

Disseminated dermatophytosis and acquired immunodeficiency syndrome: literature review and presentation of clinical experience

Dermatofitose disseminada e síndrome da imunodeficiência adquirida: revisão de literatura e apresentação de experiência clínica

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ABSTRACT

Introduction: Dermatophytosis are very common fungal infections caused by the fungal species *Microsporum*, *Epidermophyton* or *Trichophyton*, which mostly affect the skin, the interdigital region, groin and scalp. Although they do not cause serious diseases, in patients with the human immunodeficiency virus the infection manifests itself and evolves exuberantly, usually with extensive and disseminated lesions. **Objective:** To review the literature on dermatophytosis in people living with human immunodeficiency virus and to present the experience in clinical care in a patient living with human immunodeficiency virus with extensive and disseminated dermatophytosis. **Methods:** A literature review on the topic was carried out in the PubMed/National Library of Medicine – USA databases, using the keywords dermatophytosis, or dermatophytosis associated with the words AIDS, human immunodeficiency virus or immunodeficiency, from 1988–2022. The clinical experience showed a patient living with human immunodeficiency virus developing AIDS and presenting with disseminated skin lesions. Samples of the lesion were collected by scraping, which were submitted to culture and there was growth of fungi of the *Trichophyton sp* genus. A biopsy of the lesion was also performed using the Grocott-Gomori's Methenamine Silver stain. **Results:** We found 1,014 articles, of which only 34 presented a direct correlation with our paper, and were used to discuss the main themes narrated in this article. We present clinical experience in the management of a patient with human immunodeficiency virus/AIDS and low adherence to antiretroviral treatment, showing extensive and disseminated erythematous-squamous lesions with a clinical diagnosis of tinea corporis, manifesting with a clinical picture usually not found in immunocompetent patients. The diagnosis was confirmed by laboratory tests with isolation of the *Trichophyton sp* fungus. The patient was treated with oral fluconazole, with complete remission of the clinical picture after two months. She was also thoroughly encouraged to use the prescribed antiretroviral medication correctly. **Conclusion:** Dermatophytosis in patients living with human immunodeficiency virus can present extensive and disseminated forms. The antifungal treatment is quite effective, with remission of the condition. Antiretroviral therapy is an important adjuvant for better recovery of the sickness.

Keywords: Dermatophytosis. Acquired immunodeficiency syndrome. HIV.

RESUMO

Introdução: Dermatofitoses são infecções comuns, causadas pelas espécies fúngicas *Microsporum*, *Epidermophyton* ou *Trichophyton*, que acometem preferencialmente a pele da região interdigital, da virilha e do couro cabeludo. Apesar de não causar doenças graves, em pacientes portadores do vírus da imunodeficiência humana, a infecção se manifesta e evolui de forma exuberante, normalmente com lesões extensas e disseminadas. **Objetivo:** Fazer revisão de literatura sobre dermatofitose em pessoas vivendo com vírus da imunodeficiência humana e apresentar a experiência na atenção clínica em uma paciente vivendo com o vírus e dermatofitose extensa e disseminada. **Métodos:** A revisão de literatura sobre o tema baseou-se nos dados do Pubmed/National Library of Medicine, dos Estados Unidos, utilizando-se as palavras-chave dermatofitose, dermatofitose e AIDS, dermatofitose e vírus da imunodeficiência humana, e dermatofitose e imunodeficiência, de 1988–2022. Descreveu-se a experiência clínica na abordagem de uma paciente vivendo com vírus da imunodeficiência humana, a qual desenvolveu AIDS e apresentou lesões cutâneas disseminadas. Por raspado, foram coletadas amostras da lesão e submetidas à cultura, e constatou-se crescimento de fungos do gênero *Trichophyton sp*. Realizou-se também biópsia da lesão, corada pelo método da metenamina de prata de Grocott-Gomori. **Resultados:** Foram encontrados 1.014 artigos, dos quais apenas 34 apresentaram correlação direta com nosso trabalho, e foram utilizados para discorrer sobre os principais temas narrados neste artigo. Apresentou-se experiência clínica na abordagem de uma paciente com vírus da imunodeficiência humana/AIDS e baixa adesão ao tratamento antirretroviral, exibindo lacerações eritematoescamosas extensas e disseminadas, com diagnóstico clínico de *Tinea corporis*, manifestando-se com quadro clínico usualmente não encontrado em pacientes imunocompetentes. O diagnóstico foi confirmado por exames laboratoriais com isolamento do fungo *Trichophyton sp*. Tratada com fluconazol via oral, a paciente apresentou remissão parcial das infecções aos dois meses e completa aos seis meses. Também foi exaustivamente estimulada a usar corretamente a medicação antirretroviral prescrita. **Conclusão:** A dermatofitose em pacientes com vírus da imunodeficiência humana pode se apresentar de forma extensa e disseminada. O tratamento antifúngico é eficaz, com remissão do quadro. A terapia antirretroviral é importante adjuvante para melhor recuperação dos enfermos.

