CASE REPORT

Onychomycosis Caused by *Scopulariopsis brevicaulis*: Report of Two Cases

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Onychomycosis is usually caused by dermatophytes, but some nondermatophytic molds and yeasts are also associated with invasion of nails. *Scopulariopsis brevicaulis* is a nondermatophytic mold found in soil as a saprophyte. We report two cases of onychomycosis caused by *S. brevicaulis* in a 48-year-old male and a 79-year-old female. The two patients presented with a typical distal and lateral subungual onychomycosis. Direct microscopic examination of the potassium hydroxide preparation revealed fungal elements. From toenail lesions of the patients, brown colonies with powdery surface, which are a characteristic of *S. brevicaulis*, were cultured on two Sabouraud's dextrose agar plates. Three cultures taken from nail plates within a 2-week interval yielded similar findings. Numerous branched conidiophores with chains of rough walled, lemon-shaped conidia were observed in slide culture by light microscopy and scanning electron microscopy. The nucleotide sequences of the internal transcribed spacer for the two clinical isolates were identical to that of *S. brevicaulis* strain WM 04.498. To date, a total of 13 cases of *S. brevicaulis* onychomycosis including the two present cases have been reported in Korea. Mean age of the patients was 46.1 years, with a higher prevalence in males (69.2%). Toenail involvement was observed in all cases including a case involving both fingernail and toenail. The most frequent clinical presentation was distal and lateral subungual onychomycosis in 12 cases, while one case was proximal subungual onychomycosis. **(Ann Dermatol 24(2) 209～213, 2012)**

-Keywords-
Onychomycosis, *Scopulariopsis brevicaulis*

INTRODUCTION

Onychomycosis is mainly caused by dermatophytes, but is occasionally caused by nondermatophytic fungi including *Scopulariopsis brevicaulis*, *Aspergillus* spp., *Fusarium* spp. and *Acremonium* spp., which have been often considered as saprophytic or opportunistic fungi[1]. Since several cases of nondermatophytic onychomycosis have been reported, even in healthy subjects, recent increase in diseases with immune suppressed individuals as well as prominent environmental changes have brought these non-dermatophytic fungi into focus[2,3]. *S. brevicaulis* represents 1～10% of the non-dermatophytic onychomycoses[3-5]. Eleven cases of *S. brevicaulis* onychomycosis had been reported in Korea[6,7].

Here, we report two additional cases of distal and lateral subungual onychomycosis (DLSO) diagnosed by clinical features, mycological culture, microscopic observations and molecular analysis, with a review of the literature on *S. brevicaulis* onychomycosis.

CASE REPORT

A 48-year-old male presented with a 1-year history of brownish-yellow discoloration with hyperkeratosis on the toenails. There was no history of other symptoms except

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for toenail dystrophy. Dermatological examination revealed the DLSO on the right toenails (1st, 2nd, 4th and 5th) and left toenails (1st and 5th) (Fig. 1). A 79-year-old female presented with yellow discoloration with hyperkeratosis on the right and left toenails during hospitalization due to herpes zoster. This patient had experienced progressive thickening and discoloration of distal and lateral nailplate (1st and 5th toenails of both feet) for 3 years without other symptoms.

Complete blood count, peripheral blood smear, urinalysis, liver and renal function tests and stool examination were within normal limits for both patients. Venereal disease research laboratory test and serological tests for hepatitis virus and human immunodeficiency virus were also negative. Chest x-ray and electrocardiogram were unremarkable. In mycological examination, fungal elements were observed in potassium hydroxide (KOH) preparations from the toenail lesions of both patients. Nail specimens were cultured on two slants of Sabouraud's dextrose agar (SDA) without cycloheximide at 25°C for 2 weeks, which yielded several identical appearing colonies. But, there was no colony growth on slants of SDA containing cycloheximide. The moderately fast-growing colonies were initially white then turned buffy and powdery at their centers (Fig. 2). The back of each culture revealed a brownish tan center. We performed repeated (three) cultures taken from nail plates at 2-week intervals; all yielded similar findings. When the slide cultures of fungal colonies were stained with lactophenol cotton blue, numerous branched conidiophores with chains of conidia were observed by light microscopy (Fig. 3A). Structural features of rough-walled lemon-shaped conidia were observed in detail by scanning electron microscopy (Fig. 3B, C). The sequence analysis of internal transcribed spacer (ITS) 1 indicated that the two isolates were identical to *S. brevicaulis* strain WM 04.498 (GenBank accession number: AJ85377) (Fig. 4). From the light and scanning electron microscopy observation of the fungal culture in addition to the comparison of ITS 1 region, the isolates causing DLSO in two patients were identified as *S.*

