DOI: https://doi.org/10.17816/dv111992

Клинический случай

Особенности наружной терапии микоза кожи и волос, вызванного грибами рода *Microsporum*: результаты клинических наблюдений

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АННОТАЦИЯ

В статье обобщён многолетний опыт наблюдения за динамикой патологического процесса при микозе гладкой кожи у детей и взрослых, вызванном грибами рода *Microsporum* spp., на фоне применения или отсутствия топических комбинированных глюкокортикостероидов на начальном этапе лечения. При назначении топических комбинированных глюкокортикостероидов сроки излечения микроспории увеличиваются в 1,5–2 раза, чего нельзя сказать о микозах, вызванных грибами рода *Trichophyton* и *Epidermophyton*, что, по-видимому, можно объяснить особенностями спорулирования грибов рода *Microsporum* spp.: большинство дерматомицетов в момент проникновения в эпидермис и дерму делают ставку на прорастание мицелия, и только у грибов рода *Microsporum* spp. в момент инвазии активность спорулирования не снижается. В результате гриб способен одновременно инфицировать и эпидермис, и волосы.

Большинство современных терапевтических программ для наружного лечения микроспории включают препарат йода и антимикотик в форме крема или мази, которые не подавляют макрофагальную реакцию в очаге поражения, и с началом лечения спорулирование резко уменьшается. При применении топического комбинированного препарата, содержащего антимикотик и топический комбинированный глюкокортикостероид, гриб продолжает активно спорулировать, в результате чего процесс в эпидермисе останавливается, а проникшие в волос споры остаются жизнеспособными.

Ключевые слова: топические комбинированные глюкокортикостероиды; микроспория; экссудативный микоз.

Для цитирования:
Яковлев А.Б. Особенности наружной терапии микоза кожи и волос, вызванного грибами рода Microsporum: результаты клинических наблюдений // Российский журнал кожных и венерических болезней. 2022. Т. 25, № 5. С. 381–388. DOI: https://doi.org/10.17816/dv111992

Рукопись получена: 07.09.2022 **Рукопись одобрена:** 16.10.2022 **Опубликована:** 15.11.2022

ЭКО•ВЕКТОР

DOI: https://doi.org/10.17816/dv111992

Case report

Features of topical therapy of skin and hair mycosis caused by *Microsporum* genus fungi: Results of clinical observations

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ABSTRACT

The article summarizes the long-term experience of observing the dynamics of pathological process of tinea corporis caused by *Microsporum* spp. in children and adults treated at the initial stage with combined topical steroids and without them. The duration of treatment increases by 1.5–2 times when combined topical steroids are used, while with other mycoses caused by fungi of the genera *Trichophyton*, *Epidermophyton*, this does not occur. This can be explained, apparently, by the peculiarities of sporulation of fungi of the genus *Microsporum* spp.: most dermatomycetes at the time of penetration into the epidermis and dermis rely on the germination of mycelium, and only in fungi of the genus *Microsporum* spp. at the time of invasion, sporulation activity does not decrease. As a result, the fungus is able to simultaneously infect the epidermis and hair.

Most modern therapeutic programs for the external treatment of microsporia include iodine preparation and an antimycotic in the form of a cream or ointment. These drugs do not suppress the macrophage reaction in the lesion, and with the onset of treatment, sporulation decreases sharply. When using a topical combination drug containing an antimycotic and combined topical steroids, the fungus continues to actively sporulate, as a result of which the process in the epidermis stops, and the spores that have penetrated into the hair remain viable.

Keywords: topical combined steroids; microsporia; exudative mycosis.

For citation:
Yakovlev AB. Features of topical therapy of skin and hair mycosis caused by Microsporum genus fungi: Results of clinical observations. *Russian journal of skin and venereal diseases.* 2022;25(5):381–388. DOI: https://doi.org/10.17816/dv111992

Received: 07.09.2022 **Accepted:** 16.10.2022 **Published:** 15.11.2022

INTRODUCTION

Microsporia is a zooanthroponous anthropurgical mycosis of the skin, hair, and sometimes nails caused by various species of the *Microsporum* genus fungi, with a contact mechanism of transmission of the pathogen [1, 2].

