

Mucocutaneous manifestations and the relationship to CD4 lymphocyte counts among Turkish HIV/AIDS patients in İstanbul, Turkey

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Background/aim: Dermatologic findings differ among countries but no sufficient data about Turkish HIV-infected patients exist in the literature. Therefore, our aim in this study was to document the dermatologic manifestations and their relationships with CD4 cell counts among HIV/AIDS patients visiting our clinic for the first time in İstanbul, Turkey.

Materials and methods: A retrospective analysis of 306 HIV/AIDS patients (260 men, mean age: 38.3 years) was done in a tertiary hospital in İstanbul from January 2006 to September 2012. Information on age, sex, transmission routes, socioeconomic and educational status, CD4 counts, and dermatologic findings was collected retrospectively from medical records.

Results: Our analyses revealed at least 1 dermatologic disease in 111 of the 306 (36.2%) patients. Mean CD4 count of the patients was 393.64 cells/mm³ (range: 4–1270 cells/mm³). Oral candidiasis (12.4%), herpes zoster (5.9%), dermatophytosis (5.4%), hyperpigmentation (5.2%), and folliculitis (4.6%) were the most common skin problems. Statistically significant correlation ($P < 0.05$) with low CD4 cell counts was found for oral candidiasis, folliculitis, herpes zoster, hyperpigmentation, xerosis, and Kaposi's sarcoma.

Conclusion: Dermatologic manifestations in this study were identical to those described in most studies from Asia, and there were more manifestations as the HIV infection progressed and immune functions declined.

Key words: Mucocutaneous findings, HIV/AIDS, CD4 lymphocyte counts

1. Introduction

Since 1981, when the first reports about AIDS were published in the medical literature, mucocutaneous diseases have played an important role in the initial diagnosis of HIV infection and in determining the clinical stage of the disease. Skin can serve as the main indicator of other problems. In up to 90% or more of HIV-positive patients, mucocutaneous problems may develop at any stage of the disease (1,2). Patients with advanced HIV infection have more skin disorders than those in the early stages. Hence, dermatologic examinations can serve as a guide for diagnosis in terms of severity of HIV/AIDS (1,3,4).

It is well known that mucocutaneous diseases vary among countries, which may be attributable to climate, endemic diseases, and hygienic standards, as well as social, economic, and cultural factors. To date, there have been many reports issued about the dermatologic manifestations of HIV/AIDS patients in Western literature. However, there is a lack of sufficient data about

dermatologic findings in Turkish HIV-infected patients. Therefore, our aim in this study was to document the dermatologic manifestations and their relationships with CD4 cell counts among HIV/AIDS patients visiting our clinic for the first time in İstanbul, a large cosmopolitan city situated in western Turkey.

2. Materials and methods

A total of 306 newly diagnosed HIV/AIDS patients admitted to our outpatient clinic between January 2006 and September 2012 were included in this study. All patients were examined by an infectious diseases specialist, and patients who had skin, mucous membrane, nail, or hair complaints were examined by a dermatologist. All diagnoses were based on clinical criteria supplemented by laboratory procedures.

Information on age, sex, transmission routes, socioeconomic and educational status, CD4 counts, and dermatologic findings were collected retrospectively from medical records. FACSCalibur flow cytometry (Becton

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Dickinson, USA) and a concurrent complete blood count performed by standard techniques were used to evaluate CD4 T-cell count and CD4/CD8 ratio.

All analyses were performed by using GraphPad Prism 5.0 and SPSS 15.0. Data were described using mean ± standard deviation. Chi-square and Fisher's exact tests were used for categorical variables as appropriate. P < 0.05 was considered to be significant.

3. Results

Of the 306 HIV/AIDS patients included in this study, 260 (84.9%) were men, with a mean age of 38.3 ± 11.07 years and all patients being of Caucasian origin. The most frequent route of transmission was heterosexual intercourse (65.3%), followed by men having sex with men (MSM) (33.6%); intravenous drug abuse was present in only 3 cases. Almost half of the patients (141 (47.7%)) had low education. The majority of the women (30 (65%)) were housewives, whereas in men, office workers (n = 69), the unemployed (n = 25), and drivers (n = 18) constituted the largest group, at 112 in total (43%).

