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Scopulariopsis brevicaulis as the Cause of Dermatomycosis

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SUMMARY *Scopulariopsis (S.) brevicaulis* (Saccardo) Bainier 1907 is a ubiquitous fungus frequently isolated as a saprophyte from various layers of the soil, wood, straw, paper, food, and occasionally in animals and humans. This nondermatophyte filamentous fungus is multiresistant and is frequently associated with onychomycosis in humans. In the last two decades, the number of reports on its pathogenic role in different localized and disseminated infections has been on an increase. Identification was done by native KOH microscopy and culture on the Mycobios selective agar (Biolife). From January 1, 2002 till January 23, 2008, a total of 7161 samples were examined by use of mycology methods; *S. brevicaulis* accounted for 39 (2.2%) of 1834 (25.6%) positive samples. During the study period, *S. brevicaulis* was isolated from nail, skin and scalp scrapings of 39 patients (17 male and 22 female), mean age (± SD) 43.9±20.7 (range 8-87) years. Specimens were most frequently obtained from the foot (n=16; 41%), i.e. great toe nail in 10 and other foot areas in 6 cases, followed by palm and fingers in 8 (20.5%), scalp in 3 (7.7%) and other parts of the body in 12 (30.8%) cases. Most of the study subjects lived in a rural setting (n=22; 56%), working as farmers in close contact with the soil and domestic animals. Seventeen (44%) subjects were from urban setting (n=9) or unknown place of residence (n=8). Underlying risk factors were present in 29 (74%) of 39 study subjects, some of them with multiple risk factors. Besides close contact with the soil, the most common predisposing factors were various dermatoses (atopic dermatitis, psoriasis, dysseborrhea, etc.), lower extremity circulatory insufficiency, trauma, microtrauma, and metabolic disorders. Although the clinical picture of onychomycosis caused by *S. brevicaulis* shows some specific features, timely sampling for mycology is crucial to verify the diagnosis and to identify the causative agent prior to the introduction of appropriate therapy for dermatomycosis.

KEY WORDS: *Scopulariopsis brevicaulis*, onychomycosis, dermatomycosis

INTRODUCTION

The genus Scopulariopsis includes more than 30 species, of which *Scopulariopsis (S.) brevicaulis, S. candidum, S. acremonium, S. koningii, S. brumptii* and *S. fusca* are the most common causes of infection in humans (1-3). *S. brevicaulis* is widely spread in nature and is usually isolated

from the soil, especially at sites of cellulose breakdown. Although frequently considered as a contaminant, in humans it can cause infections of the skin and nail (onychomycoses), soft tissues, bone and lungs in immunocompromised (neutropenic) patients and in recipients of solid organ and bone marrow grafts (2).

MATERIAL AND METHODS

In this retrospective study, the prevalence of mold isolates from nail, skin and scalp scrapings was analyzed from January 1, 2002 till January 23, 2008. Samples for mycologic diagnosis (microscopy slide and culture) were collected at Department of Dermatology and Venereology, Dr. Josip Benčević General Hospital in Slavonski Brod, in cases suspected of fungal infection. The samples collected were in part processed for microscopy by use of 10%-20% potassium alkali (KOH) and after 30 min examined under X400 magnification with the condenser pulled down and tinted stop of the microscope. Keratin is dissolved by the alkali, thus facilitating detection of fungal forms (specific aneloconidia). The rest of scrapings and/or hairs from infected areas were seeded on the Mycobios selective agar (soy peptone, glucose, cycloheximide, chloramphenicol, agar) (Biolife Italiana s.r.l., Milan, Italy) and incubated at room temperature for 2-3 weeks. Scopulariopsis was suspected on the basis of characteristic appearance and morphology of the grown colonies, which were then referred to Department of Mycology, National Institute of Public Health in Zagreb for verification. There, the isolates were identified to the genus and/or species level according to macroscopic and microscopic characteristics and physiologic properties (4,5). Medical records of outpatients and medical history of inpatients served as the source of clinical data used in the analysis.

