A multicenter clinicomycological study evaluating the spectrum of adult tinea capitis in Egypt

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Abstract

Introduction: Tinea capitis (TC) is a common fungal infection in children but is less frequently encountered in adults. This study evaluates the clinical characteristics and mycological studies of adult TC among the Egyptian population.
Methods: A multicenter study included patients diagnosed with TC from 2002 to 2012.
Results: The study included 58 patients with a predominance of females (84.5%). The average age was 43.2 years and the mean duration of lesions was 7.1 ± 2.41 months. A history of close contact with animals was reported in 17.2% and Hepatitis C virus infection was recorded in 34.4%. Clinically, scaly scalp (37.9%), alopecia (22.4%), and pyoderma-like lesions (13.8%) were the most common presentations. The parietal (27.6%) and temporal (25.8%) regions were the most affected areas. KOH mounting showed endothrix spores in 56.9%, ectothrix spores in 34.5%, and favic chaplets (hyphae) in 8.6%. Fungal culture showed *Trichophyton violaceum* in 56.9%, *Microsporum audouinii* in 19%, *Microsporum canis* in 15.5%, and *Trichophyton schoenleini* in 8.6%.
Conclusions: *Trichophyton violaceum* is the most common cause of adult TC among Egyptians. Increased awareness of variable clinical forms of TC will help in identifying more cases, especially those with HCV infection and close contact with animals.

Introduction

Tinea capitis (TC) is a common fungal infection in children but is less frequently encountered in adults. Although the incidence of adult TC was reported early to be less than 1% (1), a higher incidence was observed in later studies (3–5%) and in other reports the incidence increased up to 11% (2). Females are known to be infected more frequently than men and there is greater predilection for the post-menopausal age group. It has also been reported that African-American women are more prone to infection than other races (3).

Clinically, TC commonly presents with variable degrees of hair loss and scalp scaling, whereas typical kerion is uncommon and favus is rare. Adult TC may show polymorphic and atypical clinical presentations leading to difficulty in diagnosis and delay in treatment. The severity of clinical presentation is usually determined by the immune status of the host and the species of the causative dermatophyte (4).

The most common dermatophytes isolated in adult TC included *Trichophyton tonsurans, T. violaceum, T. verrucosum, Microsporum canis,* and *M. gypseum*. It was found that fungi are transmitted into the hair through various methods, including contact with fungi in hairdressing equipment or in childcare settings, extensions from glabrous skin, and contact with domestic animals, which are important asymptomatic carriers that facilitate transmission of the disease to humans (5).

Diagnosis of TC is usually based on demonstration of fungi in the hair by direct microscopic examination. Histological examination is usually required in cases with atypical clinical presentations, and a culture is usually performed to identify the fungal species and to record the epidemiologic characteristics of fungal infection in the community. Molecular identification of fungi has been considered an important diagnostic approach in recent decades. Polymerase chain reaction (PCR) amplification of genomic DNA followed by se-

quencing of resulting amplicons of the internal transcribed spacer region 1 (ITS1) represents the most promising and rapid diagnostic tool, and has shown greater sensitivity and specificity than traditional methods (6). In this study we demonstrated the clinical spectrum of adult TC at five dermatology centers in Egypt and identified the causative fungal species of such disorder.

Methods

This multicenter study included patients that were diagnosed with TC at Al-Hussein, Alexandria, Dumyat, Al-Zahraa, and Tanta university hospitals from 2002 to 2012. All of the patients were subjected to a complete medical history and general examination. Routine laboratory investigations and blood tests to detect of HCV and HIV were also performed.

The selected areas for fungal examination were cleaned with alcohol, and then scraped scales or plucked hairs were collected using sterilized instruments. The collected materials were examined by direct microscopy and culture. For direct microscopy, specimens were placed on a clean glass slide and a drop of 10% KOH / 40% dimethyl sulfoxide (DMSO) mixture was added. DMSO increases the sensitivity of the preparation and softens keratin more quickly than KOH alone in the absence of heat (7). The samples were kept for 20 minutes and then examined for the presence of ectothrix or endothrix spores in addition to filamentous, septate, branched hyphae with or without arthrospores and trichospores.