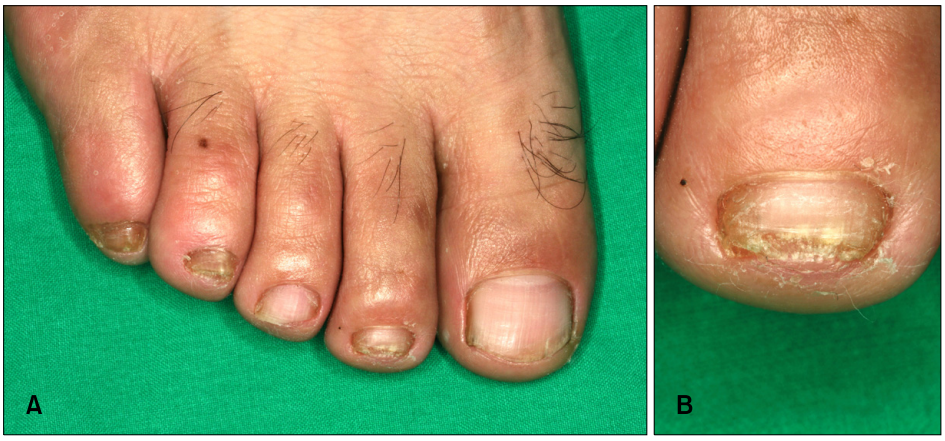

Fig. 1. (A) Brownish-yellow discoloration with hyperkeratosis on the toenails. (B) Close-up view of the right 2nd toenail.

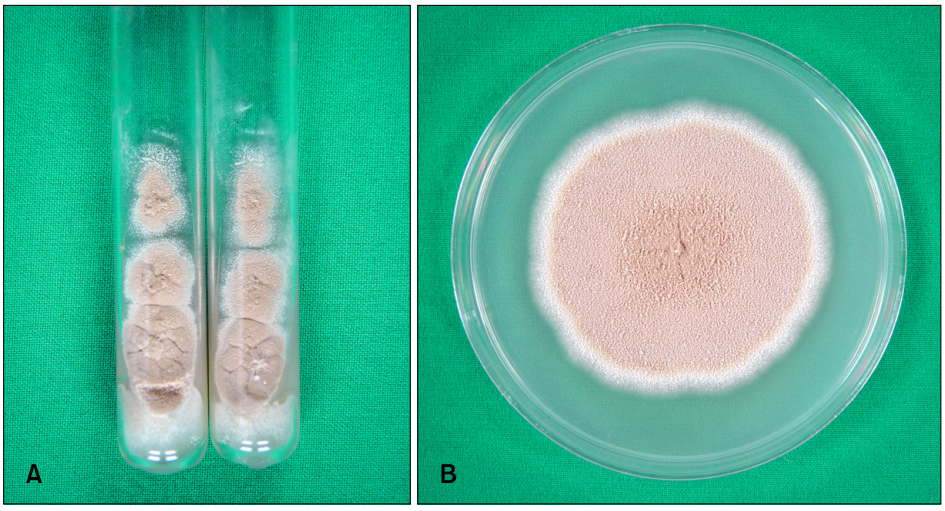

Fig. 2. Brown colonies with powdery surface after incubation at 25°C for 2 weeks. (A) Sabouraud's dextrose agar slant. (B) Sabouraud's dextrose agar plate.

