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Dermatophyte fungi: Infections, Diagnosis and Treatment

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Abstract

Problems: Dermatophyte fungi are keratinophilic pathogenic fungi which lead to superficial mycotic infection of dermatophytosis.

Experimental approach: Dermatophytosis refers to three main genera of *Epidermophyton*, *Microsporum* and *Trichophyton* which are distributed around the world. Therefore, the infection of Tinea (dermatophytosis) is one of the most important superficial infections worldwide. Dermatophytes may lead to acute or chronic diseases with high morbidity but not mortality.

Findings: The pattern of several forms of dermatophytoses are the same in Iran and worldwide.

Today, there are two main diagnostic methods of traditional and advanced molecular techniques.

Conclusion: The rapidity, sensitivity, specificity, and accuracy of diagnostic methods are important parameters to have a definitive treatment. In this mini review we tried to have an overview of dermatophyte fungi, dermatophytosis, appropriate diagnostic methods and treatment.

Keywords: Dermatophytes, Epidermophyton, Microsporum, Trichophyton, Tinea

Introduction

Dermatophyte fungi or dermatophytes comprise a vast range of filamentous pathogenic fungi including three important genera of *Epidermophyton (E)*, *Microsporum (M)*, and *Trichophyton (T)* which may lead to superficial infections in both humans and animals-zoonosis. However, *Pityriasis versicolor*, *Saccharomyces cerevisiae*, and *Candida* spp. as opportunistic pathogenic fungi are capable of causing superficial mycotic infections in human beings (1-8).

On the basis of ecologic habitat, demarophytes are divided into three groups of anthropophilic microorganisms (from person to person), zoophilic microorganisms (from animal to either animal or human), and geophilic microorganisms (transmitted from soil to animals or humans) (2, 8-10).

Dermatophytes as keratinophilic fungi are able to infect keratinous tissues of skin (the stratum corneum layer), hair, and nail in humans via their keratinase enzymes. They also degrade claws, feathers, hooves, horns, wools in animals (1, 2, 10-12).

Dermatophytes are fungal agents of dermatophytoses. Superficial mycoses of dermatophytoses are named after anatomic localization of the lesions. Dermatophytosis (tinea or ringworm) is a general name for acute to mild and chronic lesions of the outer layers of keratinized tissues caused by dermatophytes. Dermatophytoses include *Tinea barae*, *Tinea faciei*, *Tinea incognito*, *Tinea capitis*, *Tinea favosa*, *Tinea corporis*, *Tinea cruris*, *Tinea manuum*, *Tinea pedis*, and *Tinea unguium*. According to historical evidences, the Persian scientists knew about skin disease of dermatophytosis in ancient Persia (1, 2, 5, 13-15).

In recent years, there are a vast range of traditional and modern diagnostic approaches and treatments for managing superficial infections of dermatophytes (4, 16, 17).

Although dermatophytes are not life threatening microbial agents but they are distributed around the world and cause mycotic infections with high morbidity (4, 13).

In the present mini review we are tried to introduce different forms of dermatophytoses, diagnostic

approaches for dermatophyte fungi and treatment options of ring worms.

Tinea barbae, Tinea Faciei and Tinea incognito

Tinea barbae is a type of superficial mycosis which is seen in the bearded areas of face and neck in men. The infection involves the skin and the hairs (shafts and follicles) of mustache, beard and a part of neck area. Zoophilic dermatophytes such as *T.verrucosum*, *T.mentagrophytes*, *M.canis*, and *T.tonsurans* are the most common causative agent of *Tinea barbae* and anthropophilic dermatophytes like *Trichophyton rubrum*, are known as the second infectious agents of *Tinea barbae*. The clinical demonstrations of *Tinea barbae* include kerion, scaling, folliculitis, itching, burning, and inflammatory reactions (2, 8, 18-20).

Tinea faciei is seen in the same anatomic locations as well as in men, but this infection belongs to women and children. In other words, *Tinea faciei* is the pediatric and female form of *Tinea barbae*. *Tinea barbae* occurs in adult males while *Tinea faciei* involves neonates, children and women. Either *Tinea barbae* or *Tinea faciei* are low common in Iran. Sometimes, *Tinea faciei* occurs completely mild and its clinical appearance is not distinguishable. This type of dermatophytosis is named *Tinea incognito*. The most important risk factors of these groups of ring worms are low personal hygiene, moisture, contact with soil, contact with pets and contact with infected people (1, 2, 18-24).