For the culture, samples were inoculated in two types of Sabouraud's dextrose agar (SDA) culture media; one was SDA with the addition of chloramphenicol and gentamicin to inhibit the growth of bacteria, and the second was SDA containing chloramphenicol and cycloheximide (Mycosel agar) to inhibit the growth of saprophytic fungi. The sample was incubated at 27 °C for 2 weeks.

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Cultures without evident fungal growth were kept for another 3 weeks before being considered negative. The fungi were identified by noting their growth rate, colonial morphology, and microscopic structures.

Molecular studies were limited to the use of PCR test to identify and compare the isolated fungal species from the scalp area with those isolated from other areas rather than the scalp, other family members, and contact animals in order to confirm the fungal transmission by the same species. Briefly, DNA extraction was carried out after inoculation of the obtained strains in SDB overnight at 30 °C. A fungal suspension was prepared after photometrical concentration and centrifugation. The pellet was frozen at −20 °C for 1 hour then incubated at 65 °C for 1 hour in 0.5 ml extraction buffer. The lysate was extracted, and then sodium acetate and NaCl were added to the supernatant and incubated at 4 °C for 30 min. The concentration was measured by monitoring the UV absorbance at 260 nm (Gene Quant System; Pharmacia, LKB Biochrom). Serial aqueous dilutions of DNA from *T. violaceum*, *M. canis*, *T. schoenleini*, and *M. audouinii* were prepared at different concentrations (10 ng to 1 fg per 10 μl) and stored at −20 °C until used (8).

Skin biopsies were required in some cases that were not clinically suspected to be TC. Sections were routinely stained with hematoxylin-eosin, periodic acid–Schiff (PAS), and Grocott's methenamine silver (GMS) stains. Clinical and mycological follow-up was recorded for all patients with monitoring of therapeutic response to systemic antifungal treatment. After clinical clearance of the lesion, two KOH smears were performed for each case with a 1-month interval. A negative result in both smears indicated a mycological cure. Each patient signed a written consent for medical photography. The study was approved by the local ethics committee.

Results

Over 10 years, a total of 1,380 patients with TC were recorded at five dermatology centers at various locations in Egypt; out of them, 58 patients (4.2%) were adults. There were more females (84.5%) than males (ratio 5.4:1). The mean age of patients was 42.9 ± 8.54 years, and the mean duration of disease was 7.1 ± 2.41 months. Concurrent fungal infection in other family members was reported in 15.5% of cases, and 17.2% reported a positive history of close contact with animals (cattle, dogs, and cats).

The most important associated systemic diseases included Hepatitis C virus (HCV) infection (34.4%) and diabetes mellitus (22.4%). Out of 20 patients with HCV infection, nine (45%) were being treated with interferon-alpha at the time of diagnosis. Skin examination revealed associated fungal infection in 29.3% (17.2% tinea corporis, 3.5% onychomycosis, and 8.6% tinea pedis). Cervical lymphadenopathy was observed in 11 patients (15.5%).

Clinically, scalp scaling was the most common presentation (37.9%), and other clinical forms included alopecia (22.4%) either scarring (8.6%) or non-scarring (13.8%), follicular pustules (5.2%), acne keloidalis (10.3%), pyoderma-like lesions (13.8%), and folliculitis decalvans (1.7%). A typical picture of favus was recorded in five patients (8.6%). The vast majority (87.9%) of patients presented with a solitary lesion (parietal area 27.6%, temporal area 25.8%, vertex 20.7%, and occipital area 13.8%), whereas multiple lesions were recorded in 12.1% (Table 1).

KOH smear and fungal culture were the basic investigations for all cases enrolled in this study. KOH examination of extracted hair revealed endothrix spores in 56.9%, ectothrix spores in 34.5%, and favic chaplets (hyphae) in 8.6%. Fungal culture showed a predominance of *T. violaceum* (56.9%). The fungal colony of *T. violaceum* was characterized by a glabrous waxy deep violet surface and direct examination of the colonies showed irregular and bizarre segmented branched hyphae (Fig. 1) with rare or absent macroconidia.

