

Invasive dermatophytosis in HIV/AIDS patient by zoophilic *Trichophyton verrucosum*

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Abstrak. Dermatofitosis invasif adalah infeksi dermatofita yang ditandai dengan invasi jamur ke jaringan kulit yang lebih dalam termasuk lapisan dermis dan subkutan. Di sini, seorang pria yang merupakan penderita HIV/AIDS dilaporkan mengalami dermatofitosis invasif dengan manifestasi klinis yang aneh berupa nodul dan ulserasi. Hitung sel CD4⁺ pasien ini adalah 88 sel/ μ l dengan persentase 1,87%. Pengobatan mandiri dengan antibiotik topikal tidak memberi respon. Pemeriksaan mikrobiologi meliputi preparasi kalium hidroksida dari specimen kerokan lesi dan kultur jamur. Diagnosis etiologi dari kasus dermatofitosis invasif ini adalah *Trichophyton verrucosum*. Spesies ini adalah salah satu jamur zoofilik penyebab kurap pada sapi. Pasien diduga terinfeksi akibat kontak dengan material yang mengandung jamur saat bekerja sebagai pekerja bangunan. Dermatofita dapat menyebabkan infeksi atipikal dengan gambaran yang sama sekali tidak terduga pada pasien dengan gangguan imunitas. Diagnosis sangat ditentukan oleh tingkat kecurigaan klinis yang tinggi diikuti dengan pemeriksaan mikrobiologis.

Kata Kunci : Dermatofitosis invasif; *Trichophyton verrucosum*; HIV/AIDS

Abstract. Invasive dermatophytosis is a dermatophyte infection characterized by fungal invasion into deeper skin tissue including the dermis and subcutaneous areas. Herein, a man who was an HIV/AIDS sufferer was reported to develop an unusually invasive dermatophytosis in the form of nodules and ulceration. His CD4⁺ cells count was 88 cells/ μ l with a percentage of 1.87%. Self-medication with topical antibiotics did not respond. Microbiological examination was carried out including direct potassium hydroxide preparation and fungal culture. The etiologic diagnosis of invasive dermatophytosis by *Trichophyton verrucosum* was established. This is one of the zoophilic fungus that causes ringworm in cattle. It was suspected that the patient was inoculated due to contact with fomites containing fungi while working as a construction worker. Dermatophytes can cause atypical infections with a completely unexpected appearance in immunocompromised patients. The diagnosis is largely determined by a high level of clinical suspicion followed by microbiological examination.

Keywords : Invasive dermatophytosis; *Trichophyton verrucosum*; HIV/AIDS

Introduction

Dermatophytes are fungi that tend to cause benign infections worldwide. They constitute the largest group of pathogens that cause skin mycosis. Dermatophytes are cosmopolitan, filamentous, keratinophilic fungi, consisting of the genera *Trichophyton*, *Microsporum* and *Epidermophyton*.^{1,3} Each genus includes several species. These fungi are keratinophilic and colonize or infect superficial tissues containing keratin (skin, nails, and hair) in both humans and animals.² Dermatophyte species have a unique ability to cause diseases, because infection can occur due to contact with humans, animals, and fomites. Dermatophytosis remains one most prevalent contagious mycoses in the world.³

The transmission from one person to another (anthropophilic), from animals (zoophilic), or from the ground (geophilic) facilitate the infections in humans. These species causing infections differ geographically and their prevalence is dynamic over time due to population movements.³ Anthropophilic species tend to cause chronic infections with less inflammation. In contrast, zoophilic and geophilic dermatophyte species often cause severe inflammatory lesions in humans.⁵

The clinical appearance varies, determined by the causative agent and host immune status. The infection may be chronic and may be asymptomatic

or simply manifest as mild itching. Most cases manifest as blisters, fissures, scales or spots.⁶ However, it can also occur in unusual and severe forms in immunocompromised patients.¹ Grossman et al. reported invasive *Trichophyton rubrum* infections in the form of granulomas, papules, nodules and abscesses in immunocompromised patients.⁷