Palavras-chave: Dermatofitose. Síndrome da imunodeficiência adquirida. HIV.

INTRODUCTION

Dermatophytosis are common infections caused by the fungal species *Microsporum*, *Epidermophyton* or *Trichophyton*⁽¹⁾, which

mostly affect keratinized tissues, such as the interdigital region, the groin and the scalp⁽²⁾. These are superficial infections both in immunocompetent and immunocompromised patients⁽¹⁾. In patients with the human immunodeficiency virus (HIV), despite not causing severe diseases, the pathology manifests itself and evolves atypically, with extensive and disseminated lesions⁽³⁾. Considered as a universal disease, it is usually caused by the *Trichophyton rubrum*⁽⁴⁾ species, etiological agent that is more isolated in immunocompromised patients⁽⁵⁾.

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Restricted to the stratum corneum, dermatophytosis affects exposed areas of the skin, except for the palms of the hands and foot sole⁽⁴⁾; however, there are reports of dermal and lymph node invasion⁽⁶⁾. Its transmission occurs by inter-human contact or with infected animals, especially cats and dogs, and can be transmitted during sexual intercourse, self-inoculation or directly on the ground⁽⁴⁾; the latter related to animal fur that falls on the ground and become a keratin substrate for the growth of fungi, fact that is mainly observed in households.

The incubation period is from one to three weeks. The lesions present varied sizes and shapes (circinate, oval or arched), usually rounded, with elevated edges, scaly core, leading to intensive pruritus, and eventually associated with a burning sensation⁽⁴⁾.

The treatment is non-pharmacological, involving maintaining the skin clean, and pharmacological, with topical or oral medicines⁽⁷⁾. The choice of the more appropriate treatment is determined by the extension of the infection, the anatomic site that is mostly affected and the involved dermatophytic species.

OBJECTIVE

To review the current literature about dermatophytosis in patients with HIV and present the clinical experience with the treatment of a patient with AIDS and an unusual, exuberant, clinically disseminated manifestation, and satisfactory evolution caused by the prescription of fluconazole.

METHODS

This article aims at describing the experience of the clinical and therapeutic management of extensive dermatophytosis in a patient living with AIDS, as well as the treatment success. A literature review on the subject was performed based on the Medline/PubMed databases (National Library of medicine), from the United States, using the EndNote X9.3.3 software (license n. 3061984210), and the descriptors (DeCS — <https://decs.bvsalud.org/>) in English: *dermatophytosis, AIDS, HIV or immunodeficiency*. We found references from 1988 to 2022 in 1,014 articles, of which only 34 presented a direct correlation with our paper. They were used to analyze the main topics described in this article. Besides that, we used three books^(4,8,9).

RESULTS

A 38-year-old female patient, with the human immunodeficiency virus (HIV), on irregular use of antiretrovirals. She presented with CD4 T-cell count (48 cells/mm³) and viral load (22,630 copies/mm³) and went to the AIDS outpatient clinic in Hospital Universitário Gaffrée e Guinle with extensive pruritic rashes along her body, and history of eight months of evolution⁽⁸⁾ (**Figures 1 and 2**). The infections began in the abdomen and transited to other areas of the body; extensive and major lesions such as these ones are often found in patients with AIDS.

The macroscopic aspect of the lesions observed by ectoscopy and the patient's report led to the clinical suspicion of extensive dermatophytosis. To conclude the diagnosis, skin scraping on the lesions' edges was performed, and the material was analyzed with potassium hydroxide (KOH) microscopy, showing several hyphae. Another part was sent to culture, which diagnosed fungus of the *Trichophyton sp.*

Gender. The lesions' biopsy showed hyphae in the stratum corneum using the Grocott-Gomori stain⁽⁸⁾ (**Figure 3**).

First, the patient underwent treatment with 400 mg of fluconazole per day, for seven days, followed by 200 mg a day for two months. There was significant reduction of the lesions. The patient was referred to psychological treatment, which resulted in good adherence to the antiretroviral treatment. About six months after the beginning of treatment with fluconazole, the infection disappeared completely; however, there were others, this time compatible with the diagnosis of herpes simplex, possibly resulting from the immune reconstitution syndrome.

