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Случай успешной терапии микроспории у больного, заразившегося от слона, сертаконазолом

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РЕЗЮМЕ

Микроспория гладкой кожи и волосистой части головы — одна из наиболее распространенных клинических форм дерматомикозов на территории Российской Федерации. Основными источниками заражения микроспорией становятся кошки и собаки, реже кролики, мелкие грызуны и козы. В статье представлено описание редкого случая (возможно, первого) заражения мужчины 32 лет микроспорией от индийского слона на острове Пхукет в Юго-Восточной Азии. Причиной микоза кожи стал *Microsporum canis* — наиболее часто встречающийся возбудитель микроспории. Течение микроспории в описываемом случае отличалось большим количеством пустулезных элементов в очаге поражения. Молекулярно-генетический анализ возбудителя *M. canis*, выделенного от больного, показал идентичность его генотипа с генотипами местных штаммов *M. canis*, выделенных ранее у людей, заразившихся от кошек в Северо-Западном регионе, в Санкт-Петербурге и Ленинградской области. Терапия микоза кожи кремом с действующим веществом сертаконазолом и гризеофульвином оказалась высокоэффективной. В настоящее время фармацевтический рынок предлагает широкий ассортимент противогрибковых препаратов для наружного применения. Линия препаратов за счет уникального строения молекулы действующего вещества сертаконазола, обеспечивающего фунгицидный эффект и широкий спектр действия на большинство возбудителей микозов кожи, позволяет быстро и эффективно лечить микроспорию.

Ключевые слова: микроспория, Microsporum canis, индийский слон, сертаконазол.

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Successful treatment with sertaconazole of microsporia in a patient infected from an elephant

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Microsporia of skin and scalp is one of the most common clinical forms of ringworm in the Russian Federation. The main sources of microsporia infection are cats and dogs, less often rabbits, small rodents and goats. It is presented rare case report (perhaps, the first one) of a 32-year-old man infection with microsporia from an Indian elephant on Phuket Island in Southeast Asia. *Microsporum canis* as the most common cause of microsporia resulted skin mycosis in this case. The course of microsporia was characterized by a large number of pustules. Molecular genetic analysis of *M. canis* isolated from the patient confirmed identity of its genotype with the genotypes of local strains of *M. canis*. Those strains were previously isolated from people who were infected by cats in the North-West region, St. Petersburg and Leningrad region. Therapy with sertaconazole and griseofulvin was highly effective. Currently, wide range of topical antifungal drugs is available. Therapy with sertaconazole is very effective for microsporia due to unique structure of the active molecule followed by fungicidal effect and wide spectrum of action on the most of pathogens of skin mycoses.

Keywords: microsporia, Microsporum canis, Indian elephant, sertaconazole.

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The prevalence of dermatomycosis has significantly increased over the past decades. These are superficial mycoses of skin caused by microscopic fungi (dermatomycetes) [1, 2]. Maximum morbidity is noted on summer and autumn. Children usually suffer from microsporia and trichophytosis caused by zoophilic fungi, such as *Microsporum canis* and *Trichophyton mentagrophytes* [3]. However, these fungi also affect adults. Microsporia of smooth skin is one of the most common dermatomycoses caused by zoophilic fungi. *M. canis* is the main causative agent of microsporia of the scalp and smooth skin on the territory of the Russian Federation [4].

Clinical manifestations of microsporia are well known due to some distinctive features: erythematous-squamous round or oval patches with clear edges. Raised edges are observed as a rule with microvesicles or small pustules. Patches eccentrically enlarge and areas of apparent recovery occur in the center. After some time, elements *de novo* can appear inside the patches and "ring-in-ring" pattern occurs [5]. Diagnosis of microsporia is not difficult for the majority of dermatovenerologists due to characteristic manifestations, anamnestic data about contact with animals. However, microsporia may not be recognized in some cases even in case of positive mycological examination. It is true for atypical clinical picture and "unusual" source of infection, as it happened in this case report.

