

Prevalence of dermatophytes in interdigital spaces in HIV patients

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Post Dermatol Alergol 2012; XXIX, 1: 30–34

Abstract

Introduction: Human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS), both are related to higher prevalence of mycoses, especially oral candidosis, but also superficial mycoses. Fungal infections of the skin and its appendages are the most frequent dermatological complications in HIV patients and clinical manifestations of those infections are often atypical and more severe than in immunocompetent individuals.

Aim: The purpose of the study was evaluation of the presence of dermatophytes in foot interdigital spaces in HIV patients in relation with various factors concerning the patient.

Material and methods: The population under study were patients at the Infectious Diseases Clinic. The research comprised filling in questionnaires, physical examinations, evaluation of immunological status, and mycological examination of swabs from interdigital spaces.

Results: Out of the 120 HIV infected patients under study, foot skin lesions were observed in 40 cases (33.3%) while dermatophytes were isolated from 12 patients (10%). *Trichophyton mentagrophytes* was isolated from 7 patients (5.8%), and *Trichophyton rubrum* from 6 (5.0%); both of the species were isolated from 1 patient. The prevalence of dermatophytes did not depend on the patient's sex, sexual orientation, CD4 cells count, HCV co-infection, anti-retroviral therapy nor clinical manifestations on the feet.

Conclusions: The prevalence of dermatophytes in foot interdigital spaces in HIV patients amounted to 10% (similarly as in immunocompetent individuals) and did not depend significantly on any of the factors tested. It appears that contact with the fungi is the main factor responsible for infection.

Key words: dermatophytes, human immunodeficiency virus, superficial mycoses.

Introduction

Superficial mycoses are an essential epidemiological problem because they are widespread and are easily transferred from one person to another. Despite constant progress in diagnosis and management, they still remain a serious therapeutical problem. Recently a constant increase in the prevalence of both invasive and superficial mycoses has been observed, which is related to a growing population specifically susceptible to such infections.

Human immunodeficiency virus (HIV) infection is accompanied by increasing immunodeficiency, which increases the risk of various infectious diseases, including mycoses [1]. In HIV-positive and acquired immune deficiency syndrome (AIDS) patients, the main problem

is infection of mucous membranes with *Candida*; it particularly concerns the oral cavity, throat, larynx and vagina. Candidosis is the most frequent mycosis in this group of patients and is known as an "AIDS-defining illness". When the number of CD4 lymphocytes is very low, other invasive fungal infections may occur (systemic, disseminated) caused both by yeasts (invasive candidosis, cryptococcal meningoencephalitis) and by filamentous fungi (invasive aspergillosis) [2-6]. Superficial mycoses occur in HIV patients less frequently than mycoses of mucous membranes, nevertheless, they are the most frequent complications in those persons [7]. Skin infections in HIV patients may be either primary superficial infections that may disseminate to other tissues and organs or be a superficial manifestation of an invasive infection [4].

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The clinical manifestations of superficial mycoses in HIV patients are more severe, the lesions may be atypical and resistant to conventional treatment [4, 7-9]. Such infections in HIV patients may be severe and even life threatening because skin maceration in the interdigital spaces may create the entry of infection with highly pathogenic fungi and/or bacteria [10]. Moreover, superficial mycoses, similarly to other diseases of the skin and its appendages, may considerably influence functioning of the patient in various situations, increase his or her psychosocial discomfort and thus deteriorate the quality of life. Those diseases may cause a feeling of shame because of unsightly appearance, anxiety about spreading of the disease to other parts of the body, as well as anger and depression. Superficial mycoses may interfere with social activity of the patient: his or her professional activity, social contacts, rest and sexual activity. The latter is significantly limited by the underlying disease in HIV patients [10-12].

Aim

The objective of the study was evaluation of the occurrence of dermatophytes in foot interdigital spaces in HIV patients as well as analysis of the influence of CD4 cell level and other patient characteristics (sex, sexual orientation, other diseases, antiretroviral drugs) on the prevalence of dermatophytes.

Material and methods

The population under study comprised HIV patients treated at the Clinic of Infectious Diseases, Chair of Gastroenterology, Hepatology and Infectious Diseases, Jagiellonian University Medical College in Kraków, aged over 18 years who agreed in writing to participate in the study.

An agreement of the Bioethical Committee of the Jagiellonian University was obtained (KBET/24/B/2009, KBET/56/B/2010). The financial support was obtained from the Jagiellonian University Medical College research grant K/ZBW/000569.

The patients had to fill in an anonymous questionnaire concerning their age, residence (urban/rural), education, job, sexual orientation, route and time of HIV infection, concomitant diseases and actual medication. Additionally, the medical history was taken and physical examination of the foot skin was performed.