The term "anthropurgical" (Greek) means "associated, one way or another, with human activity": usually this term refers to epizootics of fungal diseases among synanthropic animals [2, 3].

The causative agent of the disease was first described in Paris by the Hungarian scientist Gruby (1843).

Until July 2018, *Microsporum* genus fungi were divided into 3 non-systematic groups: anthropophilic, zoophilic and geophilic [1, 4].

Anthropophilic: *M. audoinii*, *M. langeroni*** — distributed in North Africa and Western Europe [5]; *M. ferrugineum* — predominates in Eastern Europe, Southwest Asia, West Africa; *M. rivaliery* (*M. audoinii var. rivaliery**) — endemic to the Congo.

Zoophilic: *M. canis (felineum*, *lanosum*, *equinum*) is the most frequent causative agent of human and animal microsporia, it is widespread locally; the natural reservoirs are stray cats, dogs, less often other mammals; *M. galinae (Lophophyton galinae*)* — chickens; *M. persicolor* (*Nannizia persicolor**) — mice and other small rodents; *M. distortum*** — monkeys, cats, dogs; *M. nanum* (*Nannizia nana**) — monkeys [6].

Geophilic: *M. gypseum* (*Nannizia gypsea**), *M. racemosum* (*Nannizia racemosa**), *M. qookey* (*Paraphyton qookey**), *M. magellanicum***. This group of fungi does not play a significant role in the formation of the epidemic process, nevertheless it is described in the literature as the causative agent of "mycosis of predators".

The sign * indicates new species of the *Microsporum* genus, which were included after the classification revision based on genetic studies [7, 8].

The sign ** indicates the species of the *Microsporum* genus, whose systematic affiliation has not yet been determined [7, 8].

Microsporum canis (*felineum*) — canine or, better, feline *Microsporum* — is the main fungus that forms *Microsporum* spp. epidemiological situation [2, 9].

The main sources of zoophilic *M. canis* infection for people are cats (80%), especially kittens [1, 10] due to:

- the kitten's immune system imperfection — a high probability of developing the disease;
- well-developed and tender undercoat — a nutrient medium for microsporums;
- great attractiveness for children.

Infection with anthropophilic species *M. audoinii* and *M. ferrugineum* is possible in children, and even among adults. The probability of infection transmission is up to 20%: for comparison, the probability of infection transmission with the zoophilic *M. canis* from person to person is only 4% [10], but it increases slightly in the circumstances of a very close physical contact, for example when practicing freestyle or Greco-Roman wrestling [4, 11].

Up to 80% of all cases of infection occur through direct contact [1, 10, 12].

Tinea caused by *Microsporum* spp. is most commonly observed in children aged 6–14 years [13]. The proportion of adults with tinea corporis caused by *Microsporum* spp. ranges annually from 9 to 20%; tinea capitis caused by *Microsporum* spp. occurs in adults almost exclusively when lesions are localized along the edge of hair growth, in the ophiasis zone [10].

Most pathogenic fungi, and especially dermatomycetes, follow one of the clinical mycology basic rules: zoophilic fungi cause more pronounced inflammation during invasion than anthropophilic ones. In this regard, the most striking examples are seen with the *Trichophyton spp.* fungi: anthropophilic fungi cause hair loss, which is often undiagnosed for years, and zoophilic fungi cause infiltrative and suppurative tinea capitis. *Microsporum* spp. fungi generally follow this rule, and *M. canis* causes exudative and inflammatory forms more frequently than *M. ferrugineum* [10].

The incubation period varies from 3 to 8 days for zoonotic *Microsporum* spp. infection, from 4 to 6 weeks (or from 28 to 45 days) for anthroponotic *Microsporum* spp. infection [2, 14].

DESCRIPTION OF CLINICAL CASES

The typical tinea capitis clinical findings are characterized by the formation of an erythematous-squamous patches, with clear boundaries (**Fig. 1**); hairs break off at the level of 6–8 mm above the skin in zoonotic and at different levels in anthroponotic *Microsporum* spp. infection [4].

Examination with a Wood lamp reveals a green fluorescence of affected hairs (look Fig. 1).