Microsporum audouinii was isolated in 19% of cases. The colony of *M. audouinii* was flat and had a brown velvety surface, and microscopically it showed thick-walled chlamydospores either terminal or intercalary (Fig. 2). *Microsporum canis* was identified in 15.5% and the colony was characterized by a cottony-white appearance. Macroconidia were abundant with a large spindle-shaped appearance, thick walls, and curved ends (Fig. 3). *Trichophyton schoenleini* was detected in 8.6%. The colonies were characterized by a yellowish-white to brown color and antler-like hyphae (Fig. 4).
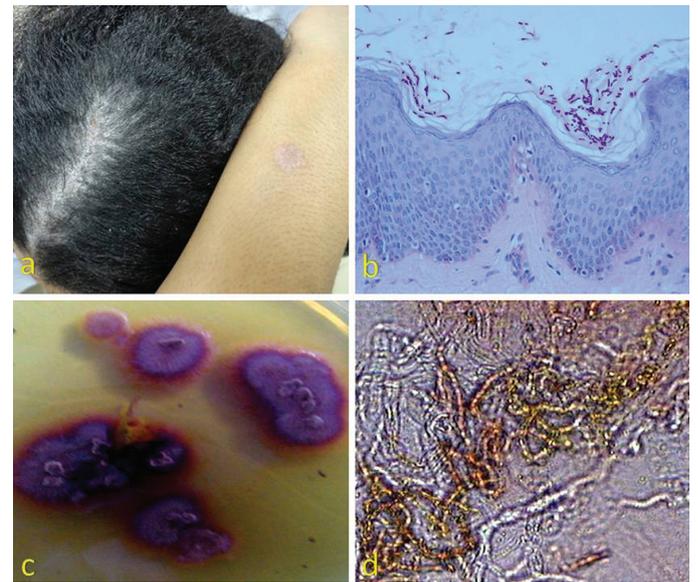

Figure 1 | (case 10) A – Scaly tinea capitis and tinea circinata on the left forearm in a female patient. B – Lesional skin biopsy: numerous hyphae in the stratum corneum (PAS, × 400). C – Mycological culture: glabrous waxy colonies with deep violet color (*T. violaceum*). D – Culture mount: irregular, bizarre segmented and branched hyphae.
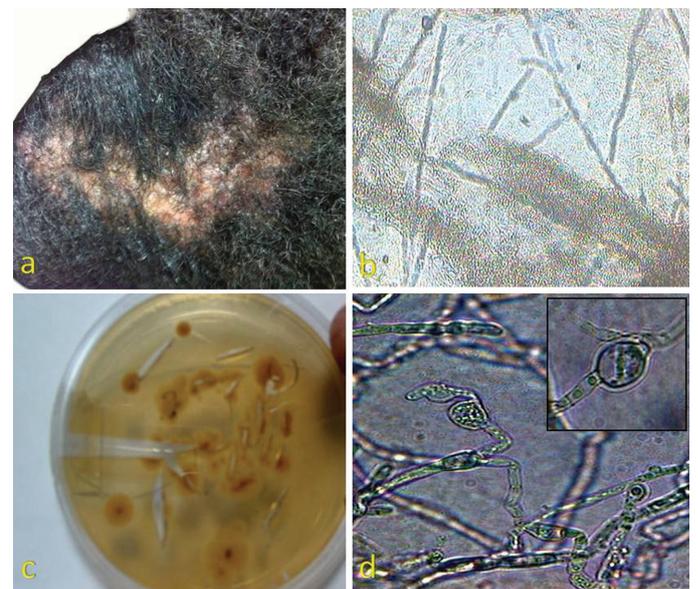

Figure 2 | (case 18) A – Female patient presented with pustular crusted alopecia. B – KOH examination of affected hair: ectothrix pattern. C – Mycological culture: flat colonies with brown velvety surface (*M. audouinii*). D – Culture mount: thick-walled intercalary chlamydospores and the terminal ones have pointed tips.