At physical examination, smears from the left and right foot interdigital spaces were taken with a spatula with cotton wool rinsed with sterile saline. The clinical materials were cultured on two microbiological media: Sabouraud medium with chloramphenicol, and Sabouraud medium with chloramphenicol and cycloheximide. The cultures were incubated at 27°C for 4 weeks. The fungi grown in the cultures were identified phenotypically on the basis of colony morphology, micromorphology in

preparations from the culture and slide microculture as well as using biochemical tests.

The data were processed statistically using the language and environment R, version 2.9.1 (2009). The results were considered as significant when $p \leq 0.05$.

Results

A total of 120 HIV patients were included into the study: 91 males aged 20-73 years (mean age 37.7 ± 9.8 years), and 29 females aged 24-44 years (mean age 34.6 ± 4.8 years). The mean age in the entire group was 37.0 ± 8.9 years.

Out of the males, 51 (56.0%) declared that they are heterosexuals, 30 (33.0%) – homosexuals, and 10 (11.0%) bisexuals. In the group of females, 26 (89.7%) declared their heterosexuality and 1 (3.4%) – homosexuality. One woman refused to answer this question.

At the clinical materials to mycological examinations sampling moment, the number of CD4 varied from 2/μl to 1065/μl. Patients with CD4 count between 200/μl and 499/μl dominated.

The most frequent disease in the group was hepatitis C virus infection (HCV). It was detected in 35 (29.2%) patients: in 26 males (28.6%) and in 16 females (55.2%). During sampling smears from the interdigital spaces, 85 patients (70.8%) were under antiretroviral treatment: 63 males (69.2%) and 22 (75.9%) females.

On physical examination, skin lesions of the feet were observed in 40 patients (33.3%): flare, scaling, discoloration, dermatorrhesis, pachyderma, discharge. Six patients (5.0%) complained about itching, pain, burning and sweating.

Dermatophytes were isolated from 12 patients (10.0%): 11 males (12.1%) and 1 female (3.4%). Two dermatophyte species were detected in the clinical materials: *Trichophyton rubrum* and *T. mentagrophytes*. *Trichophyton rubrum* was found in 6 patients (5.0%), and *T. mentagrophytes* in 7 (5.8%), while in 1 patient, colonization with both of the species was found.

Dermatophytes were isolated from 6 (15.0%) out of the 40 patients with foot skin lesions. Dermatophytes were also isolated from 6 (7.5%) of the remaining 80 patients (66.6%) with no foot skin lesions. The prevalence of dermatophytes did not depend on the presence or lack of skin lesions (Table 1).

Dermatophytes were isolated only in one of the 6 patients complaining about symptoms from their feet, while they were present in 11 (9.6%) of the 114 symptomless patients. No relationship was found between the presence of symptoms and the prevalence of dermatophyte isolations (Table 1).

It was also found that the number of CD4 does not influence the occurrence of dermatophytes. Moreover, no significant relationship was found between the prevalence of dermatophytes vs. HCV co-infection and/or antiretroviral treatment (Table 1).

Table 1. The occurrence of dermatophytes in foot interdigital spaces in HIV patients in relation to various factors

Factors		Number of patients	Number and percentage of patients in whom dermatophytes were isolated	Fischer test
Sex	Male	91	11 (12.1%)	$p = 0.2894$
	Female	29	1 (3.4%)	
Sexual orientation	Heterosexual	77	5 (6.5%)	$p = 0.1104$
	Homosexual	31	5 (16.1%)	
	Bisexual	11	2 (18.2%)	
Foot skin lesions	Present	40	6 (15.0%)	$p = 0.2113$
	None	80	6 (7.5%)	
Symptoms	Present	6	1 (16.7%)	$p = 0.4761$
	None	114	11 (9.6%)	
CD4 cell count	$\leq 199/\mu\text{l}$	35	5 (14.3%)	$p = 0.4452$
	200-499/ μl	60	6 (10.0%)	
	$\geq 500/\mu\text{l}$	25	1 (4.0%)	
HCV co-infection		35	2 (5.7%)	$p = 0.5078$
Antiretroviral therapy		85	8 (9.4%)	$p = 0.7286$

Discussion

Both HIV infection and AIDS are related to higher prevalence of mycoses [1]. Candidosis of mucosa is usually diagnosed in HIV patients, however, mycoses of the skin and its appendages are also frequent [4, 13]. Mycoses of the skin and its appendages are the most frequent complications in HIV patients; clinical manifestations of those infections are often atypical and more severe than in immunocompetent individuals [4, 6, 8, 9].

Foot mycosis is the most frequent skin mycosis in the general population and accounts for 30% of all of the fungal skin infections [14]. The international epidemiological study (Achilles project) revealed that as many as 42% of the Polish population suffers from foot mycosis [15]. The most frequent causative agents of those infections, similarly to other superficial mycoses, are undoubtedly dermatophytes. Macura *et al.* [16] analyzed the prevalence of dermatophytes in clinical materials sampled from outpatients suspected of superficial mycosis in Krakow in the years 1998-2007. They detected presence of those fungi in 38.6% of the toenail specimens and in 22.8% of foot skin scrapings. Dermatophyte infections are also common in HIV patients, however, there is no evidence that they are more frequent in HIV-positive than in HIV-negative patients [13].