The typical tinea corporis clinical presentation is that of rounded or oval shape lesions, with a peripheral border that consists of small papules, vesicles and crusts. Due to the partial death of the fungal colony and subsequent autoinoculation, "ring in the ring" or "iris" lesions (resemble the iris of the eye) may be seen (**Fig. 2**). It is believed that the "iris" lesions are more characteristic for the *M. ferrugineum* [10].

Atypical forms [15]:

- tinea capitis: trichophytoid, seborrheic, asbestos-like lichen type, parasitic achromia;
- tinea corporis: abortive, parasitic achromia, erythematous-edematous, papular-squamous, deep, transformed due to topical steroids.

Complicated forms [9, 16]:

- tinea capitis: infiltrative, suppurative (deep), exudative;
- tinea corporis: erythematous-edematous, deep.

Histological examination is used relatively rare. Microscopic examination of affected hairs (mixed type

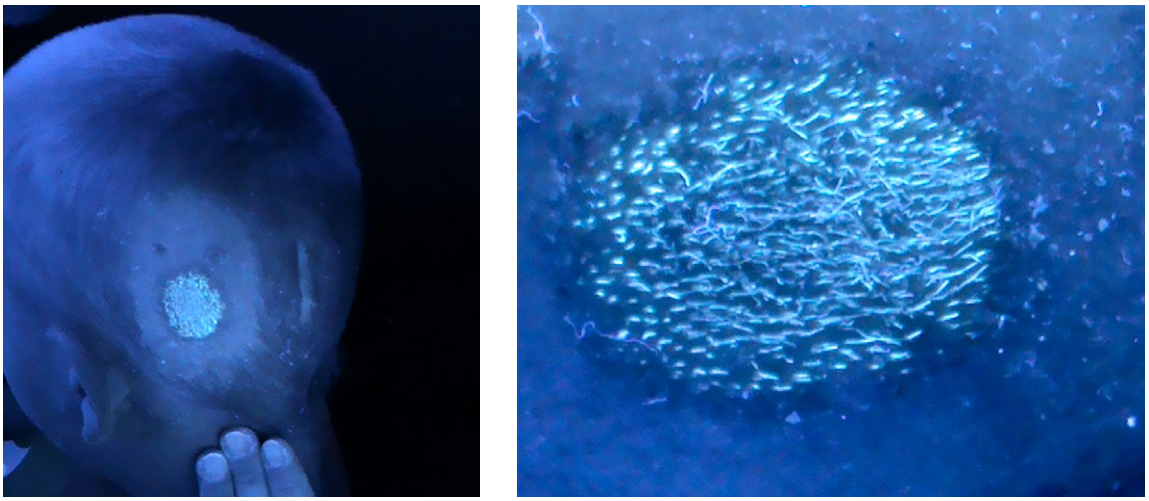

Fig. 1. Tinea capitis caused by *Microsporum* spp. in an 8-year-old patient. Observation together with PhD Yu.A. Nikolenko.

Fig. 2. The «ring in the ring», or «iris» lesion; the causative agent according to the laboratory results is *M. canis*. Own observation.

Fig. 3. Widespread tinea corporis caused by *Microsporum* spp. with an exudative component in a 40-year-old patient. Own observation.

of ectothrix/endothrix) in combination with the characteristic fluorescence in a Wood lamp make it possible to establish a diagnosis quickly [2, 14].

In cases of widespread lesions of tinea corporis caused by *Microsporum* spp. (more than 20 lesions), a large number of vesicular eruptions is usually seen. Compared with localized forms, this type of tinea corporis has a more acute course (**Fig. 3**).

Fungal culture isolation from a "dry" lesion is the "golden standard" of cultural diagnostics — the culture of a pathogenic fungus grows in 95% of cases (the method has high sensitivity and specificity). Fungal culture isolation from an exudative or infiltrative lesion allows to get a culture in 75% and 67% of cases respectively. The fungal culture can be isolated only in 25–30% of cases if suppuration takes place in the lesion, as suppurative process destroys the majority of the fungal colony-forming units [17].

Histological features of infiltrative and suppurative forms of tinea capitis caused by *Microsporum* spp. [17]: in the suppurative stage (kerion), fungal spores surrounding the hair follicle and hyphae inside the hair shaft may be evaluated. An inflammatory infiltrate is detected in the dermis; a giant cell reaction may occur due to the destruction of follicles. To confirm the diagnosis, Schiff's acid fuchsin staining may be used.

