manifestations after taking informed consent of the patients between November 2005 and July 2007. Ethical clearance was obtained from the institutional ethics committee. CD4 and CD8 count was performed in every patients using FACS count system (Becton Dickinson Immunocytometry systems, USA). Questionnaire was filled in all patients which included demographic details, details of present and past illnesses as well as the examination findings. Diagnosis was made clinically. Laboratory investigations like skin biopsy were done wherever necessary to aid the diagnosis. Data was evaluated using IBM SPSS (software package for statistical analysis) 21 software (USA). Prevalence of each diagnosis in the study was calculated. Continuous variables were summarized as means and standard deviations and were compared by unpaired t-test. Categorical variables were assessed as percentages and proportions and were compared by Chi-square test. A p value of less than 0.05 was considered significant.

RESULTS

Out of the 200 patients examined, 64.5% (n=129) were found to have mucocutaneous manifestations. Out of

those 129 patients 70 (54.3%) were male and 59 (45.7%) were females. Age of the patients ranged from 5 to 62 years with a mean±S.D of 32.08±11.48 yrs. Patients under metric were found to be of the highest percentage (34.9%), followed by under-graduates (18.6%). Occupation wise maximum patients were unemployed (45%), followed by the self-employed (35.7%). Among the risk factors heterosexual contact had the highest percentage (51.2%), followed by IVDU (27.1%), fetomaternal (12.4%) and blood transfusion (7.0%).

Table 1: Distribution of different types of mucocutaneous manifestations.

Type of mucocutaneous manifestation	Number of cases (n=129)	%
Fungal		
*Candidial infection	29	22.5
*Seborrhoeic dermatitis	15	11.6
*Dermatophyte	9	6.9
Infection		
*M. furfur infections	4	3.1
*Cutaneous penicilliosis	10	7.8
Viral		
*Herpes simplex	1	0.8
*Herpes zoster	12	9.3
*Kaposi's sarcoma	1	0.8
*OHL	10	7.8
*Molluscum contagiosum	2	1.6
*HPV infections	9	6.9
Parasitic		
*Scabies	17	13.2
Bacterial		
*Furunculosis	2	1.6
Miscellaneous		
*Eosinophillic pustular folliculitis	8	6.2
*Pruritic Papular eruptions	12	9.3
*Xerotic eczema and Ichthyosis	6	4.7
*Photosensitive dermatitis	9	6.9
*Drug eruptions	5	3.9
*Atopic dermatitis	4	3.1
*Psoriasis	1	0.8
*Others	3	2.32

Infectious dermatoses outnumbered noninfectious (121 v/s 48) ones (Table 1). Fungal infections (n=67, 51.9%) were the most common infectious dermatoses, followed by viral infections (n=35, 27.1%), scabies infestations (n=17, 13.2%) and bacterial infections (n=2, 1.6%). Of all the fungal infections, candidiasis (43.28%) was the commonest in which oropharyngeal candidiasis (38.8%) was much prevalent than genital candidiasis (4.5%). Malassezia associated infections were seen in 28.35% of all the fungal infections with 22.4% cases of seborrhoeic dermatitis, 4.4% of pityrosporum versicolor and 1.5% of pityriasis folliculitis. This was followed by cutaneous penicilliosis at 14.92% of the cases [widespread (11.9%)

and localized (2.9%)] and dermatophyte infections (13.43%). Of the viral infections (n=35, 27.1%), herpes zoster (34.28%) was commonest [multidermatomal (20%), localized herpes and recurrent herpes (5.7% each), ulceronecrotic (2.8%)], followed by oral hairy

leukoplekia (28.57%), human papilloma virus (HPV) infections (25.71%) [verruca plana (14.28%), verruca vulgaris (5.7%), genita warts and condyloma acuminata (2.8% each), molluscum contagiosum (5.7%), and herpes simplex (2.8%).

Table 2: Association of mucocutaneous manifestations and CD4 count.

Mucocutaneous manifestation	Number of cases	Median (CD4 count)	Range (CD4 count)
*Candidial infection	29	136.00	23 - 561
*Seborrhoeic dermatitis	15	168.00	41 - 561
*Dermatophyte infection	9	201.00	59 - 516
*M. furfur	4	157.00	120 - 428
*Herpes simplex	1	24.00	24 - 24
*Herpes zoster	12	102.50	45 - 494
*Kaposi sarcoma	1	149.00	149 - 149
*OHL	10	100.00	12 - 202
*Molluscum contagiosum	2	160.00	121 - 199
*HPV infections	9	163.00	52 - 426
*Scabies	17	223.00	47 - 644
*Eosinophillic pustular folliculitis	8	189.00	113 - 313
*Pruritic papular eruptions	12	167.00	23 - 313
*Cutaneous penicilliosis	10	44.00	23 - 238
*Xerotic eczema	6	120.00	36 - 251
*Photosensitive dermatitis	9	204.00	66 - 407
*Drug eruptions	5	99.00	55 - 154
*Atopic dermatitis	4	195.50	13 - 644
*Psoriasis	1	5.00	5 - 5
*Bacterial infections	2	154.00	140 - 168
*Others	3	240.00	170 - 337
Total	169	157.00	5 - 644

Table 3: Frequency distribution of mucocutaneous manifestation with respect to CD4 count.