Tinea capitis

Tinea capitis is known as the most considerable dermatophytosis between childish populations in Iran and worldwide. The infection involves scalp, hair shafts and hair follicles. *Tinea capitis* is the most occurred superficial dermatophyte infection in crowded urban societies. It is the predominant infection among young and school-age children. The etiological dermatophyte genera of *Tinea capitis* contain *Trichophyton* and *Microsporum*. *T.violaceum*, *M.canis*, *T,verrucosum*, *T.mentagrophytes*, *T.interdigitale* and *T.tonsurans* are the most common species isolated from patients with *Tinea capitis* in Iran and other countries (1, 2, 4, 20, 23, 25-38).

Tinea capitis is categorized into three main types of ectothrix, endothrix and favus. The ectothrix form of *Tinea capitis* is often recognized via the presence of arthroconidia on the outside of infected hair shafts; while the endothrix hair invasion form of *Tinea capitis* is distinguished by the presence of

arthroconidia in the inner side of infected hair shafts. The hair infection of favus which is known as *Tinea favosa* is detectable by the presence of fungal mycelia of *T.schoenleinii* within infected hair shafts (2, 26, 34, 39).

Clinical signs of *Tinea capitis* include a wide range of demonstrations from asymptomatic, subtle and mild flaked scalp to severe broken infected hairs, inflamed patches, pustules, kerions and scutula on different areas of head. *Tinea capitis* with kerion lesions is known as *Tinea profunda*. Direct contacts of heads (especially in children), utilization of personal belongings of infected individuals, and low hygiene are the most reported risk factors for *Tinea capitis* (1, 2, 8, 26).

Tinea corporis

Tinea corporis as a type of dermatophytosis, is produced by the three genera of *Trichophyton*, *Microsporum*, and *Epidermophyton* which involves the trunk. *Tinea corporis* is characterized via uni- or multiple circular reddened edge lesions. *T.rubrum*, *T.tonsurans*, *T.interdigitale*, *T.mentagrophytes*, *E.floccosum*, and *M.canis* are important dermatophyte etiological agents for *Tinea corporis* in Iran and worldwide. *Tinea corporis* is most observed in the neighborhood of the Persian Gulf (1, 2, 5, 8, 20, 40, 41).

Tinea corporis occurred in wrestlers is known as *Tinea gladiatorum* which infection spreads via skin to skin and wrestling mats to skin. *T.tonsurans*, *T.rubrum*, *E.floccosum*, and *T.mentagrophytes* are the most frequent reported etiological agents in Iran (42, 43).

Also, *Tinea corporis* caused by anthropophilic dermatophyte fungus of *T.concentricum* is called *Tinea imbricata* which is rare in Iran but common in South America. *Tinea imbricata* is known as genetic and race dependent dermatophytosis (2, 44, 45).

Sometimes, women who consume corticosteroids and shave their legs are susceptible to a typical form of *Tinea corporis* which is known as Majocchi's granuloma. In accordance with previous reports, *Tinea corporis* is the predominant form of dermatophytosis in some parts of Iran (40, 46, 47).

Tinea cruris

Tinea cruris or "jock itch" is a common dermatophytosis of groin. It affects adults and occurs three times more in men than women. The most important causative dermatophyte agents of *Tinea cruris* are *T.rubrum*, *E.floccosum*, *T.interdigitale*, *T.mentagrophytes*, and *T.verrucosum* in Iran and other

countries(1, 2, 8, 19, 20, 48-54).

Moisture, low hygiene, high temperatures, tight-fitting cloths are the most common predisposing factors which may lead to *Tinea cruris* appearance (2, 8, 50, 53).

In chronic cases, no inflammation is seen, while the acute infections are correlated with inflammation and sever itching. Lesions progression and erythema appear centrifugally and are seen symmetrically or asymmetrically. Erythematous rashes with vesicles at the lesions edges are common clinical demonstrations for *Tinea cruris* (1, 8, 53).