Table 1 | Demographic and clinical data of adult Egyptians patients with tinea capitis.

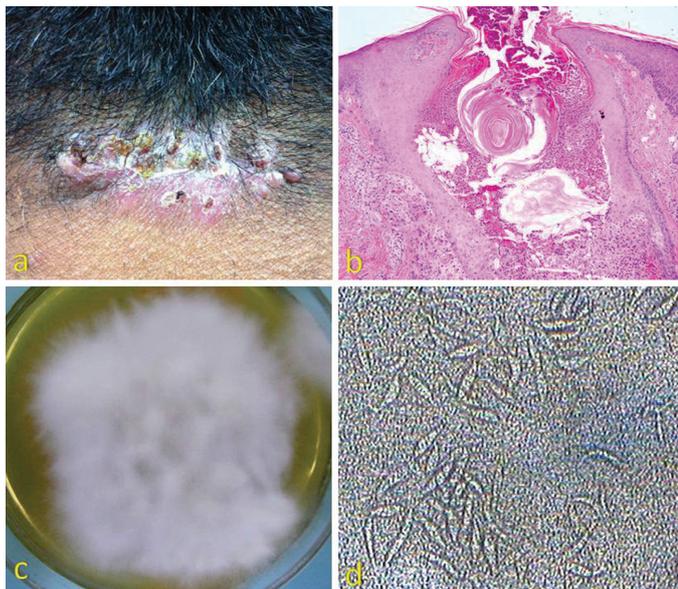|	Trichophyton violaceum (n = 33)	Microsporum audouinii (n = 11)	Microsporum canis (n = 9)	Trichophyton schoenleini (n = 5)	Total (n = 58)
Sex					
Male	7	0	0	2	9 (15.5%)
Female	26	11	9	3	49 (84.5%)
Age (years)					
Range (average)	19 – 78 (45)	30 – 56 (42)	21 – 70 (47)	28 – 49 (39)	19 – 78 (43.2)
Mean ± SD	45.6 ± 9.35	41.8 ± 7.22	49.1 ± 10.86	35.4 ± 6.74	42.9 ± 8.54
Duration (month)					
Range (average)	2 – 24 (10)	3 – 11 (6)	5 – 26 (11)	3 – 13 (5)	2 – 26 (8)
Mean ± SD	7.5 ± 4.29	5.6 ± 1.8	8.7 ± 2.77	6.6 ± 3.12	7.1 ± 2.41
Family history					
Positive	7	1	1	2	11 (15.5%)
Negative	26	10	8	3	47 (84.5%)
Animal contact					
Positive	0	2	8	0	10 (17.2%)
Negative	33	9	1	5	48 (82.8%)
Associated systemic diseases or infections					
Hepatitis C virus infection	15	1	3	1	20 (34.4%)
Diabetes mellitus	7	2	3	1	13 (22.4%)
Internal malignancy	2	1	0	0	3 (5.2%)
Rheumatoid arthritis	1	0	0	1	2 (3.4%)
Chronic renal disease	1	0	1	0	2 (3.4%)
Ulcerative colitis	1	0	0	0	1 (1.7%)
Associated fungal infection					
Positive	12	4	1	0	17 (29.3%)
Negative	21	7	8	5	41 (70.7%)
Clinical presentation					
Alopecia	13	0	0	0	13 (22.4%)
Scaly scalp	19	0	3	0	22 (37.9%)
Favus	0	0	0	5	5 (8.6%)
Pyoderma	1	5	2	0	8 (13.8%)
Folliculitis decalvans	0	1	0	0	1 (1.7%)
Pustular eruption	0	2	1	0	3 (5.2%)
Acne keloidalis	0	3	3	0	6 (10.3%)
Location					
Vertex	9	0	2	1	12 (20.7%)
Parietal	11	1	3	1	16 (27.6%)
Temporal	8	4	2	1	15 (25.8%
Occipital	3	4	1	0	8 (13.8%)
Multiple	2	2	1	2	7 (12.1%)