DISCUSSION

Dermatophytosis are universal diseases caused by three genders of fungi: *Microsporium*, *Trichophyton* and *Epidermophyton*, which belong to the *Arthrodermataceae* Family. Among them, the most found species is *Trichophyton rubrum*⁽¹⁰⁻¹³⁾. These fungi affect keratinized tissues of the skin, hair and nails^(13,14), causing superficial infection both in immunocompetent and immunocompromised patients^(11,15); however, they are more often found among immunocompromised patients with skin barrier dysfunction^(12,16,17).



Figure 1. Extensive and disseminated erythematous-squamous plaques, with circinate and high edges and intense pruritus. There are areas of broadly distributed lichenification, especially on the posterior side of the body, possibly indicating long term chronic injuries.

Ouédraogo et al.⁽¹⁸⁾ state that the dermatophytosis are the second most common skin rashes among patients with HIV, and the prevalence is of *Tinea corporis*⁽¹⁾. In patients with AIDS, the CD4 T-lymphocyte count below 200/mm³ is a risk factor for fungi infections^(14,16). The correlation between immunosuppression caused by low lymphocyte count and generalized dermatophytosis was described in 1991 by Wright et al.⁽¹⁹⁾. All of the aforementioned reports are compatible with the case of the patient approached in this article.

The pathogenesis of dermatophytosis is shared by the tinea species (**Table 1**); the infection begins with the deposition and adherence of fungal spores on the external layer of the skin, followed by the secretion of specific proteases (subtilisins), which enables adherence to keratin; then, the produced keratinase allows the hyphae to enter the stratum corneum. The diffusion of fungal metabolic products through the stratum basale leads to an inflammatory process that results in the classic appearance of squamous, annular and pruritic injuries⁽¹⁾. Fungi growth is centrifugal, and the hyphae are found in the inflamed edges of the lacerations, which are the chosen locations to collect samples or tissues for the biopsy.



Figure 2. Scaly aspect of the lacerations and their elevated and delimited edges.

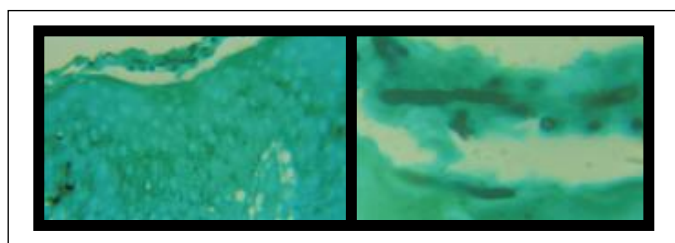


Figure 3. Histopathology demonstrating many hyphae in the corneum layer. Grocott-Gomori methenamine silver staining. Objectives of 40 and 100x, respectively.

The dermatophytes also produce sulfite and reducing agents to allow proteases to degrade keratin, which works as a nutrient. The secreted proteases were also identified as virulence factors. Adhered to human keratinocytes, the dermatophytes penetrate in the stratum corneum⁽²⁰⁾. This process can be facilitated by a change in the structure or environment of the stratum corneum (humidity, trauma), which, together with the environment of the follicular ostium, provide nutrition and proper pH for the dermatophyte to grow. A series of substances that are locally produced by the hosts, such as β -defensins, unsaturated transferrin from sweat and fat, besides long chain unsaturated fatty acids produced by sebaceous glands, inhibit the growth of dermatophytes on the epidermis⁽²¹⁾.

As in patients with AIDS, the physiopathology mechanisms are not well established, and some authors considered that the loss of function in CD4+ T lymphocytes, the changes in balance between the Th1 and Th2 responses, and the damage in cellular immunity could explain the peculiar clinical forms^(1,3).

Dermatophytosis can be transmitted directly through physical contact with animals and infected humans, and indirectly by the exposure to fungi in the ground or contaminated items (bath towels, shoes, brushes, hats, among others)⁽²²⁾. Therefore, Moriarty et al⁽¹²⁾. correlated the species of dermatophytes, which can have anthropophilic, zoophilic and/or geophilic origin, and concluded that the disease caused by antropophilic species usually presents with less inflammatory characteristics than those caused by zoophilic and geophilic species⁽¹²⁾.