Mucocutaneous manifestations	CD4 count 0-200 cells/mm ³	CD4 count ≥200 cells/mm ³	Number of cases
*Candidial infection	18	11	29
*Seborrhoeic dermatitis	10	5	15
*M. furfur	2	2	4
*Dermatophyte	4	5	9
*Herpes simplex	1	-	1
*Herpes zoster	9	3	12
*Kaposi's sarcoma	1	-	1
*OHL	9	1	10
*Molluscum contagiosum	1	1	2
*HPV	5	4	9
*Scabies	8	9	17
*Eosinophillic pustular folliculitis	4	4	8
*Pruritic papular eruption	7	5	12
*Cutaneous penicilliosis	9	1	10
*Xerosis	5	1	6
*Photosensitive dermatitis	4	5	9
*Drug eruptions	5	-	5
*Atopic dermatitis	3	1	4
*Psoriasis	1	-	1
*Bacterial infections	2	-	2
*others	1	2	3
Total	109 (64.5%)	60 (35.5%)	169

Overall median for CD4 count is found to be 157.00, with a range of 3 to 644. The group titled others which includes cases like aphthous stomatitis, lichen planus and secondary syphilis has the highest CD4 median (240) while herpes simplex (24) had the lowest CD4 (Table 2). There were more mucocutaneous manifestations seen with CD4 count of <200 cells/mm³ (64.5%) than with CD4 count ≥ 200 cells/mm³ (35.5%) (Table 3). Diseases like penicilliosis (9:1), oral hairy leukoplakia (9:1), drug eruptions (5:0), xerosis (5:1), herpes zoster (9:3) atopic dermatitis (3:1), seborrheic dermatitis (10:5) and candidal infections (18:11) were present more often with CD4 count <200 cells/mm³ whereas the diseases like dermatophyte infections (4:5), molluscum contagiosum (1:1), human papilloma virus (HPV) infections (5:4), scabies (8:9), eosinophilic pustular folliculitis (4:4), pruritic papular eruptions (7:5), photosensitive dermatitis (4:5) and others (1:2) were distributed almost equally across the two spectra of CD4 counts. The percentage of patients with lower CD4 count (<200) is higher in males (48.6%) compared to females (45.8%) and the difference was found to be statistically strongly significant ($p < 0.009$). Patients with age ≥ 34 years showed significantly higher proportion of lower CD4 count (<200 cells/mm³) than those < 34 years ($p < 0.041$). Similarly significance was noted in CD4 count with respect to penicilliosis and OHL ($p < 0.044$).

The overall median CD8 count was 944.50 cells/mm³. Molluscum contagiosum had the highest median value (1643) while herpes simplex showed the least (415).

Hair was not affected in maximum cases (70.5%) while diffuse loss was seen in 26.4%. Among 86.85% of the patients nail changes were not observed while 11.6% had pigmentary changes. Similarly, 63.6% of the patients had no oral changes. Oral candidiasis was observed in 24.8%, OHL in 5.4% and the combination of both was seen in 2.3% of patients.

DISCUSSION

Mucocutaneous findings are common in HIV-infected patients. Certain characteristic skin changes can help clinicians to recognize previously undiagnosed HIV infection. In addition, skin disorders in patients with unknown HIV status, may lead to HIV testing.

In the present study 64.5% of the subjects had mucocutaneous manifestation which falls somewhere between the incidence observed by Wiwanitkit (80%) and Shobana et al (40%).^{4,5} Slight preponderance of male patients (M:F=1.2:1), similar to observations made by Prabhakaran et al, may be due to higher chances of risk exposure and other factors like occupation, lifestyles etc.⁶ In our study, the maximum number of patients was in the 30-40 years of age (52.7%), same as study by Maryam et al.⁷ Very high proportion of less educated patients supports the importance of education with respect to awareness and prevention of HIV/AIDS. Unemployment

was maximum among the study group. In a study conducted by Kar on sexual behaviour in patients with STDs, 58% of the men reported sexual contact during a period of unemployment.⁸

In our study candidial infection was commonest manifestation seen at 22.5%, followed by scabies infestations (13.2%). Studies conducted by Shobhana et al and Sachin et al also observed maximum prevalence of candidiasis in HIV patients.^{5,9} Herpes zoster was the commonest viral infection in the present and the above mentioned studies. There were two cases of Norwegian scabies, both in patients with CD4 count <200 cells/mm³. Most of the other cases were eczematized scabies. Scabies is a common infestation with a high prevalence in Manipur even in the HIV-negative population and hence our study showed a higher percentage as compared to the above quoted studies.¹⁰ There was no case of infestation other than scabies in the present study.