Tinea manuum

Tinea manuum is superficial infection of dermatophytosis which involves hands, palms and interdigital parts unilaterally or bilaterally. *Tinea manuum* appears mostly with *Tinea pedis*. *T.rubrum*, *T.mentagrophytes*, *T.interdigitale*, and *E.floccosum* are the most etiological agents of *Tinea manuum* in Iran and worldwide (1, 2, 8, 20, 53).

Humidity and moisture, pre-infection of *Tinea pedis* are the most important risk factors for *Tinea manuum*. Clinical demonstrations of *Tinea manuum* include dryness and scaly hand(s) which is similar to eczema. Sometimes, finger nails may be infected in the following of *Tinea manuum* (2, 53).

Tinea pedis

Tinea pedis which is known as athlete's foot is the most frequent dermatophytosis around the world. According to estimations, nearly 70% of people have been infected in a period of their life worldwide. The incidence of *Tinea pedis* in adults is significantly more than children and it occurs more in men than women (1-3, 8, 53, 55).

Mostly, *Tinea pedis* is produced by *T.rubrum*, *T.mentagrophytes*, *T.interdigitale*, and *E.floccosum* in Iran and other countries (2, 20, 53).

Clinical signs of *Tinea pedis* are appeared in different forms including inflammation and ulcer (with putules and vesicles on sole), moccasin (with scaly and thick keratinized sole and heel), and interdigital spaces (with itching and burning). Clinical manifestations may be seen unilateral, bilateral, symmetrical, asymmetrical, acute or chronic. Humidity, high temperature, low hygiene, and, wearing footwear for long period are known as important risk factors for dermatophytosis of *Tinea pedis* (1-3, 8, 53, 55, 56).

Tinea unguium

The infection of bed or plate of the nail caused by pathogenic dermatophyte fungi leads to *Tinea unguium* or dermatophyte onychomycosis. The most common causative dermatophytes of *Tinea unguium* are *T.rubrum*, *T.mentagrophytes*, *T.interdigitale*, and *E.floccosum* which are reported from Iran and other countries around the world (2, 20, 53, 57-61).

Typical clinical demonstrations of *Tinea unguium* comprise deformity and discoloration of the nails. Trauma, tight wearing shoes, humidity, pre-*Tinea mannum*, pre-*Tinea pedis* are the most frequent risk factors for dermatophyte onychomycosis (2, 8, 53, 55).

Diagnostic techniques

In accordance with progression in mycological diagnostic approaches, today there are two diagnostic categories including traditional and advanced molecular diagnostic tools available. Accuracy, availability, rapidity, sensitivity, specificity and cost effectiveness are important items for diagnostic procedures. Nevertheless, routine traditional diagnostic tools are not able to warrant adequate sensitivity and specificity (62).

Traditional diagnostic techniques

Traditional mycological diagnostics involve specimen direct microscopy, Wood's lamp test, fungal culture medium, and biopsy. (2, 5, 63, 64).

Specimen direct microscopy

Direct microscopic observation of fungi in clinical samples is obviously a cheap and short-time diagnostic method. Clinical specimen must be prepared by scalpel, moving to a clean glass slide with a drop of 10%-20% KOH. Mild heat may help to increase the lytic activity of KOH on fungal α -(1,3) and α -(1,4) cross linkages in cell wall glucan polymers to have a clear and transparent vision of dermatophyte fungal elements including filamentous, septate, and branched hyphae with or without conidia among the specimen (1-3, 8, 9, 17, 65).

Providing suitable samples is an important part of direct microscopy. Accuracy in isolation of scale from peripheral border of suspected lesion, obtaining infected hair shafts or hair follicles, scraping from infected nails are the primary procedures for preparing valuable samples to have a successful observation to confirm the presence or absence of dermatophyte fungi. According to previous studies,

sensitivity and the specificity of direct KOH microscopy are ~65% and >45% (1, 2, 8, 17, 66, 67).

Wood's lamp test

Wood's lamp tool is a limited diagnostic method which can be used for detecting *Tinea capitis* caused by fluorescent metabolite producing dermatophyte of *M.canis* (fluorescence blue-green) and *M.audouinii* (fluorescence grey-yellow) in a dark room (1, 2, 8, 53, 68).