The incubation period is from one to three weeks⁽⁵⁾, and the disease may be classified according to the anatomic location of the lesion, followed by the anatomic site of infection, as described in **Table 2**⁽²³⁾. The dermatophytoses are called *Tinea*. In a study by Kaviarasan et al.⁽²⁴⁾, including 185 patients with HIV, 41 (22.2%) were diagnosed with dermatophytosis, and *Tinea corporis* was the most common infection in 22 cases (53.7%).

The lesions usually present themselves as well delimited, circumscribed, oval or circular plaques, discreetly erythematous, squamous and with high edges, with asymmetrical distribution, affecting regions where the skin is exposed, especially the trunk. It starts as a spot that spreads centrifugally, leaving the central region hypochromic and forming a characteristic annular lesion⁽¹⁾. In immunocompromised patients, however, the clinical presentation can be more extensive, involving a larger area of the body surface⁽¹⁾ or presenting atypical lesions, with areas of poorly delimited hyperkeratosis, few signs

Table 1. Fungi species that cause dermatophytosis, according to classification and mode of contamination.

	Anthropophilic	Zoophilic	Geophilic
Mode Of Transmission	Human to human	Animal to huma	Ground to human or animal
Species	<i>T. rubrum</i> <i>T. tonsurans</i> <i>T. interdigitale</i> <i>T. schoenleinii</i> <i>T. soundanense</i> <i>T. violaceum</i> <i>M. audouinii</i> <i>E. floccosum</i>	<i>M. canis</i> <i>M. nanum</i> <i>M. ferrugineum</i> <i>M. distortum</i> <i>M. nanum</i> <i>T. equinum</i> <i>T. verrucosum</i>	<i>M. gypseum</i>

Source: Adapted from Leung AKC, et al.⁽¹⁰⁾

of inflammation⁽²⁰⁾, characterizing anergic dermatophytosis⁽²⁴⁾, as observed in **Figures 1 and 2**.

In most cases, diagnosis is clinical and can include dermoscopy. Doubts can be clarified through culture, considered as gold standard, or mycological test with potassium hydroxide (KOH)^(5,22). The histopathological evaluation is also an option (**Figure 3**).

The clinical forms range according to the etiological agent and the affected anatomic site, presenting with varied shapes and sizes^(5,22), which increases the chances of differential diagnoses: pityriasis (rosea, versicolor and lichenoides chronica), psoriasis, dermatitis (atopic, contact and seborrheic), granuloma annulare, lupus erythematosus (subacute and discoid), rash, lichen planus, erythema (migrans and multiforme) and secondary syphilis, Among others^(1,5).

According to Rouzaud et al.⁽⁶⁾, severe dermatophytosis is associated with innate or acquired immunodeficiencies, and can affect the dermis and the lymph nodes. Also according to this author, several subjacent conditions are associated with severe dermatophytosis: infection with HIV, solid organ transplant, systemic treatments with corticosteroids and other immunosuppressants, including topic corticoids, hematologic malignancy, liver disease, Cushing's syndrome, congenital adrenal hyperplasia, atopy, diabetes mellitus and CARD9 (Caspase Recruitment Domain Family Member 9) innate deficiency.

Extensive and disseminated erythemasquamous plaques, with circinate and high edges, and intense pruritus, were common findings in this case. Besides, there were broadly distributed areas of lichenification, especially on the posterior side of the body, possibly indicating long term chronic lesions (**Figure 1**).

Clinical treatment is divided in pharmacological measures, with the indication of topical or oral medicines, and non-pharmacological actions, such as the orientation to maintain a clean and dry skin

and to wear light and large clothes. The located or superficial lesions respond well to topical antifungal cream, if applied once or twice a day, for a period of two to four weeks. The most used topical agents are: azoles (econazole, ketoconazole, clotrimazole, miconazole, oxiconazole, sulconazole e sertaconazole), allylamines (terbinafine), benzylamine (butenafine), ciclopirox and tolnaftate. Even though nystatin is indicated to treat for infections by *Candida*, it is not efficient against dermatophytosis⁽¹⁰⁾.

Side effects from the topical treatment are unusual, and contact dermatitis is rarely registered. Flaws in the treatment can be explained by low adherence, resistance to medication, reinfection by contact or self-inoculation and incorrect diagnosis⁽¹²⁾. To treat the lesions with inflammation, some authors suggest the concomitant use of topical corticosteroid^(7,25).