In our study, 10 (7.8%) out of 129 patients were affected by cutaneous penicilliosis which were culture and biopsy confirmed. They accounted for 14.92% of fungal infections. Clinically they appeared in 2 distributions; as multiple discrete, flesh-coloured umbilicated papules with necrotic centres, of variable sizes on the face, secondly a more wide spread pattern with involvement of the upper and lower extremities and parts of the chest. Sivayathorn et al, in their study on the prevalence of skin disease in HIV-infected patients in Bangkok found that 3.2% of their study subjects were diagnosed as having cutaneous penicillium marneffei infection.¹¹ Shobhana et al, in their study conducted in Calcutta, on mucocutaneous manifestations of HIV/AIDS did not detect a single case of penicillium marneffei infection among their study subjects.⁵ Findings with regard to penicillium marneffei in the present study are more similar with reports from other studies in Southeast Asia than those in India.¹² The morphology and pattern of manifestation was no different from findings in other studies where cutaneous penicilliosis was detected except that there was not a single case with involvement of the oral mucosa.

Herpes zoster was the most common viral infection (overall incidence was 9.3%) at 34.8% of viral cases {multidermatomal (20%), localized herpes and recurrent herpes (5.7% each), ulceronecrotic (2.8%)}, close to the findings in the study by Das et al (11.8%).¹³

In our study, 10 cases of OHL were detected in overall 5% of patients in our study, accounting for 28% of all viral infections. Most of the cases were detected in patients with CD4 count <200 cells/mm³. It falls in between the observations were made by Wiwanitkit et al (12.5%) and Kumaraswamy et al (2.5%).^{4,14} Only one case of Kaposi's sarcoma was detected in our study, who presented with multiple purplish red growths in the hard palate, external meatus and face.

Two cases of furunculosis were the only bacterial infections detected in our study accounting for 1.6% of all mucocutaneous findings similar to study by Criton et al (1.7%).¹⁵ It was very less compared to study by Sukumaran et al, but the study was carried out on only pediatric population.¹⁶ Biopsy-confirmed cases of eosinophilic pustular folliculitis were detected in 6.2% of patients. The lesions mostly appeared as discrete, erythematous papules on the face and upper arms and they were severely pruritic. Wiwanitkit et al, in their study on Thai HIV-infected patients, detected folliculitis in 11.67% of their patients, in which eosinophilic pustular folliculitis was included.⁴ These findings suggest that eosinophilic pustular folliculitis should be considered as a probable diagnosis in an HIV⁺ patient with itchy folliculitis of the facial area.

The incidence of pruritic papular eruptions (9.3%) in our study is comparable to the incidence in the study conducted by Shashi et al (7%).¹⁷ The patients usually find the pruritus disturbing and some of them considered the post inflammatory hyperpigmentation disfiguring. Photosensitive dermatitis (6.9%) was relatively common in our study population and this could be due to several factors like increased sun exposure due to outdoor activities, climatic conditions in the state etc.

There were a striking low number of sexually transmitted diseases detected in our study population and this could be due to various reasons like the active intervention of nongovernmental organizations which have set up special HIV and STD clinics in the city.

Majority (64.5%) of the mucocutaneous manifestations were seen in patients with CD4 count <200 cells/mm³ and difference in CD4 count was significantly associated with cutaneous penicilliosis and oral hairy leukoplakia (p<0.044). A study by Thira et al showed penicilliosis was associated persistently in patients with <50 cells/mm³.¹⁸ A definite pattern comparable to other studies for any of the manifestations in relation to CD8 count could not be deduced. A very wide range in CD8 counts was noted in pruritic papular eruptions (338-3285), but the significance is not known.

CONCLUSION

Pattern of dermatoses can differ widely in HIV patients on HAART and those without. While non infectious dermatoses and HAART related adverse drug reactions are the dominant dermatoses on the former group, infectious dermatoses remains as the far most common skin manifestations in HAART naïve patients. Incidence of many of the dermtoses significantly depends on CD4 counts of the patients. Lower the CD4 higher will be the incidence. While candidiasis remains as the most common infectious dermatoses across the country, rare endemic infections like penicilliosis should be considered from this region.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee of RIMS, Imphal

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