Figure 3 | (case 26) A – Male patient had an acne keloidalis–like plaque on the occipital area. B – Lesional skin biopsy: acute superficial folliculitis (HE, × 200). C – Fungal culture: cottony-white colonies (*M. canis*). D – Mounting of the colonies: abundant large spindle-shaped macroconidia with thick walls and curved ends.
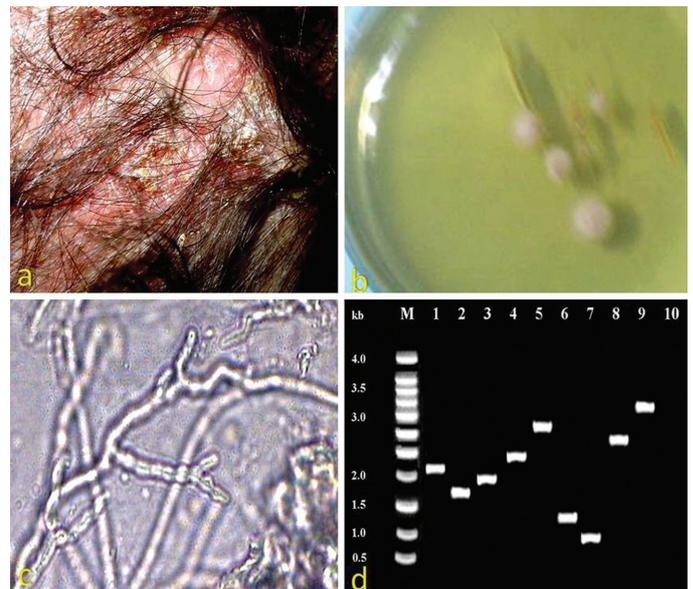

Figure 4 | (case 23) A – Erythematous scaly alopecic plaque with pustules and scaring in a female patient. B – Fungal culture: yellowish-white to brown colored colonies (*T. schoenleini*). C – Mounting of the colonies: antler-like hyphae. D – PCR result: agarose 1.5% gel electrophoresis showing DNA products amplified from *T. schoenleini* isolate in lane 7 (0.9 kb).

PCR was performed in 38 patients (65.5%). The results of a PCR test proved a similarity of fungal species between patients and contact animals in 80%, whereas samples from other body sites and from other infected family members showed a similar species in 17.6% and 18.2%, respectively. *Trichophyton violaceum* isolates showed bands of 1.9, 2.3, and 3.2 kb, *M. canis* showed bands of 1.7 and 2.8 kb, *M. audouinii* showed bands of 2.1, 1.3, and 2.6 kb, and *T. schoenleini* showed a band of 0.9 kb. A skin biopsy was performed for 17 patients (29.3%) and it showed various grades of folliculitis (70.6%) and peri-folliculitis (29.4%). Hyphae and/or spores were observed in 17.6% of specimens (Table 2).

Follow-up of the patients showed clinical improvement and mycological cure in 47.9% of patients after treatment with griseofulvin (500 mg/d), 80.8% after treatment with itraconazole (200 mg/d), and 70% after treatment with terbinafine (250 mg/d). A total of 25 patients (52.1%) failed to respond to griseofulvin therapy; 14 of them were shifted to itraconazole and 11 were shifted to terbinafine treatment. In addition, five patients (19.2%) failed to respond to itraconazole and they were shifted to terbinafine. The failure rate for terbinafine was 30% (six patients) and these patients were shifted to itraconazole therapy. The initial response was faster with itraconazole (2 to 3 weeks) compared to griseofulvin (3 to 5 weeks) and terbinafine (3 to 4 weeks). However there was no significant difference between the duration of complete clearance after treatment with itraconazole or terbinafine (6 to 8 weeks for both; Table 3).

All of the drugs were well tolerated by the patients and no significant side effects or complications necessitated withdrawal of any treatment. The most frequently reported side effects included nausea, gastric upset, fatigue, and headache. Other laboratory changes that were observed in these patients included anemia, lymphopenia, mild elevation of liver enzymes, and erythrocyte sedimentation rate.