RESULTS

The prevalence of *S. brevicaulis* isolates in the samples collected for mycology and comparison with dermatophyte and other fungal isolates during the study period is shown in Table 1. In a total of 7161 samples, 1834 (25.6%) samples were positive for fungi. Out of 1834 mycologically positive samples, molds and other medically relevant fungi beyond the scope of the present study accounted for 962 (52.4%) isolates, whereas *S. brevicaulis*, *Epidermophyton floccosum*, *Trichophyton* spp. and *Microsporum* spp. accounted for 39 (2.2%), 7 (0.4%), 342 (18.6%) and 484 (26.4%) isolates.

Thirty nine subjects (22 female and 17 male), mean age (±SD) 43.9±20.7 (range 8-87) years, were analyzed during the study period. Suspicion of *S. brevicaulis* was based on the growth of characteristic colonies of specific cinnamon-brown, earthen color. Subculture of the *S. brevicaulis* strain isolated from foot scrapings of the patient M.M. on Mycobios selective agar (Biolife) after 3-week incubation at room temperature is shown in Fig. 1.

The anatomic areas sampled for mycology that resulted in the growth of *S. brevicaulis* are presented in Fig. 2. The most common localization was great toe nail (n=10), followed by foot (n=5)

Table 1. Rate of *Scopulariopsis brevicaulis* isolates *versus* dermatophytes and other fungi during study period (January 1, 2002 – January 23, 2008)

Year	All samples tested for fungi	Samples positive for fungi	*Scopulariopsis brevicaulis*		Dermatophytes						Other fungi	
					Epidermophyton		*Trichophyton*		*Microsporum*			
	N	N=100%	n	%	n	%	n	%	n	%	n	%
2002	1239	383	6	1.6	0	0	50	13.1	135	35.2	192	50.1
2003	1184	284	6	2.1	2	0.7	50	17.6	86	30.3	140	49.3
2004	1245	265	13	4.9	0	0	53	20.0	66	24.9	133	50.2
2005	1184	328	5	1.5	0	0	71	21.7	91	27.7	161	49.1
2006	1067	282	2	0.7	5	1.8	55	19.5	54	19.1	166	58.9
2007	1149	272	5	1.8	0	0	55	20.2	44	16.2	168	61.8
2008*	93	20	2	10.0	0	0	8	40.0	8	40.0	2	10.0
Total	7161	1834	39	2.2	7	0.4	342	18.6	484	26.4	962	52.4

*January 1, 2008 – January 23, 2008

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Figure 1. *Scopulariopsis brevicaulis* on nutrient Mycobios selective agar.

and toes (n=1), i.e. 16 (41%) samples in total; the extremities and trunk accounted for 12 (30.8%), hand for 8 (20.5%) and scalp for 3 (7.7%) positive samples.

Results of sample analysis by use of direct KOH microscopy showed the majority of samples to be microscopically negative (n=28; 71.8%), 6 (15.4%) samples were suspect of *S. brevicaulis*, 4 (10.2%) were positive, and one (2.6%) sample was found to be inadequate for microscopy. Microscopic examination is always considered preliminary, and in case of skin, hair and nail samples it also depends on patient immunocompetence, duration of therapy and sample localization. Three of the four microscopically positive samples were obtained from great toe nail, a typical site of *S. brevicaulis* infection. Patients with positive microscopy finding had onychomycoses and more severe clinical picture, and had been treated with antimycotic polytherapy for a longer period of time.

According to the place of residence, 22 (56%) subjects were from rural setting and nine (23%) from urban setting, whereas reliable data were lacking for eight (21%) subjects. Data on the risk factors and associated factors for the development of mycosis in study subjects were obtained from medical records of subjects examined as outpatients and from medical history of inpatients. A total of 51 risk factors were recorded, indicating that some of 39 patients were exposed to multiple risk factors. Dermatoses were the most common predisposing factor found in 24/51 (47.1%) cases, whereas psoriasis, contact dermatitis and other types of dermatitis were less common. Metabolic and other chronic diseases were present in 15 (29.4%) and cardiovascular factors including lower extremity circulatory insufficiency in 12 (23.5%) cases.