Kerion is characterized by neutrophilic and granulomatous infiltrates in the early stages and fibroblast reaction in the late stages. There are four types of histological patterns associated with kerion [17]:

1) purulent folliculitis — perifollicular inflammatory infiltrate, spongiosis and infiltrates composed of neutrophils, lymphocytes and plasma cells; most hair follicles are in the catagen stage (the stage of slow metabolism extinction);
2) purulent folliculitis with purulent dermatitis — perifollicular and perivascular neutrophilic infiltrate with edema in the papillary dermis; hair follicles are infected, with a small number of destroyed follicles;
3) purulent folliculitis with purulent and granulomatous dermatitis — infiltration withneutrophils, lymphocytes and plasma cells, formation of granulomatous reaction — in fact, this is the beginning of a trichophytosis granuloma (like Majocca) formation; the number of intact hair follicles is reduced;
4) purulent and granulomatous dermatitis with fibroblast reaction — an inflammatory infiltrate composed of neutrophils, lymphocytes and plasma cells with granuloma formation, increased number of collagen fibers and the absence of hair follicles.

Clinically this stage corresponds to the formation of scarring alopecia. In the majority of cases, the latter two histological variants are characterized by the absence of fungal structures, and Shiff's fuchsin staining is negative [11, 17].

Topical therapy of tinea caused by *Microsporum* spp. fungi has some specific features, and the main one is the prohibition on the use of combined topical steroids (cTS) to relieve excessive inflammation.

In clinical cases of *Microsporum* spp. infection associated with a pronounced exudative component, microsporides and vesiculation, it is recommended to replace vaseline or lanolin-vaseline based preparations with Unguentum Zinci (zinc ointment) at the beginning of treatment, which will ensure anti-inflammatory and drying effects [10].

Since 2015, we use 5% povidone-iodine solution widely in our clinical practice for the treatment of *Microsporum* spp. lesions. We recommend using this drug instead of 2% alcohol iodine tincture, which is known to cause contact dermatitis.

Even if a pronounced exudation is present, we do not recommend treating lesions caused by *Microsporum* spp. fungi with combined ointments and creams containing topical steroids [2, 14], including combined topical creams and ointments of the type "topical steroid/antimycotic". At the same time, the presence of an antibiotic or another component (dexpanthenol) in a cream is possible, as these additives do not reduce the effectiveness of treatment. This is the main feature of the *Microsporum* spp. fungi topical therapy: the use of topical combined drugs of the type "topical steroid / antimycotic" is contraindicated at any stage of the disease.

The use of combined topical steroids (cTS) for the management tinea corporis caused by *Microsporum* spp. fungi leads to the vellus hair infestation — the fungi literally "catch fire in the hair", even if vellus hair were not involved in the infectious process before treatment.

Current studies on the pathogenesis of tinea capitis and corporis have shown that low concentration of TNF-alpha (21.9±2.23 pg/ml) in lesions is associated with a low concentration of INF-γ and an insufficient number of activated Th1 lymphocytes. At the initial stages of fungal invasion, the main production of IL-2 is provided by antigen-recognizing T-lymphocytes during the initiation of immunogenesis, which leads to the formation of cellular immunity in patients. The increased production of IL-2 indicates the activation of cell-mediated immunity, which ensures pathogen elimination and recovery. The INF-γ insufficiency leads to a slowdown of this beneficial effect to a certain extent [18].

At the same time, the pathogenesis peculiarities of tinea caused by *Microsporum* spp. and *Trichophyton spp.* fungi remain completely unexplored.

The fact remains! According to our observations, the duration of tinea treatment with the use of cTS increases by almost 85%: instead of 12 days, patients need 20 days of topical therapy. At the same time, with tinea caused *Trichophyton spp. fungi*, this does not happen [18].

Besides, after the initial treatment of tinea caused by *Microsporum* spp. with cTS fungi are detected in 77% of cases [10], while the use of an antifungal drug without

steroids makes it necessary to perform a number of diagnostic techniques to detect the pathogen.