Discussion

Tinea capitis is an uncommon infection in adults. In 1946, the first cases of adult TC were reported by Goodman (9) and then Andrews (10), and since that time many reports have focused on studying the incidence, clinical characteristics, and etiological factors of adult TC (11). The incidence of adult TC varies in different communities. In the United States, Pipkin (12) reported an incidence of 4.9% in the southwest area, and Silverberg et al. (3) found a higher incidence of 11.4%. In Europe, adult TC represented only 2.7% of all TC among Italians (13), whereas the incidence was higher in Greece (5.8%) (14) and in France (11%) (2).

In Asia, Lee and Hsu (15) reported the highest incidence (63%) of adult TC among Taiwanese patients, whereas in China the incidence ranged from 6% to 13.6% (16). In Africa, Mebazaa et al. (17) reported an incidence of 5.27% among Tunisian patients. In this study, we encountered an incidence of 4.2% among Egyptian patients. This incidence may be the most relevant in Egypt because the study was carried out at five dermatology centers with various locations that included most of the population variation (urban and rural). The rarity of adult TC in general was explained by the higher resistance of adults' scalp hair to dermatophyte colonization due to the fungistatic properties of sebum, which is mainly formed of long-chain fatty acids (18).

There are many suggested predisposing factors for adult TC (19, 20). We observed that contact with animals was a common predisposing factor in rural areas, whereas transmitted infection from other family members was more common among urban patients. We also found a higher incidence of adult TC (46.4%) among menopausal women, and this was explained by the involution of sebaceous glands following decreased blood estrogen levels during menopause (2).

Table 2 | Results of diagnostic techniques in adult tinea capitis.

Test	Total number of tested patients	Number (%) of Positive cases	Findings
KOH smear	58 (100%)	33 (56.9%)	Endothrix
		20 (34.5%)	Ectothrix
		5 (8.6%)	Favic chaplets
Culture	58 (100%)	33 (56.9%)	*T. violaceum*
		11 (19%)	*M. audouinii*
		9 (15.5%)	*M. canis*
		5 (8.6%)	*T. schoenleini*
PCR	38 (65.5%)	13 (34.2%)	Similar species (isogenic)
		- 3 (17.6%)	- from other body sites
		- 2 (18.2%)	- from other infected family members
		- 8 (80%)	- from closely contact animals
		25 (65.2%)	Different species (heterogenic)
Skin biopsy	17 (29.3%)	12 (70.6%)	Folliculitis
		- 3 (17.6%)	- positive spores or hyphae
		5 (29.4%)	Perifolliculitis

Table 3 | Therapeutic response of adult tinea capitis to systemic antifungal therapy.

Drug (dose)	Total number of treated patients	Number of patients with history of previous treatment	Failure rate Number (%)	Cure rate Number (%)	Time of Initial response (w)	Time of Complete improvement (w)	Side effects Number (%)
Griseofulvin (500 mg/d)	48	Previously treated patients (0) Naïve patients (48)	25 (52.1%)	23 (47.9%)	3-5	6-12	7 (14.6%)
Itraconazole (200mg/d)	26	Previously treated patients (20) - Griseofulvin (14) - Terbinafine (6) Naïve patients (6)	5 (19.2%)	21 (80.8%)	2-3	6-8	3 (11.5%)
Terbinafine (250 mg/d)	20	Previously treated patients (16) - Griseofulvin (11) - Itraconazole (5) Naïve patients (4)	6 (30%)	14 (70%)	3-4	6-8	3 (15%)

Systemic diseases such as diabetes mellitus (21), immunosuppressants (22), and long use of topical or systemic steroids (23) were reported in association with adult TC. In this study, HCV infection was most commonly (34.4%) associated systemic disorder. However, treatment with interferon-alpha seems to have a significant role in increased incidence of TC in HCV patients. It was reported that interferon-alpha therapy was associated with other dermatophytosis (tinea manus) and this contributed to the alteration of a delayed-type hypersensitivity reaction and the possible ability of interferon-alpha to influence the cytokine cascade towards increased Th1 expression and also the cutaneous manifestation of dermatophytosis (24).

