CLINICAL SPECTRUM OF MUCOCUTANEOUS MANIFESTATIONS IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION REFERRED TO A DERMATOLOGIST

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ABSTRACT

BACKGROUND

In today's era of HIV pandemic, it is vital for the physician and the dermatologist to be aware of the wide spectrum of cutaneous manifestations of HIV, as they could be one of the earliest indicators of retroviral illness warranting a prompt diagnosis and early initiation of antiretro viral therapy.

AIMS

To study the mucocutaneous manifestations of HIV and correlate it with CD4 counts.

SETTINGS AND DESIGN

All the HIV positive patients referred from an HIV physician to a dermatologist for screening of mucocutaneous manifestations of HIV were included for a period of 6 months.

MATERIALS AND METHOD

The anonymised records of 36 patients were accessed for relevant demographical and dermatological data including details of ART and the CD4 counts within the last 6 months.

STATISTICAL ANALYSIS USED

The data was collated on Microsoft Excel 2010 and was analysed using SPSS version 21. Descriptive statistics included frequencies, proportions and Chi sq. test.

RESULTS

There were 24 males (66.7%) and 12 females (33.3%). The mean CD4 counts were 237cells/mm^3. The common mucocutaneous manifestations of HIV were oral candidiasis (58.3%), seborrhoeic dermatitis (30.6%), generalised xerosis (25%), longitudinal melanonychia and dermatophytosis (16.7%), bacterial infections and brittle nails (13.9%) and onychomycosis (11.1%). The other less common manifestations were pruritic papular eruptions of HIV (8.3%), koilonychia, paronychia, lichen planus, acquired ichthyosis and shiny nails (5.6%). Oral candidiasis was noted to be more common in men than in women. The CD4 counts decreased as the HIV clinical staging increased.

CONCLUSIONS

Certain dermatoses tend to occur more commonly in an HIV infected patient. The mucocutaneous manifestations of HIV often correlate with the CD4 counts and in a resource limited health setup help to judge the immune status of an HIV patient, prompting early initiation of ART which decrease morbidity and mortality and improve the quality of life of these patients.

KEYWORDS

Mucocutaneous Manifestations of HIV, Oral Candidiasis, Seborrhoeic Dermatitis, CD4 Counts.

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INTRODUCTION

The majority of the patients infected with Human Immunodeficiency Virus (HIV) pandemic are from developing countries. According to WHO, the total number of adults above 15 years of age living with HIV in 2013 was 1,900,000.(1) The cutaneous manifestations of HIV are well known.

Approximately, 90% of the HIV positive patients develop cutaneous manifestations during the natural course of illness.(2)

In today's era of HIV pandemic, it is vital for the physician and the dermatologist to be aware of the wide spectrum of cutaneous manifestations of HIV, which could be as common as oral candidiasis to as rare as Kaposi's sarcoma in an Indian setting. Mucocutaneous manifestations could be one of the earliest indicators of retroviral illness warranting a prompt diagnosis and early initiation of Anti-Retro Viral Therapy (ART).

Skin is the largest organ of the body and the common dermatosis could be easily classified under natural sunlight without the need of highly specialised equipment.

The mucocutaneous manifestations of HIV can be classified as infectious, non-infectious and neoplastic dermatoses. The commonest infections which plague HIV infected individuals include MRSA infections, Herpes Simplex

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Virus infections, Human Papilloma Virus infections and Syphilis to name a few.[3] Kaposi's sarcoma, lymphomas and squamous cell carcinomas are the common neoplastic dermatoses.

The frequently noted primary non-infectious dermatoses affecting the HIV-type1 infected individuals include seborrhoeic dermatitis, psoriasis and atopic dermatitis.[4] Therefore, it is prudent for all the medical health professionals to be sensitised to these common dermatoses, especially in a resource poor setting where they could help in assessing the immune status of these patients if the facility for doing the CD4 counts is not available.

METHODS

In this case series, all the HIV positive patients referred from an HIV physician to a dermatologist for screening of mucocutaneous manifestations of HIV were included from September 2014 till February 2015. The anonymised records were accessed for relevant demographical and dermatological data including details of ART and CD4 counts within the last 6 months which were noted on a pro forma. The data was collated on Microsoft Excel 2010 and was analysed using SPSS version 21. Descriptive statistics included frequencies, proportions and Chi sq. test. P value <0.05 was considered clinically significant.