Mean CD4 count of the patients was 393.64 cells/mm³ (range: 4–1270 cells/mm³) and one-third of the patients (33%) had CD4 counts of lower than 200/mm³. There was at least 1 dermatologic disease in 111 (36.2%) patients. The mean CD4 count in patients with dermatologic problems

was 292 cells/mm³ (range: 4–1189 cells/mm³). The frequency of infectious and noninfectious manifestations, in line with the classification of the World Health Organization (WHO) in terms of the immunological groups, is shown in Tables 1 and 2.

A statistically significant correlation with low CD4 cell counts was found for oral candidiasis, folliculitis, herpes zoster, hyperpigmentation, xerosis, and Kaposi's sarcoma.

Out of 306 patients, 44 (14.3%) had been diagnosed with HIV infection due to mucocutaneous diseases before. Oral candidiasis (n = 18), Kaposi's sarcoma (n = 7), folliculitis (n = 6), and herpes zoster (n = 5) were the most common diseases in these patients.

4. Discussion

In HIV infection, as a consequence of decline in the number of antigen-presenting cells and CD4 lymphocytes, the skin becomes vulnerable to opportunistic infectious agents and neoplastic disorders (5). Many studies have reported mucocutaneous manifestations in 33%–95% of HIV-infected patients (2,4,6,7). The prevalence of dermatologic findings among our patients (36.2%) is close to that of reports from Iran and India. The only study from Turkey was published in 2007 and the rate of skin manifestations in HIV/AIDS patients was 90% in that report (8). The causes of this difference might be that the study in 2007 included

Table 1. Prevalence of infectious mucocutaneous manifestations and their relationship to CD4 counts (according to WHO immunological staging).

Dermatologic manifestations	Number of patients, n = 306 (%)	CD4 counts (/mm ³)				P-value
		≥500, n = 67	499–350, n = 56	349–200, n = 82	<200, n = 101	
Fungal infections						
Oral candidiasis	38 (12.4)	5	4	7	22	0.0001
Onychomycosis	9 (2.9)	1	2	2	4	0.042
Tinea pedis	6 (1.9)	-	1	1	4	0.046
Tinea corporis	2 (0.6)	-	-	2	-	0.046
Bacterial infections						
Folliculitis	14 (4.6)	2	3	1	8	0.011
Acne vulgaris	7 (2.3)	3	-	1	3	0.161
Tuberculosis	1 (0.3)	1	-	-	-	-
Viral infections						
Herpes zoster	18 (5.9)	4	1	4	9	0.02
Condylomata acuminata	8 (2.6)	1	2	2	3	0.72
Herpes simplex	3 (0.9)	1	-	1	1	0.72
Molluscum contagiosum	1 (0.3)	-	-	-	1	-
Infestations						
Scabies	2 (0.6)	1	-	1	-	-
Pediculosis corporis	1 (0.3)	-	-	-	1	-

Table 2. Prevalence of noninfectious mucocutaneous manifestations and the relationship to CD4 counts (according to WHO immunological staging).

Dermatologic manifestations	Number of patients, n = 306 (%)	CD4 counts (/mm ³)				P-value
		≥500, n = 67	499–350, n = 56	349–200, n = 82	<200, n = 101	
Noninfectious diseases						
Hyperpigmentation	16 (5.2)	-	1	4	11	0.0001
Xerosis	15 (4.9)	2	1	3	9	0.0016
Seborrheic dermatitis	13 (4.2)	2	3	2	6	0.108
Kaposi's sarcoma	8 (2.6)	-	-	1	7	0.0001
Psoriasis	2 (0.6)	-	-	1	1	-
Lichen planus	2 (0.6)	-	2	-	-	-
Alopecia	1 (0.3)	-	-	1	-	-

inpatients, that the number of the cases was very limited, and that the study was made in a different geographic region in Turkey. Nevertheless, reports from different regions of India declared the cutaneous manifestations to be between the range of 40%–87.6% (6,9).