Clinical manifestations are also largely determined by host factors such as the location of the invasion, the physiological variations of host skin barrier, patient age, body weight, immune states, and acquired conditions such as over-washing or sun exposure. The anatomical characteristics of the affected site including the presence of skin folds, sebaceous glands, thickness of the corneum layer, and involvement of the hair follicles also influence characteristic of centripetal development, inflammation and crusting.⁸

Problems that considered as trivial skin infections have become complicated. Dermatophytosis at this time is classified into difficult to treat skin diseases in conjunction with psoriasis, vitiligo, pemphigus, and erythroderma. Skin dermatophytosis sometimes mimics other skin diseases and some atypical clinical variability has been reported. Although it is more common in individuals with compromised immune systems, atypical forms can also be seen in people who have a competent immune system.⁸

Case Report

A 46-year-old man who worked as a construction worker had a complaint of having lumps on both his upper and lower limbs for more than two months. The lumps which were initially small and itchy slowly getting bigger and painful. He was an HIV / AIDS sufferer. He started taking anti-retroviral drugs (ARV) in Fixed Dose Combination (FDC) consisting of Tenofovir, Lamivudin and Efavirens since the last six months.

This patient has a thin stature. His physical examination revealed normal vital signs. Dermatologic finding on the left and right forearms, as well as on the lower legs was multiple nodules with ulceration on the upper part. The diameter of the nodules ranges from 3 to 5 cm. The nodules are lined by an erythematous area and skin scales. The nodule is hard in consistency and when pressed will release serous secretions. Some of the nodules are crusted. The skin on the edges of the nodules that have grown earlier appears blackened.



Figure 1. The appearance of lumps on the patient's forearms.



Figure 2. The confluent lesion with serous secretion.

The results of routine blood laboratory tests showed hemoglobin 13.5 g/dl, leukocytes 9500 cells/ μ l, with a count of 0% eosinophils, 0% basophils, 4% stem neutrophils, 54% segment neutrophils, 32% lymphocytes and 10% monocytes. The result of examination of CD4 + cells was 88 cells/ μ l with a percentage of 1.87%.

The patient has tried to treat his sore skin using antibiotic ointment but there was no response. Furthermore, mycological examination of the lesion scraping was carried out including direct potassium hydroxide preparation and fungal culture. The following figure 3 is the result of the direct specimen microscopy of potassium hydroxide 20% preparation. It showed irregular hyphae and the structure of chlamydospores.



Figure 3. Irregular hyphae formation was seen on 20% potassium hydroxide preparation.

Furthermore, the scraping specimen of the lesion with obvious inflammation was inoculated on Sabouraud dextrose agar slant medium with the addition of gentamicin, chloramphenicol and cycloheximide supplements. Then incubated at room temperature and $35\pm 2^{\circ}\text{C}$. Colony observations were made every two days. Optimal growth noted after the second week. Then a slide culture was carried out to clarify the morphological observations of the fungus.

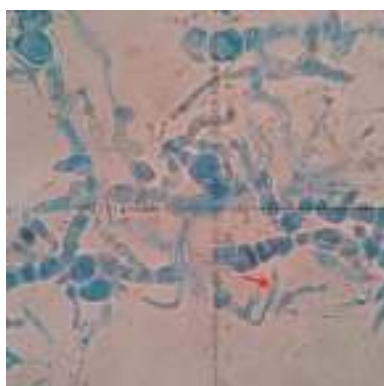


Figure 4. Lactophenol cotton blue preparations, arrow indicates the characteristic string bean shaped macroconidia of *T. verrucosum*.

The aetiologic diagnosis of invasive dermatophytosis by *Trichophyton verrucosum* as the causative agent was established. The patient was then directed to the dermatology department for appropriate management.