RESULTS

Of the 36 HIV positive patients studied, there were 24 males (66.7%) and 12 females (33.3%). The mean age was 41.1years (SD±11.5years). Sixteen patients were on ART. The CD4 counts were available for 32 patients. The mean CD4 counts were 237 cells/mm.^{3} The commonest mucocutaneous manifestation of HIV was oral candidiasis found in 58.3% of the cohort. The second most common cutaneous disorder was seborrhoeic dermatitis (30.6%) followed by generalised xerosis noted in 25% of the study group.

The other frequently diagnosed dermatosis included longitudinal melanonychia and dermatophytosis in 16.7%, bacterial infections and brittle nails in 13.9% and onychomycosis in 11.1% of the study group. Of the other less common manifestations seen in this study group were pruritic papular eruptions of HIV in 8.3% of the patients. Koilonychia, paronychia, lichen planus, acquired ichthyosis and shiny nails were present in 5.6% of the patients. Oral candidiasis was also noted to be more common in men than in women. (P value=0.031) (Table: 1).

The commonest infectious dermatosis was fungal infections occuring in 41.7% of the study group followed by Viral (19.4%) and Bacterial infections (13.9%). The commonest fungal infection was dermatophytosis (16.7%) and the commonest viral infection was herpes simplex infection (11.1%). (Table: 2). The majority of HIV positive patients with fungal infections were found in the age group of 21-40 years. Bacterial infections and generalised xerosis were more common in the age group of 41-60 years. (Table: 3).

There was significant increase in prevalence of oral candidiasis in WHO clinical stage 3 and 4 (p value 0.025) and with decreasing CD4 counts. (P value 0.023) (Tables: 4 and 5). There was also an indirect correlation between prevalence of oral candidiasis and worsening CD4 counts.

Oral candidiasis was more prevalent in those patients, who had CD4 counts <50cells/mm.^{3} (P value=0.023). Seborrhoeic dermatitis was more prevalent in patients with CD4 counts >350cells/mm.^{3} The common dermatological manifestations which were more common in patients with CD4 counts <50cells/ in our study included herpes genitalis, molluscum contagiosum, fungal infections of the skin and haemorrhoids. (Table: 5).

On correlating the HIV clinical staging and the CD4 counts, we found that the CD4 counts decreased as the HIV clinical staging increased. (P value=0.067) (Table: 6) In our study, majority of the patients who were on ART were found to be in WHO clinical stage 1. (P value=0.043) (Table: 7) This could be explained on the fact that the WHO clinical stage improved once the patient was started on ART. In our study, the majority of the patients on ART were found to have CD4 counts between 101-200cells/.

The fact that 8 out of 11 patients with CD4 counts <100 cells/ were not on ART, could be explained on the fact that they were newly diagnosed to have HIV infection at the time of the referral to the dermatologist. (Table: 8) There was no correlation between the WHO clinical staging, CD4 counts, ART and gender, highlighting the fact that ART is considered as a treatment option based on the clinical manifestations and immune status rather than the gender. (Tables: 8 and 9).

Dermatological Manifestations	Male (24)	Female (12)	Total (Percentage)	Chi sq	P value
Oral candidiasis	17	4	21(58.3)	4.629	0.031
Seborrhoeic dermatitis	5	6	11(30.6)	3.207	0.073
Generalized xerosis	4	5	9(25)	2.667	0.102
Viral infections	5	2	7(19.4)	0.08	0.4
Longitudinal Melanonychia	4	2	6(16.7)	0.0	1
Dermatophytosis	3	3	6(16.7)	0.9	0.343
Bacterial infections	4	1	5(13.9)	0.465	0.496
Brittle nails	2	3	5(13.9)	1.858	0.173
Onycomycosis	4	0	4(11.1)	2.25	0.134
Others	21	12	33(91.7)	2.16	0.10