Case report

A 32-year-old patient N. appealed for medical care in the clinical-diagnostic department of the mycological clinic of the Mechnikov North-Western Medical University. The patient complained about slightly itchy lesion on the back of the right thigh.

It was found that signs of disease appeared 2 weeks after return from Thailand and 1 month before his visit to the mycological clinic. First, a large pustule appeared on the back of the right thigh. Then, this pustule opened and erosion covered with a crust occurred. Pink patch with a diameter of 2 cm was observed within 7–10 days after initial manifestations. There were more intensely colored raised scalloped edges, pustules were located along the edges and inside the patch. Subjectively, the patient was disturbed by a slight itch. The man turned to a commercial medical center, where he was examined by a dermatologist. Scrapings for mycological research and pustule content sampling for bacteriological examination were carried out. A doctor prescribed local antibiotic therapy with mupiracine until examination data will be obtained because physician determined lesion as impetigo. The second consultation was 10 days later. The patient told that the doctor found mycelium in skin scraping and growth of *Staphylococcus epidermidis* in content of pustules. Next, amoxiclav 1000 mg twice a day for 5 days was prescribed instead of antibacterial ointment. The doctor orally justified his appointment by a growth of staphylococcus (i.e. pyoderma). Moreover, he said that so many pustules are extremely unusual for mycoses. Presence of mycelium was recognized as an artifact. Focal lesion on the thigh was enlarged by 3 times within 5 days after amoxiclav administration. The same was true for the number of pustules.

The patient appealed to the consultative and diagnostic department of the mycological clinic of the Mechnikov North-Western Medical University considering unsatisfactory results of the treatment. He complained about itching and rash on the back of the right thigh at admission. Primary examination revealed an erythematous patch 6–7 cm with irregular shape and polycyclic scalloped edge. The edge was more intensely colored than the central part of the patch and slightly raised above the skin. Folliculitis with a diameter from 0.5 to 1.0 mm within focal lesion was diagnosed **(Fig. 1)**. Wood lamp examination revealed emerald green fluorescence of some flakes and hair. Microscopic examination of skin flakes and hair found mycelium of micromycetes and hair damage by ectotrix type. Scraping material (hair, skin flakes and pus) was sown in Sabouraud agar to identify pathogen. Physical and microscopic examination determined preliminary diagnosis as "Mycosis of smooth skin, microsporia (?)". The patient was interviewed in detail in order to determine the source of infection. The patient categorically denied contact with cats, dogs, any rodents. However, he remembered riding an elephant on a holiday on the Phuket island. The patient wore shorts during the tour, and he rubbed the back surface of the right thigh strongly (in the projection of the lesion) on the skin of the animal. The man told his first attending physician about this fact, but the doctor did not attach any importance to this.

Griseofulvin 1000 mg per day and sertaconazole cream topically twice a day were prescribed. The patient was again invited for examination after 2 weeks.

Culture examination showed the growth of the pathogen in Sabouraud agar with 2% glucose. The colony was flat, white, velvety. The piles were located radially from the center to the periphery. The reverse side of the colony was light brown **(Fig. 2)**. Microscopy of the culture revealed a colorless, septate, branched mycelium 2.8–

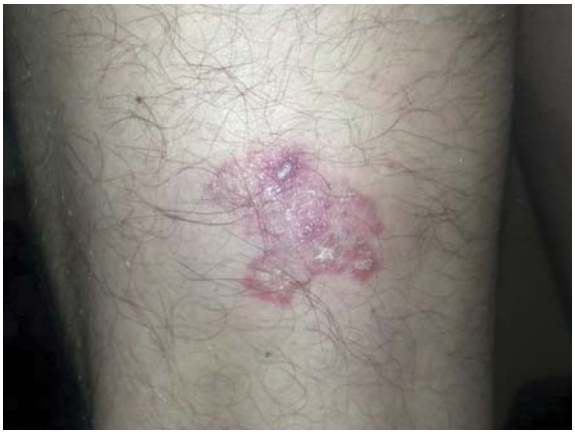

Fig. 1. **Microsporia of skin (*M. canis*) in patient *N*. aged 32 years.**

Fig. 2. M. canis **culture isolated from the patient *N*. (Sabouraud agar with 2% glucose).**

4.3 μm wide, as well as spindle-shaped thick-walled 4–7-cell macroconidia 13-15 × 53-68 μm with a narrowing at both ends. Microconidia were not found **(Fig. 3)**. Causative agent was identified as *M. canis*.