In our study, infectious and noninfectious dermatologic manifestations were recorded (see Tables 1 and 2). The most common infections were fungal, with oral candidiasis being the most frequent. Azfar et al. and Spira et al. showed similar rates and results; nevertheless, other studies reported higher incidence rates of oral candidiasis, up to 54.1% (3,10,11). The prevalence of dermatophytosis depends on sociocultural level, climate, clothing, and profession; there is no significant difference between the HIV-negative and HIV-positive population (12). In our study, dermatophytosis was documented in 5.4% of the patients.

The most common viral infection was herpes zoster, followed by condylomata acuminata. Shobana et al. reported herpes zoster with a frequency of 6%, similar to our study (6). In previous studies, condylomata acuminata rate was determined as 3.1%–12.8% among HIV-infected patients (13,14).

In bacterial infections, as observed in our patients, studies have revealed frequencies of folliculitis ranging from 3.3% to 32.9% (11,15). One of the 2 patients with scabies was diagnosed with HIV infection due to the crusted form of this infestation. The rate of scabies infection has been reported to be up to 10%, especially in pruritic eruptions (1).

Out of all the noninfectious diseases, generalized hyperpigmentation was the most frequent finding observed in patients. Hyperpigmentation incidence has been reported as being low in European populations, but

high rates of incidence have been reported in Asian studies (9,16,17). Dry skin has been noted as a common finding in studies ranging from 22% to 73% in HIV-infected patients (3,9,10,17). The prevalence of xerosis in our patients was considerably lower than in the other studies.

Seborrheic dermatitis may be an early clinical marker for HIV infection and the incidence of disease changes by 14% to 74% (4,9). In our patients, seborrheic dermatitis was observed in all stages of HIV infection. Very high incidences of psoriasis have been reported from Asia (up to 25%) in HIV-infected populations (18). In Western studies, on the other hand, 2%–4% incidences of psoriasis have been published (6). In this study, psoriasis, lichen planus, and alopecia were also rarely observed.

Compared to its prevalence in the 1980s and early 1990s, the rate of Kaposi's sarcoma was relatively low (19). Among the HIV-infected patients, MSM were the most affected by Kaposi's sarcoma. In our study, Kaposi's sarcoma was observed in 8 patients, 5 of whom were MSM.

Dermatological manifestations increased both in frequency and severity with progression of HIV and decline in CD4 cell counts. There was a significantly high occurrence of oral candidiasis, hyperpigmentation, Kaposi's sarcoma, xerosis, folliculitis, and herpes zoster among patients with low CD4 cell counts, which was similar to many previous studies (3,6,9,14,20).

Here, we presented the types of skin diseases, as well as their stages among Turkish HIV/AIDS patients. The results suggested that oral candidiasis, Kaposi's sarcoma, folliculitis, and herpes zoster are useful clinical predictors of HIV infection or signs of the presence of advanced HIV infection. Dermatological manifestations may be the first clue of an HIV infection and may also be helpful in monitoring the immune status of the patient.