Immunodepressed patients should be treated with systemic antifungal medication, as well as those with extensive dermatophytosis or the type that is refractory to the topical treatment⁽⁹⁾. In the article by Palacio et al., from 1991, the griseofulvin was pointed out as the most efficient medication Against extensive dermatophytosis⁽¹¹⁾. Vilela et al. attributes the success against dermatophytosis of a patient with HIV to fluconazole⁽²⁶⁾. According to Belda⁽⁹⁾, the most used one in this case is terbinafine, however, fluconazole, griseofulvin and itraconazole are therapeutic options⁽⁹⁾. Its administration must be maintained for two to four weeks, n doses suggested according to the Table 3 below.

Even though there are therapeutic options, we did not find, in the literature, one that is universally recommended to treat dermatophytosis in patients with HIV. In this report, our patient was treated with oral fluconazole and presented with partial involution of the lacerations in two months of therapy, and their complete disappearance after six months. However, the backside showed lesions that were compatible with herpes, possibly due to the immune reconstitution syndrome (**Figure 4**).

Strength: we report the richness of the clinical experience found in patients living with HIV at Hospital Universitario Gaffrée e Guinle, in addition to the extensive findings on dermatophytosis in the literature and the effectiveness of the treatment performed in our patient.

Limitation: the main limitation was the little information that the literature offers on the pathophysiology and a specific treatment of choice for dermatophytosis in patients with HIV.

CONCLUSION

There can be many clinical manifestations of dermatophytosis in patients with HIV, and most of them show extensive and disseminated lesions, such as the experience of our case report. Some publications describe rare cases, with not so usual clinical presentations; however, there is a common factor: the HIV diagnosis, which can be associated with immunosuppression.

Table 2. Types of *Tinea*, etiological agent and site of infection.

Types Of Tinea		
Tinea	Species of dermatophytosis	Site of infection
<i>Tinea corporis</i>	<i>Trichophyton rubrum</i>	Body (chest, face, Arms and/or legs)
	<i>T. tonsurans</i>	
	<i>Microsporum canis</i>	
<i>Tinea pedis</i>	<i>T. Rubrum</i>	Feet (dorsum or interdigital space)
	<i>T. interdigitale</i>	
	<i>Ephydermophyton floccosum</i>	
<i>Tinea capitis</i>	<i>T. tonsurans</i>	Scalp
	<i>M. canis</i>	
	<i>T. violaceum</i>	
<i>Tinea cruris</i>	<i>T. soudanense</i>	Groin
	<i>T. rubrum</i>	
<i>Tinea unguium</i> (onychomycosis)	<i>T. rubrum</i>	Nails
	<i>T. interdigitale</i>	

Source: Adapted and translated from Petrucelli MF, et al.⁽²³⁾

Table 3. Systemic therapies to treat dermatophytosis in adults and children.

	Fluconazole	Griseofulvin	Itraconazole	Terbinafine
Adults	150–200 mg/week	10–20 mg/kg/day	200 mg/day	250 mg/day
Children	6 mg/kg/week	15–20 mg/kg/day	3–5 mg/kg/day	<25 kg: 125 mg/day
	Maximum dose: 200 mg/week		Maximum dose: 200 mg/dia	25–35 kg: 187,5 mg/day >25 kg: 250 mg/day

Source: Adapted from Leung AKC, et al.⁽¹⁰⁾.



Figure 4. In the upper image, the patient was at the beginning of treatment; in the central photo, the injuries were reduced, with partial involution two months after the beginning of treatment with oral fluconazole; and the bottom picture shows the complete disappearance of the lacerations after six months of treatment; However, there were injuries compatible with herpes, possibly caused by the immune reconstitution syndrome.

In literature review, according to most authors, the main etiological agent that was found was the *Trichophyton sp fungus*, in patients with or without HIV, corroborating with the case of the described patient.

In the treatment of patients with dermatophytosis and HIV there can be refractoriness; however, in the study case, the therapy of choice was oral fluconazole, with remission of lesions in two months. Besides, it is important to stimulate the adherence to the antiretroviral treatment in order to improve the CD4 T lymphocyte count, thus reducing the changes of recurrence of the disorder.

Approval by the Human Research Ethics Committee

During hospitalization, patients sign a term allowing the report of cases in articles and conferences, as well as the use of their images. They signed a term authorizing the use of their image in scientific productions. As this is not a research, approval by the ethics committee is not required.

Participation of each author

VKL: Writing – review & editing. IMHG: Writing – review & editing. PMSE: Writing – review & editing. CJM: Data curation. RBL: Data curation. RNM: Data curation. FRAF: Conceptualization, Data curation, Formal Analysis.

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Conflict of interest

The authors declare no conflicts of interest.

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