In HIV patients, *tinea pedis* is thought to be the most frequent skin mycosis, together with *tinea corporis*, *tinea cruris* and *onychomycosis* [13]. In the present study, we have detected the presence of dermatophytes in foot interdigital spaces in 10.0% of HIV patients. The finding

is comparable to the prevalence of dermatophytes in a group of soldiers (unpublished data), who are also predisposed to development of superficial mycoses. Similar findings were obtained by di Silverio's *et al.* [17] who evaluated the occurrence of dermatophytes in selected sites on the HIV patients' skin: in sportsmen vs. control group. The prevalence of their dermatophyte isolations from interdigital spaces was similar to ours: 12.5%. They did not detect the difference of the prevalence of dermatophytes in HIV+ patients vs. sportsmen (20% vs. 28.1%), however, dermatophytes were most often isolated in the HIV patients' group than in the control group (20% vs. 6%) [17]. Lohoué Petmy *et al.* [18] diagnosed *tinea pedis* in HIV patients in somewhat lower percentage than it was found by us or di Silverio *et al.* [17]. Foot mycosis was diagnosed in 7.4% of the patients; it was one of the most frequent mycosis in those patients, just after oral candidosis, *tinea corporis* (8.8%) and *tinea versicolor* (8.1%) [18]. A considerably lower prevalence of foot mycosis in HIV patients was found by Kaviarasan *et al.* [19]. In their study on 185 HIV patients, the most frequent skin mycosis was *tinea corporis* (11.9%), next to it *tinea cruris* (9.7%). *Tinea pedis* was detected only in 3.8% of the patients. The above findings are controversial to those obtained by Rodwell *et al.* [1] and Korting *et al.* [20]. Rodwell *et al.* detected *tinea pedis* in 52 out of 105 HIV patients (49.5%) while Korting *et al.* detected presence of dermatophytes in foot skin scrapings in 42% of 105 HIV patients.

In our investigations, only two dermatophyte species were isolated: *T. rubrum* and *T. mentagrophytes*, and their

prevalence was comparable. We have established in our investigations, carried out since the 1970s that just those two species constantly dominate in our region and that *T. rubrum* considerably outnumbers *T. mentagrophytes* [16, 21]. The preponderance of *T. rubrum* in HIV patients was also reported by other researchers' teams, among others, Rodwell *et al.* [1] and Korting *et al.* [20].

The CD4 cell count in HIV patients is an index of their immunological status. The influence of CD4 cell count on the occurrence of mycoses: on mucosa, superficial and deep-seated was tested many times. Even though the influence of those lymphocytes on infections with yeasts *Candida* is not controversial [4], in the case of dermatomycoses, the available data appear to be contradictory. Gregory [22] claims that decrease of CD4 count causes occurrence of various skin lesions, e.g. onychomycosis develops at CD4 count around 450/ μ l. Similarly, Aly and Berger [13] and Gupta *et al.* [10] established that onychomycosis occurs at the early stage of HIV infection, at CD4 count around 400/ μ l. In our study, similarly as in that by Rodwell *et al.* [1] no relationship was found between the presence of dermatophytes in foot interdigital spaces and CD4 count (Fisher test, $p = 0.4452$), however, dermatophytes more often were present in patients with $CD4 < 500/\mu$ l.

Previous investigations gave evidence of relationship between sexual orientation and the presence of dermatophytes [1, 23]. Torssander *et al.* [23] noted that dermatomycoses occur more often in homosexuals. Rodwell *et al.* [1] also found a higher prevalence of dermatophyte in patients who reported homosexual contacts. In our findings, the prevalence of dermatophytes in homo- and bisexuals was 16.1% and 18.2%, respectively. In heterosexuals the prevalence was lower: 6.5%, however, the difference was not significant (Fisher test, $p = 0.1104$).

Conclusions

Our study on the prevalence of dermatophytes in the foot interdigital spaces in HIV patients did not reveal the relationship between the immunological status of the patient, his or her sexual orientation, and antiretroviral treatment. The prevalence of dermatophyte isolations in the group under study was 10.0%. It was comparable with that in a group of soldiers (unpublished data) and was twice lower than in patients referred to our institution by dermatologists because of clinical manifestations of foot mycosis. It may be concluded that HIV infection is not an important factor conducive to foot dermatophytosis. The main factor, similarly as in individuals with normal immunity, may be contact with the pathogen.

Acknowledgments

We would like to thank Mr. Paweł Krzyściak, Doctor of Medical Science for statistical processing of the data.

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