It was reported that TC may mimic variable forms of folliculitis such as bacterial folliculitis (25), tufted hair folliculitis (26), and folliculitis decalvans (27). Other atypical forms of adult TC included more inflammatory presentation such as pyoderma (28) and dissecting cellulitis (29). The variable clinical presentations of adult TC increased our belief that more awareness and careful examination of inflammatory scalp diseases is highly recommended, especially for conditions that do not respond or respond poorly to treatment.

In this study, the most common fungal pathogen was *T. violaceum* (56.9%), and this was in agreement with previous studies (30). *T. violaceum* was also reported as the most common fungal pathogen (71.1%) in all dermatophytosis among Egyptian patients (31).

In Tunisia, *T. violaceum* was reported as the most common fungal pathogen (60%) in adult TC (16). Recently, Zaraa et al. (32) also reported that *T. violaceum* is still the most common pathogen of TC in northern Tunisia. In Morocco, *T. violaceum* was also reported as the most common pathogen in both childhood and adult TC (33).

In comparison with north African studies, TC in the Pakistani population also showed a predominance of *T. violaceum* (69.4%) in both children and adults, followed by *T. tonsurans* (16.7%) (34). Controversially, the spectrum of fungal species in adult TC among Chinese showed a predominance of *T. mentagrophtes* (55.6%), followed by *M. canis* (13.3%) (16).

In Europe, *M. canis* is still the most common reported causative agent. The highest incidence of *M. canis* infections were reported in the Mediterranean region in addition to more distant countries such as Austria, Hungary, Germany, and Poland. In addition to the increase in *Microsporum*-induced TC, there is a shift towards anthropophilic TC mainly in urban areas in Europe. The largest overall increase in anthropophilic dermatophytes has been noted with *T. tonsurans* mainly in the UK and with *T. soudanense* and *M. audouinii* in France (35).

In the United States, *T. tonsurans* was reported as the most prevalent causative species in both children and young adults (36). The change of spectrum in the United States from *M. audouinii* to *T. tonsurans* was explained by the sensitivity of *M. audouinii* to griseofulvin treatment and the importing of *T. tonsurans* by people emigrating from geographic areas where that vector had been the prominent cause of TC (37). These studies may prove that TC is a classic example of the changing geographic patterns of dermatophytosis and prove the role of geographic distribution in modulating the fungal spectrum among different populations.

Molecular identification of fungi by using PCR amplification showed a great advantage in evaluating fungal transmission all over the world. In Japan, Mochizuki et al. (38) reported that the recent influx of non-transcribed spacer region (NTS) I, II, V, VI, and VII strains of *T. tonsurans* infection (the main causative agent of tinea capitis and tinea corporis worldwide) primarily originated from abroad and was transmitted to the general community through athletes: wrestlers and martial arts participants in international sports. In this study, PCR test proved a higher fungal transmission from animals to human with isogenicity of the two isolates in 80% of cases. Mapelli et al. also used PCR test to confirm a rare transmission of *T. rubrum* from a mother with tinea corporis to her newborn causing TC (39).

With regard to treatment, we found that itraconazole and terbinafine were more effective than griseofulvin in the management of adult TC. Itraconazole was reported as an effective treatment of adult TC caused by *T. tonsurans* (21), whereas terbinafine was reported as an effective therapy in TC caused by *T. violaceum* (40) and *M. audouinii* (41). Although griseofulvin showed less therapeutic effect, it was reported as an effective treatment in the treatment of adult TC caused by *M. canis* (42).

Conclusion

Trichophyton violaceum is the most common cause of adult TC among Egyptians. We believe that increased awareness of variable clinical forms of TC will help in identifying more cases, especially those with associated risk factors such as HCV infection and close contact with animals. The PCR technique will be a rapid, more accurate, and sensitive method in identifying transmitted species and demonstrating hidden sources of infection. Itraconazole is superior to other systemic antifungal treatments and remains the drug of choice in managing adult TC.

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