Considering unusual source of infection, it was decided to determine genotype of the pathogen and compare it with genotypes of *M. canis* isolated from microsporia patients infected from the cats (St. Petersburg and Leningrad region). The objective was comparison of the genotype of D15P91 specimen (patient N.) of *M. canis* with the genotypes of "local" 19 specimens. Microsatellite analysis was applied to solve the problem. Four loci were amplified. Polymorphism was present only in one locus (McGT (15)), minor variations were found in McGT locus (17). McGT (15) amplification showed that three specimens (D15P91, RKPG-1300 and RKPG-1403) had 4 more mutable alleles than the others. RKPG-1410 and 1461 strains were isolated in the sample, which were not stably amplified in McGT (13), (14) and (15) loci. Bruvo's genetic distance matrix was calculated considering allele lengths of McGT (15) and (17) loci. Polysat 1.5 package for R environment was applied. This matrix was used to analyze the main components in the same package. A tree was built in the Mega 6.06 program using neighbor joining method (NJ). DNA sequencing by the locus BT2 and analysis of microsatellite allele lengths in the Structure program confirmed homogeneity of the sample. Analysis of electrophoretic profiles of PCR products by microsatellite loci revealed specimens D15P91, RKPG-1300 and 1403, as well as a group of RKPG-1410 and 1461. The group of RKPG-1410 and 1461 was also well determined by analysis of genetic distances. Thus, these data did not confirm the uniqueness of D15P91 specimen (*M. canis* isolated from the patient N.) in comparison with local strains of *M. canis*. Its genotype turned out to be similar to the genotypes of local strains.

Fig. 3. **Colorless, septate, ramous mycelium with width of 2.8—4.3 microns, spindle-shaped, thick-walled, 4—7-cellular macroconidia 13—15×53—68 microns with narrowing at both ends.**

Significant positive changes were observed in 2 weeks after therapy onset. Patch turned pale and completely recovered on the one side. The same was true for folliculitis. The patient reported good tolerance to therapy and convenient application of sertaconazole cream. He asso-

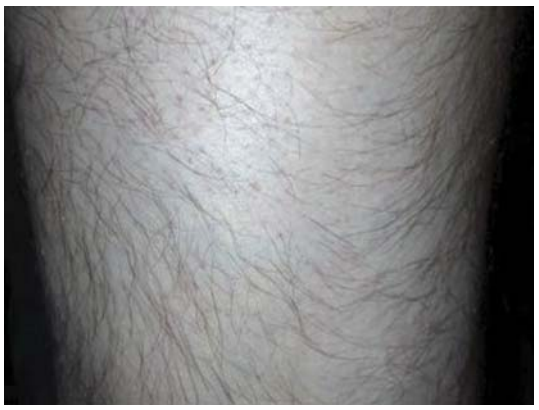

Fig. 4. **1.5-month outcome of microsporia management in patient *N*.**

ciated rapid recovery with sertaconazole cream. The patient said that even first application of the cream resulted disappearance of itching and less redness. Pustules were resolved in 5 days after onset of sertaconazole cream application. Any adverse events during the treatment were absent. Local twofold depilation under fluorescent lighting was performed over the next 2 weeks. Complete recovery was observed in 4 weeks after onset of the treatment (**Fig. 4**). Complete mycological recovery was confirmed by subsequent 3-fold mycological examination.