References

1. Sud N, Shanker V, Sharma A, Sharma NL, Gupta M. Mucocutaneous manifestations in 150 HIV-infected Indian patients and their relationship with CD4 lymphocyte counts. *Int J STD AIDS* 2009; 20: 771–774.
2. Sivayathorn A, Srihira B, Leesanguankul W. Prevalence of skin disease in patients infected human immunodeficiency virus in Bangkok, Thailand. *Ann Acad Med Singapore* 1995; 24: 528–533.
3. Wiwanitkit V. Prevalence of dermatological disorders in Thai HIV-infected patients correlated with different CD4 lymphocyte count statuses: a note on 120 cases. *Int J Dermatol* 2004; 43: 265–268.
4. Foroughi M, Koochak HE, Roosta N, Paydary K, Khatami A, Shahriari S, Payvarmehr T, Seyed Alinaghi S. Prevalence of dermatologic manifestations among people living with HIV/AIDS in Imam Khomeini Hospital in Tehran, Iran. *J AIDS HIV Res* 2012; 4: 56–59.
5. Cedeno-Laurent F, Gomez-Flores M, Mendez N, Ancer-Rodriguez J, Bryant JL, Gaspari AA, Trujillo JR. New insights into HIV-1-primary skin disorders. *J Int AIDS Soc* 2011; 14: 5.
6. Shobhana A, Guha SK, Neogi DK. Mucocutaneous manifestations in HIV infection. *Indian J Dermatol Venereol Leprol* 2004; 70: 82–86.
7. Josephine M, Issac E, George A, Ngole M, Albert SE. Patterns of skin manifestations and their relationships with CD4 counts among HIV/AIDS patients in Cameroon. *Int J Dermatol* 2006; 45: 280–284.
8. Boztepe G, Akoğlu G, Şahin GO, Güven GS, Ünal S, Şahin S. HIV/AIDS and skin: 7-year of experience at Hacettepe. *Turk Derm* 2006; 40: 46–51 (article in Turkish with English abstract).
9. Singh H, Singh P, Tiwari P, Dey V, Dulhani N, Singh A. Dermatological manifestations in HIV-infected patients at a tertiary care hospital in a tribal (Bastar) region of Chhattisgarh, India. *Indian J Dermatol* 2009; 54: 338–341.
10. Azfar NA, Khan AR, Zia MA, Humayun A, Malik LM, Jahangir M. Frequency of mucocutaneous manifestations in HIV positive Pakistani patients. *J Pak Assoc Dermatol* 2011; 21: 149–153.
11. Spira R, Mingard M, Doutre MS, Molart P, Dabis F. Prevalence of cutaneous disorders in a population of HIV-infected patients. *Arch Dermatol* 1998; 134: 1208–1212.
12. Esser S, Schoefer H. HIV-associated skin and mucocutaneous diseases. In: Hoffman C, Rockstroh JK, editors. *HIV 2010*. Hamburg, Germany: Medizin Fokus Verlag; 2010. pp. 568–580.
13. Huang XJ, Li HY, Chen DX, Wang XC, Li ZC, Wu YS, Zhang T, Gao YQ, Wu H. Clinical analysis of skin lesions in 796 Chinese HIV-positive patients. *Acta Derm Venereol* 2011; 91: 552–556.
14. Kim TG, Lee KH, Oh SH. Skin disorders in Korean patients infected with human immunodeficiency virus and their association with a CD4 lymphocyte count: a preliminary study. *J Eur Acad Venereol* 2010; 24: 1476–1480.
15. Garbe C, Husak R, Orfanos CE. HIV-associated dermatoses and their prevalence in 456 HIV-infected patients. Relation to immune status and its importance as a diagnostic marker. *Hautartz* 1994; 45: 623–629.
16. Munoz-Perez MA, Rodriguez-Pichardo A, Camacho F, Colmenero MA. Dermatological findings correlated with CD4 lymphocyte counts in a prospective 3 year study of 1161 patients with human immunodeficiency virus disease predominantly acquired through intravenous drug abuse. *Br J Dermatol* 1998; 139: 33–39.
17. Jing W. A retrospective survey of mucocutaneous manifestations of HIV infection in Malaysia: analysis of 182 cases. *J Dermatol* 2000; 27: 225–232.
18. Goh BK, Chan RK, Sen P, Theng CT, Tan HH, Wu YJ, Paton NI. Spectrum of skin disorders in human immunodeficiency virus-infected patients in Singapore and the relationship to CD4 lymphocyte counts. *Int J Dermatol* 2007; 46: 695–699.
19. Franceschi S, Maso LD, Rickenbach M, Polosel J, Hirschel B, Cavassini M, Bordoni A, Elzi L, Ess S, Jundt G et al. Kaposi sarcoma incidence in the Swiss HIV Cohort Study before and after highly active antiretroviral therapy. *Br J Cancer* 2008; 99: 800–804.
20. Nnoruka EN, Chukwuka JC, Anisui B. Correlation of mucocutaneous manifestations of HIV/AIDS infection with CD4 counts and disease progression. *Int J Dermatol* 2007; 46: 14–18.