Discussion

The main reservoirs of zoophilic dermatophytes are livestock and domestic animals. The infections usually evoke violent inflammatory reactions in humans.⁹ Most of this inflammation is produced by activated lymphocytes and macrophages that are involved in a delayed-type hypersensitivity reaction to the trichophytin glycopeptide. Increased proliferation of skin in response to inflammation is the final mechanism in an attempt to remove fungi from the skin via epidermal desquamation.¹⁰ It has been reported that dermatophyte infections can be eliminated from the skin by accelerating epidermal turnover.¹¹

Many infections by zoophilic dermatophytes seem to be acquired indirectly from objects contaminated with fungi, often from apparently healthy animal carriers.¹¹ In this case, it was suspected that the patient was inoculated due to contact with fomites containing arthrospores while working as a construction worker. Arthrospora can survive several months outside the host. It is scattered in the

environment, comes from shed skin scales. After inoculation, the arthrospores attach to keratinocytes, then proteases such as subtilisin are secreted by the dermatophytes to enter the penetration phase. Dermatophytes produce sulfites and reducing agents to allow proteases to degrade keratin, which serves as its nutrient. This protease has been identified as a virulence factor. Once they are attached to human keratinocytes, dermatophytes will easily penetrate into the stratum corneum.¹

In severely immunosuppressed AIDS patients, the lesions showed unusual inflammatory response, lack the raised margins and central healing typical of common tinea. This kind of clinical manifestation called anergic tinea.¹² The severity of dermatophytosis and variability in presentation were more common in HIV/AIDS patients. Goodman et al. observed that the prevalence of dermatophytosis was four times higher among the HIV-infected population with more diverse atypical forms.¹³

The cutaneous manifestations of infection are sometimes not specific enough and the presentation may be polymorphic, therefore the clinical diagnosis can be difficult to establish.¹ The diagnosis was confirmed by the finding of a hyphae corresponding to the dermatophyte, namely short, irregularly thick hyphae derived from the skin scraping specimen and positive culture. Skin biopsy for microbiological examination may be necessary if the diagnosis cannot be made immediately leading to more extensive involvement. Surgical debridement may also be required in severe cases.¹⁴

Severe skin inflammation can result from infection with zoophilic organisms such as *Trichophyton verrucosum* as in the case above. This infection can produce large pustular lesions, kerion, or bullae formation causing tinea bullosa.¹⁵ Human infections result from direct contact with infected cattle or fomites and usually cause severe inflammation of the scalp, beard or exposed areas of the body. Infections of the skin are common and most of these infections respond well to topical antifungal medications. Systemic antifungal drugs such as terbinafine and the azole group of fungal drugs respond effectively.¹

The diagnosis of invasive dermatophytosis is largely determined by a high level of clinical suspicion followed by a skin biopsy examination with correlation to fungal culture. Delay in diagnosing deep dermatophyte infections can lead to scarring, alopecia, and disability secondary to severe pain.¹⁶ Unfortunately, examination of fungal cultures in order to determine the etiology of infection requires a relatively long time. Morphological examination of

fungal structures from direct microscopy such as the potassium hydroxide test in this case can be very helpful for early diagnosis of fungal infections.

Microscopic observations revealed wide and irregular hyphae with many terminal and leap chlamydospores. The tips of some hyphae are wide and club-shaped, and sometimes split, giving an antler effect. Affected hairs show ectothrix infection and fluorescence response to Wood lamps ultraviolet light has been found in livestock but not in humans.¹⁷

T. verrucosum cultures showed very limited growth, with small colonies. *T. verrucosum* microscopy showing chlamydosporic chains.^{17,18} Morphological description of colonies are characterized by slow growth, small size, button shape, white to cream in color, with a suede to velvety surface, raised central portion, and a flat edge with some submerged growth. Reverse pigment may vary from colorless to yellow.¹⁷

Molecular biology tests for dermatophytosis can provide accurate results in a short time. However, these require more resources and are not easily available. Indications of fungal genome validation is now one of the main challenges in the field of molecular biology of dermatophytes.

This case is unique because its appearance is not like tinea in general which is characterized by polycyclic macules with active papules on the margins and a central healing. Even at first it was suspected of being a bacterial infection, so the patient received antibiotic therapy instead of anti-fungal drugs.

The prevalence of severe forms may be overlooked. Its low frequency of occurrence is in stark contrast to the high prevalence of dermatophytosis worldwide. Better knowledge of this entity in different groups of immunosuppressed patients will help improving our understanding of the pathogenesis of dermatophytosis. Since dermatophytes tend to cause atypical infections in immunocompromised patients, diagnosis without clearly identifiable risk factors should lead to screening for evidence of immunodeficiency.

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