Discussion and conclusion

M. canis is more common cause of microsporia of scalp and smooth skin than other *Microsporum spp*. Microsporia of smooth skin is the second mycosis of skin and its appendages after trichophytia. However, the last is true for mycoses of smooth skin while microsporia is the most common mycosis of scalp in the North-West region. Children are more susceptible to microsporia. Maximum morbidity is noted on the end of summer and autumn, when children return from vacation.

Animals is the most common source of infection in children. Cats is frequent source in the Russian Federation. The authors of the review devoted to fungal infections in animals reported dogs and rabbits as possible sources of infection in humans [6]. *M. canis* is one of the causative agents of dermatophytosis in rabbits at the Italian farms [7]. This species was found in 26 (3.2%) out of 810 examined animals at 5 (21.7%) out of 23 farms. It should be noted that clinical manifestations of microsporia may be absent in infected cats and rabbits. Nevertheless, human infection may be caused by arthroconidia even from infected animals without clinical manifestations.

Data regarding microsporia in elephants are presented only in two articles of Chinese scientists. They described the case of microsporia among elephants in the Hong Kong Zoo [8, 9]. We have not found any literature data regarding possible infection of humans from the elephants.

Treatment of microsporia of the skin is not difficult as a rule. However, combination of systemic and topical antifungal agents is required in patients with lesion of hair. It was true for our patient too. Duration of therapy may be over 12 weeks if hairs are involved. However, duration of treatment did not exceed 4 weeks in our case. In our opinion, this is primarily associated with topical application of sertaconazole cream. The effectiveness of sertaconazole is determined by the unique structure of its molecule. Sertaconazole is the only among all azole antimycotics with fungicidal effect on micromycetes and activity against dermatophytes, yeast and mold. Unlike other imidazole derivatives, sertaconazole molecule consists of benzothiophene in addition to imidazole. Benzothiophene is incorporated into the structure of the fungal cell membrane instead of tryptophan. The last amino acid is essential structural part of fungal cell wall. This results violation of integrity and permeability of the wall and death of the fungus [10]. Sertaconazole has similar effect not only on dermatomycetes and yeast, but also on the pathogens of opportunistic infections including *Aspergillus fumigatus, Chaetomium atrobrunneum* and *Scedosporium prolificans* [11]. There was a high antifungal activity of sertaconazole against *Microsporum canis*. MIC50 and MIC90 were 0.25 and 0.5 μg/ml, respectively [12]. Sertaconazole has a direct toxic effect on the fungal cell membrane in 10 min after exposure onset and ensures death of 90% of fungal cells within an hour of sertaconazole exposure with a concentration of 0.008 g/ml [13]. The effectiveness of sertaconazole was proven both in vitro and in vivo. Clinical efficacy of sertaconazole for dermatomycoses was confirmed in meta-analyses and systematic reviews with a low risk of errors. The Cochrane review (2015) enrolled eight articles devoted to the effectiveness of sertaconazole in the treatment of dermatophytosis of smooth skin and folds [14]. I. Rotta et al. in meta-analysis reported effectiveness of sertaconazole in patients with mycoses of skin of other localizations including mycosis of the feet [15]. Thus, effectiveness of sertaconazole is 62.3-95.6%, that is similar to terbinafine and exceeds miconazole and butenafine [10].

We reported clinical and mycological efficacy of sertaconazole against *M. canis*. We have previously described effective administration of sertaconazole in monotherapy of microsporia of smooth skin [16]. In our report, microsporia of smooth skin was complicated by deep fungal folliculitis and hair lesion. Therefore, griseofulvin was required besides sertaconazole. Griseofulvin is usually prescribed for 6-8 weeks if micosporia affects hairs. In our case, duration of treatment was only 4 weeks because sertaconazole was additionally prescribed for topical application. Thus, high therapeutic efficacy of sertaconazole was demonstrated once again.

Conclusion. The first case of human infection with microsporia from an elephant was described in this case report. It is also interesting that genotype of the pathogen was identical to genotype of the local species. However, griseofulvin and sertaconazole were effective for medication despite certain diagnostic difficulties.

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