Table 1: Gender Distribution of Common Mucocutaneous Manifestations

Type of Infection	Dermatological Manifestation	Total (%)
FUNGAL	Dermatophytosis	6(16.7)
	Onychomycosis	4(11.1)
	Paronychia	2(5.6)
	Anguar chelitis	1(2.8)
	Pityriasis versicolor	1(2.8)
	Genital candidiasis	1(2.8)
	Total	**15(41.7)**
VIRAL	Herpes labialis	2(5.6)
	Herpes genitalis	2(5.6)
	Herpes zoster	1(2.8)
	Mollucum cantagiosum	1(2.8)
	Genital warts	1(2.8)
	Total	**7(19.4)**
BACTERIAL	Ecthyma	2(5.6)
	Folliculitis	2(5.6)
	Cellulitis	1(2.8)
	Total	**5(13.9)**

Table 2: Clinical Spectrum of Infective Dermatosis

* Each patient may have more than one infection

Dermatological Manifestations		AGE GROUPS (Years)				Chi sq	P value
		0-20 (n=)	21-40 (n=)	41-60 (n=)	61-80 (n=)		
Oral candidiasis	YES	1	11	8	1	1.920	0.589
Seborrhoeic dermatitis	YES	1	6	4	0	3.639	0.303
Longitudinal Melanonychia	YES	0	3	1	2	6.240	0.100
Onychomycosis	YES	0	2	1	1	1.744	0.627
Bacterial infections	YES	0	1	4	0	5.760	0.124
Generalised xerosis	YES	0	2	5	2	7.289	0.063
Dermatophytosis	YES	0	4	2	0	0.960	0.811
Brittle nails	YES	0	2	3	0	2.137	0.545

Table 3: Clinical Spectrum across Different Age Groups

Dermatological Manifestations		WHO STAGING				Chi sq	P value
		1 (n=8)	2 (n=4)	3 (n= 15)	4 (n=9)		
Oral candidiasis	YES	2	1	10	8	9.371	.025*
Seborrhoeic dermatitis	YES	3	1	3	4	1.846	.605
Longitudinal melanonychia	YES	0	1	4	1	3.080	.379
Onychomycosis	YES	1	2	1	0	7.566	.056
Bacterial infections	YES	0	0	3	2	2.926	.403
Generalised xerosis	YES	2	0	5	2	1.926	.588
Dermatophytosis	YES	2	1	3	0	2.520	.472
Brittle nails	YES	1	1	1	2	1.603	.659

Table 4: Correlation between Dermatological Manifestations and WHO Clinical Staging

Dermatological Manifestations		CD4 Counts (cells/mm^3)					Chi sq	P value
		<50 n=8	51-100 n= 2	101-200 n=10	201-350 n=4	>350 n=8		
Oral candidiasis	YES	7	0	8	2	2	11.375	0.023**
Seborrhoeic dermatitis	YES	1	1	3	0	4	4.916	0.296
Longitudinal Melanonychia	YES	3	0	0	2	1	7.385	0.117
Onychomycosis	YES	1	0	1	0	2	2.057	0.725
Bacterial infections	YES	1	0	2	1	0	2.514	0.642
Generalised xerosis	YES	2	1	3	1	1	1.467	0.833
Dermatophytosis	YES	2	0	1	0	2	2.418	0.659
Brittle nails	YES	0	0	1	1	2	3.200	0.525

Table 5: Correlation between the Dermatological Manifestations and CD4 Counts

CD4 Counts(cells/mm^3)	WHO Clinical staging				Chi sq	P value
	1	2	3	4		
<50	0	0	5	3	20.000	0.067
51-100	0	0	1	1		
101-200	1	2	4	3		
201-350	1	0	3	0		
>350	5	2	1	0		

Table 6: Correlation between the CD4 counts and WHO Clinical Staging

	WHO Clinical Staging				Chi sq	P value
ART	1	2	3	4	8.168	0.043*
YES	6	3	3	4		
NO	2	1	12	5		

Table 7: Correlation between WHO Staging and ART

		ART		Chi sq	P value
		Yes	No		
CD4 counts (cells/mm^3)	<50	1	7	5.994	0.200
	50-100	1	1		
	101-200	6	4		
	201-350	1	3		
	>350	5	3		
Gender	Male	9	15	1.406	0.236
	Female	7	5		