DISCUSSION

In the last decade, an increasing rate of characteristic brown colonies of powder-velvet appearance, identified as the mold *S. brevicaulis* from the family Moniliaceae, has been recorded at Laboratory of Mycology, Department of Microbiology, Dr. Josip Benčević General Hospital in Slavonski Brod. During the study period, *S. brevicaulis* was isolated from 39 (2.2%) of 1834 samples positive for fungi (Table 1). *S. brevicaulis* belongs to the fungi that cause dermatomycoses, mostly onychomycoses, and has recently been demonstrated to act as a pathogen in disseminated skin lesions in acquired immunodeficiency syndrome (AIDS) patients and in other immunocompromising conditions (3,6-9). Scopulariopsis often causes proximal onychomycosis and may cause deep superficial

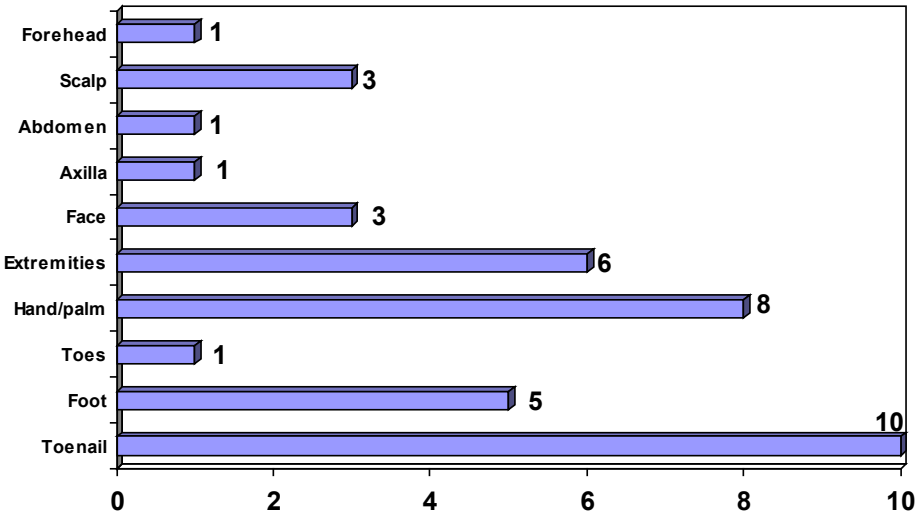

Figure 2. Localization of *Scopulariopsis* positive samples.

onychomycosis (10-13). Mycotically altered, yellow-striated toe nail without interdigital mycosis is indicative of Scopulariopsis causation; the lesion generally occurs post-traumatically in young male subjects with trophic disorders (11). We had only two young patients with trauma of the great toe and foot, along with microtraumas. Lower extremity circulatory deficiency, hypertension and other cardiovascular disorders were more common than trauma.

Scopulariopsis was also isolated in six children aged 8-16 from rural setting, which is consistent with literature data (10,14). Most of our study subjects (n=22; 56%) were from rural setting, thus being frequently in contact with the soil and animals. Besides close contact with the soil, other predisposing factors for onychomycosis reported in the literature are familial dermatoses, trauma, diabetes mellitus and peripheral circulatory insufficiency (15). In our study, underlying risk factors were present in 29 (74%) of 39 subjects. A total of 51 risk factors were identified because some patients were exposed to multiple risk factors. The leading risk factor was atopic dermatitis, found in nine (18%) patients, followed by lower extremity circulatory insufficiency in five (10%), psoriasis in four (8%), and frequent infections and chronic diseases in three (6%) patients. Other risk factors including diabetes mellitus, carcinoma, etc. were only identified in individual cases.