According to our data, the negative impact of cTS on the course of tinea corporis caused by *Microsporum* spp. fungi may be observed if cTS are used for more than 5–6 days [10, 19].

The antimycotic action of the antifungal component in the combined cream is sometimes insufficient to inhibit fungal proliferation, while the immunosuppressive and antiproliferative action of topical steroids prevents the local reaction of macrophages.

Microsporum spp. fungi, unlike *Trichophyton* spp., continue to sporulate actively in the lesion, which damages hair [10, 19]. This, in turn, increases the duration of treatment.

Thus, it is contraindicated to use cTS for the treatment of tinea caused by *Microsporum* spp. [2]. However it is possible to use cTS for the treatment of tinea caused by other fungal genuses for a relatively long time (but also, as a rule, no more than 10 days).

In case of a tendency to exudative or infiltrative process, it is possible to use other drugs that reduce exudation: Fucorcin solution — contains resorcinol, which causes local vascular spasm and reduces exudation; povidone-iodine 5% — does not cause irritant dermatitis, can be prescribed for any forms of tinea; zinc paste — has a drying effect, can be used for no more than 1–2 days, since zinc has no antifungal effect, and it is necessary to switch to a real topical antimycotic in a timely manner; the solution "tannin – polydocanol – zinc oxide" has both anti-inflammatory and antipruritic effect; terbinafine spray and naphthyphine solution have an anti-inflammatory effect comparable to hydrocortisone; bifonazole solution — acts fungicidal when applied topically [2, 14].

For the treatment of tinea with an infiltrative component, the prescription of sulfur-tar ointment based on Ung. Zinci (salicylic acid in this recipe is a non-permanent component) may be used:

Rp: Sulfuris pp	*5,0*
Ac. salicylici	*1,5*
Ol. Rusci	*2,5*
Ung. Zinci	*ad 50,0*
M. f. ung.	
D.S. Topical for skin lesions	

When infiltration and suppuration are reduced, it is possible to switch to conventional modern cream with antimycotics. Of these, the most preferred are (in the descending order): azoles (e.g. clotrimazole, bifonazole); cyclopyroxolamine; allylamines (naphthyphine, terbinafine). As a rule, topical antifungal creams are prescribed in combination with an iodine preparation, preferably povidone-iodine: an antifungal cream is applied in the morning, a povidone-iodine solution is applied in the evening [20]. Both drugs can be prescribed twice a day throughout the course of treatment if tolerated well — in the morning and in the evening, iodine is applied first, 20–30 minutes later — an antimycotic cream [10].

For the treatment of tinea corporis with affected vellus hair, topical therapy with keratolytic agents should be used, which leads to the removal of hair: 5% urea ointment, 10%-sulfur–3%-salicylic ointment, 12%-salicylic–6%-milk ointment of A.M. Arievich. The use of these ointments is possible only after the regression of acute inflammatory process in the lesion [10].

In multiple lesions, it is recommended to prescribe systemic therapy with griseofulvin or itraconazole for 2–3 weeks [21, 22].

The follow-up duration after the *Trichophyton* spp. or *Microsporum* spp. infection cure is currently not regulated, but it is recommended to focus on the following timeframes [4, 10]:

- tinea corporis without vellus hair involvement — 1 month;
- tinea corporis withvellus hair involvement — 2–3 months;
- tinea capitis — from 3 months;
- favus — 1 year.

CONCLUSIONS

Topical therapy is the most important component of the tinea corporis treatment.

The use of topical preparations has specific features that distinguish *Microsporum* spp. infection from tinea corporis caused by other fungi genuses.

In *Microsporum* spp. infection, the tendency of the fungus to actively sporulate is especially pronounced, unlike fungi of the genus *Trichophyton*.

cTS are relatively contraindicated in the treatment of *Microsporum* spp. infection.

Povidone-iodine preparations successfully replace Fucorcin in exudative lesions.

ADDITIONAL INFORMATION

Funding source. This work was not supported by any external sources of funding.

Competing interests. The author declare that he has no competing interests.

Authors contribution. The author made a substantial contribution to the conception of the work, acquisition, analysis of literature, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

Patient permission. Patient voluntarily signed an informed consent to the publication of personal medical information in depersonalized form in the journal "Russian journal of skin and venereal diseases".

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