Table 8: Correlation of ART with CD4 Counts and Gender

		Gender		Chi sq	P value
		Male	Female		
WHO Clinical Staging	1	4	4	1.425	0.700
	2	3	1		
	3	11	4		
	4	6	3		
CD4 Counts (cells/mm^3)	<50	6	2	4.405	0.354
	50-100	1	1		
	101-200	8	2		
	201-350	3	1		
	>350	3	5		

Table 9: Correlation of Gender with WHO Clinical Staging and CD4 Counts

DISCUSSION

Skin manifestations are the presenting symptom of HIV infection in approximately 39.3% of the patients.[5] The commonest mucocutaneous manifestation in our study was oral candidiasis (58.3%), followed by dermatophytosis (16.7%) and seborrhoeic dermatitis (11%), which is similar to the study done by Attili et al.[5] However, drug induced cutaneous reactions were not observed in our study.

Among the cutaneous infections commonly associated with HIV, we found that the majority of the patients suffered from a spectrum of fungal infections {dermatophytosis (16.7%), onychomycosis (11.1%), paronychia (5.6%), angular chelitis (2.8%)} similar to the study done by Vasudevan et al.[6] Next to follow were viral infections in 19.4% and bacterial infections in 13.9% of our study group.

According to Munoz–Perez et al. certain dermatoses correlate well with disease progression due to their strong association with CD4 counts like herpes genitalis, herpes simplex infection, molluscum contagiosum, common warts, PPE and seborrhoeic dermatitis.[7] Our results corroborate their findings.

On correlating the mucocutaneous manifestations with CD4 counts, it was found that there was a negative association between the two. As the CD4 counts decreased, the prevalence of oral candidiasis was noted to be higher, similar to the study done by Attili et al.[5] It is also known that infectious mucocutaneous manifestations occur when the CD4 counts fall below 200 cells/mm^3, whereas non-infectious dermatosis like seborrhoeic dermatitis are more prevalent when the CD4 counts are >350cells/mm.[3],[8] which was noted in our study too.

The commonest non-infectious dermatoses noted in our study were seborrhoeic dermatitis (30.6%) and generalised xerosis (25%). Singh et al. had reported xerosis in 52.5% of their study population and seborrhoeic dermatits in 74.16%.[9] The prevalence of pruritic papular eruptions in our study was 8.3%, whereas other studies report a prevalence ranging from 7.7% to 35.8%.[9-11]

We observed longitudinal melanonychia in 16.7% of the patients similar to that reported by Cribier et al.[11] whereas Kore et al. reported nail discoloration in 5.4% of their study population.[12]

We also noted that when there was a decrease in the CD4 counts, the patient tended to be in a higher HIV clinical staging, consistent with other studies.[13] This re-emphasizes the importance of clinical assessment of the patient to know the underlying immune status even in resource limited setting where the monitoring of CD4 counts is not possible.

In our study, the dermatoses tending to be more common in patients with CD4 counts <50cells/mm^3 included herpes genitalis, molluscum contagiosum and fungal infections of the skin. Kaposi's sarcoma, cutaneous cryptococcosis, bacillary angiomatosis, proximal onychomycosis which are considered AIDS defining illnesses were absent in our study population stressing the fact that the spectrum of cutaneous manifestations in India vary from those seen in the west.[6][14] Oral hairy leukoplakia was not observed in our study.

CONCLUSION

It is important for the physician and the dermatologist to be aware of the mucocutaneous manifestations of HIV, especially oral candidiasis which is its most common mucocutaneous manifestation. Dermatologists should be aware of the various presentations of oral candidiasis so as to screen them for HIV infection early in the course of the disease, leading to prompt diagnosis and referrals to the Infectious Disease physician.

This case series further emphasises the fact that there are certain dermatoses, which tend to occur more commonly in an HIV infected patient. The mucocutaneous manifestations of HIV often correlate with the CD4 counts and in a resource limited health setup, it is possible to judge the immune status of an HIV patient based on this. The early initiation of ART decrease morbidity and mortality and improve the quality of life of these patients.

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