Our study population showed a female predominance (F 22 *vs*. M 17). Six of ten subjects with onychomycosis were women. Study subjects from rural setting were predominantly women (F 13 *vs*. M 9). However, these data could not be considered conclusive due to the small sample size. The average age of our study subjects was 44 years, which is consistent with literature reports. In the present study, foot and great toe nail were confirmed as the most common sites of *S. brevicaulis* detection (n=16; 41%) (Fig. 3).

Demonstration of the association of onychomycosis and Scopulariopsis also depends on the diagnostic procedures used (3,12,13,15). Molecular identification is superior to and more sensitive than culture (84% *vs*. 22%). In addition, the time of causative agent identification has been reduced to 48 h as compared with 2-4 weeks required for the classic method of cultivation (16). The relatively late development of characteristic brown-powder configuration of *S. brevicaulis* colonies poses a diagnostic problem. Clinically, colonization that precedes *S. brevicaulis* infection, only later followed by onycholysis and total nail plate dystrophy, may be difficult to recognize (17,18). Therefore, the earliest possible sampling is of paramount importance (in children in particular) to make the diagnosis, identify the causative agent and initiate appropriate therapy on time. Thus, nail dystrophy and dissemination of infection with the respective pathogen can be prevented (7,9,14,18). In the present study, *S. brevicaulis* was isolated from foot sample in only one of our young patients (and from the face, scalp or hand samples in the others). The patient has been followed up by a dermatologist and treated with topical clotrimazole and planned to continue with terbinafine. While onychomycosis caused by *S. brevicaulis* has been efficiently treated in some countries (17), numerous studies of *in vitro* activity of antifungal agents and their combinations against clinical isolates of *S. brevicaulis* have confirmed it to be a multiresistant pathogen (6,9,20-24). According to clinical records, our study subjects were prescribed long-term antimycotic monotherapy or a combination of several antimycotics. The treatment of fungal infections included topical therapy and/or systemic antimycotics, depending on the lesion localization, number of foci, type of infection and patient age. The efficacy of therapy prescribed could not be reliably assessed because of deficient follow up of subjects generally treated at outpatients (n=34; 87%). Miconazole, clotrimazole and terbinafine were most frequently used as topical agents, while amorolfine hydrochloride, econazole and ketoconazole were less frequently prescribed.

Along with topical therapy, systemic therapy with terbinafine, itraconazole pulse therapy, and rarely fluconazole are mostly administered for onychomycosis. Our patients with onychomycosis had used two or more antimycotics over long periods of time (for years) and were exposed to numerous risk factors. Their microscopic samples were positive for *S. brevicaulis*. In two patients, the introduction of terbinafine after treatment with miconazole and clotrimazole resulted in improvement of the toe nail and foot clinical picture. In one patient with onychomycosis, therapy with itraconazole following miconazole and fluconazole led to improvement after months of treatment. Another patient with the same clinical picture and on long term therapy with miconazole, then with fluconazole and three pulses of itraconazole failed to improve, while also complaining of abdominal pain. A female patient with bilateral onychomycosis was first treated with fluconazole, which only resulted in a discrete nail shift to the right. Then she was administered oral terbinafine, followed by

itraconazole pulse therapy. Her right nail recovered within a year, whereas the left nail improved slowly. Currently, the patient has been treated with amorolfine hydrochloride (nail polish).

Successful pathogen eradication and optimal therapy for *Scopulariopsis* induced infections, extraungual infections in particular, remain unknown (3,8,9).

CONCLUSION

Our study confirmed the presence of the opportunistic fungus *S. brevicaulis* in the area, especially in onychomycosis patients and those with multiple risk factors for the development of dermatomycosis. As these are refractory infections with the potential for disseminated infections caused by this universal pathogen, the earliest possible mycologic diagnosis made at a laboratory of microbiology is necessary. Large clinical trials using the methods of molecular diagnosis and determination of the pathogen sensitivity to antifungal agents are needed to reduce the time of diagnostic work-up and to introduce appropriate therapy on time.

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Innoxa - put your skin in “milky” condition; year 1930.
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