Fungal culture medium

Culture is an expensive and time consuming technique with low sensitivity (30%-35%) and higher specificity. In mycological methodology, it is important to have adequate amounts of samples to increase the accuracy of results. In traditional diagnostics, clinical samples including scale, hair and nail scraping must be used simultaneously for direct microscopy and culture medium. For positive result of culture technique usually takes two weeks while a negative result of culture method normally needs a period of 6 weeks. Sabouraud Dextrose Agar (SDA) is recommended for the most in culture medium technique (1, 2, 8, 17, 63, 64).

Biopsy

Biopsy from nail or skin is used when the clinical manifestations of dermatophytosis are present but results of direct microscopy and culture are negative or even treatment did not respond to ring worm (2, 8).

Advanced molecular tools

Advanced molecular diagnostics provide successful approaches for rapid diagnosis of pathogenic dermatophytes with high accuracy, sensitivity and specificity (3, 17, 62, 69).

In molecular diagnostic methods, DNA molecules extracted from clinical samples are amplified by universal primer sets that targeting the regions of 18S rDNA and Internal Transcribed Spacer (ITS). The ITS regions are species-specific for the three dermatophyte genera of *Epidermophyton*, *Microsporum* and *Trichophyton*. Conventional Polymerase chain Reaction (PCR), Nested-PCR, Real-Time PCR, Multiplex PCR, Restriction Fragment Length Polymorphism (RFLP), Amplified Fragment Length Polymorphism (AFLP), Random Amplified Polymorphic DNA (RAPD), DNA microarray and other nucleic acid based techniques provide faster, easier, and confident species-level diagnostic approach which may lead to an effective treatment at early stage of dermatophytosis. Simple and

standard molecular diagnostic methods make them easier to use in routine clinical diagnostic techniques with a high applicability and capability to represent reliable results with high level of sensitivity and specificity. Each molecular assay has its particular application and validity; therefore, the use of a molecular diagnostic approach is completely depended on the purpose of the assay (1, 3, 17, 20, 53, 62, 70).

Treatment

There are two treatment methods comprising topical or systematic antifungal agents for dermatophyte infections. To achieve a definitive and successful pharmacotherapy of dermatophytosis, there is an essential need for an accurate identification of pathogenic agent at species level (4, 53, 55, 62, 71).

According to different reports, several types of *Tinea* show insufficient response to topical medication. Thus, there are many kinds of *Tinea* which must be treated with systemic antifungal drugs. Amphotericin, azole antifungal agents including clotrimazole, fluconazole, itraconazole, ketoconazole, miconazole, voriconazole), griseofulvin, and terbinafine are predominant good choices with satisfied effective antifungal activities (4, 53, 55, 72).

Conclusion

Pathogenic dermatophytes are etiologic agents of superficial mycotic infections of dermatophytoses. On the basis of predisposing factors and geographic regions, the level of anatomical infections may vary. However, *Tinea pedis* is the most important dermatophytosis worldwide. *Tinea* is not a life threatening infection, but it is known as an irritating infection.

Dermatophytoses are not easy to be detected and identified only via clinical demonstrations. Therefore, it is necessary to utilize suitable diagnostic techniques for an appropriate diagnosis and treatment. Today, there are two particular mycological laboratory diagnostics including traditional and advanced molecular techniques.

As mentioned through the text, advanced molecular diagnostic tools are preferable because of their rapidity, accuracy, sensitivity, specificity; but sometimes, they are not available or may be expensive. Thus, direct KOH microscopy is an acceptable diagnostic method yet. Simultaneous application of direct microscopy and culture are used as a best choice in some countries worldwide.

We purpose that, the use of direct microscopy, culture medium and molecular diagnostics

simultaneously is the best choice until now. In addition, by detection of fungal elements via direct microscopy and molecular diagnostic approaches, pharmacotherapy must be started and the respond of culture medium is a confirmation test for an accurate diagnosis.

Although different types of antifungal drugs are available today; we believe that topical pharmacotherapy is the first choice. Negative respond to topical treatment, may be a good evidence for administering systematic antifungal drugs.

Conflict of interest

The authors declare no conflict of interests.

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Authors Column



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