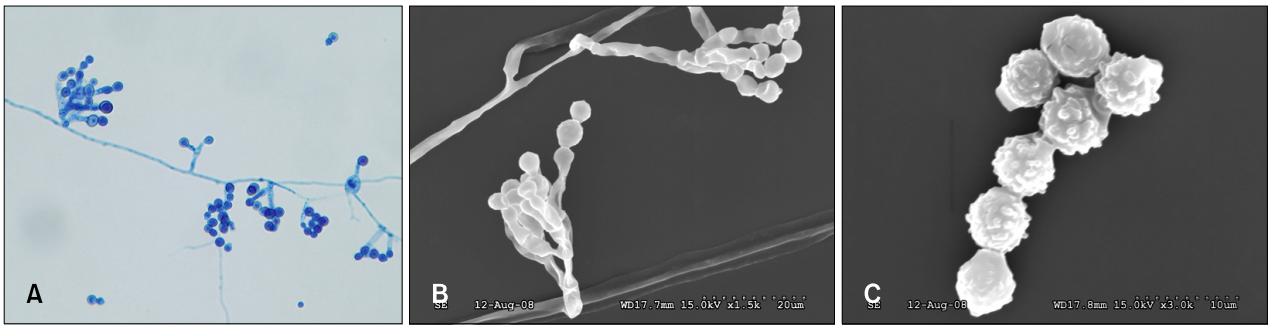

Fig. 3. (A) Slide culture of *Scopulariopsis brevicaulis* showing numerous branched conidiophores with chains of lemon-shaped conidia (Lactophenol-cotton blue stain, ×400). (B) Numerous branched conidiophores with chains of lemon-shaped conidia (scanning electron microscop [SEM], ×1,500). (C) Lemon-shaped conidia with a rough walled feature (SEM, ×3,000).

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S. brevicaulis_WM_04.498_AJ85377 GATCATTACCGAAGTTACTCTTCAAAACCCATTGTGAACCTTACCTCTTGCCGCGCGTTGCCTCGGCGGGGAGGCGGGGT [ 80]
080911-R2_K01_Oh-ITS1.ab1_951_.. ----------------.................................................... [ 80]
080812-19_K02_Kwon-ITS4.ab1_929_ .................................................................... [ 80]

S. brevicaulis_WM_04.498_AJ85377 CTGGGTCGGCGCGCCCCTCACCGGGCCGCCGTCCCCGTCCCCGTCCCCGCCGGCCGCGCCAAACTCTAAATTTGAAAAAG [160]
080911-R2_K01_Oh-ITS1.ab1_951_.. .................................................................... [160]
080812-19_K02_Kwon-ITS4.ab1_929_ .................................................................... [160]

S. brevicaulis_WM_04.498_AJ85377 CGTACTGCACGTTCTGATTCAAAACAAAAAACAAGTCAAAACTTTTAACAACGGATCTCTTGGTTCTGGCATCGATGAAG [240]
080911-R2_K01_Oh-ITS1.ab1_951_.. .................................................................... [240]
080812-19_K02_Kwon-ITS4.ab1_929_ .................................................................... [240]

S. brevicaulis_WM_04.498_AJ85377 AACGCAGCGAAATGCGATAAGTAATGTGAATTGCAGAATTCAGTGAATCATCGAATCTTTGAACGCACATTGCGCCCGGC [320]
080911-R2_K01_Oh-ITS1.ab1_951_.. .................................................................... [320]
080812-19_K02_Kwon-ITS4.ab1_929_ .................................................................... [320]

S. brevicaulis_WM_04.498_AJ85377 AGCAATCTGCCGGGCATGCCTGTCCGAGCGTCATTTCTTCCCTCGAGCGCGGCTAGCCCTACGGGGCCTGCCGTCGCCCG [400]
080911-R2_K01_Oh-ITS1.ab1_951_.. .................................................................... [400]
080812-19_K02_Kwon-ITS4.ab1_929_ .................................................................... [400]

S. brevicaulis_WM_04.498_AJ85377 GTGTTGGGGCTCTACGGGTGGGGCTCGTCCCCCCCGCAGTCCCCGAAATGTAGTGGCGGTCCAGCCGCGGCGCCCCCTGC [480]
080911-R2_K01_Oh-ITS1.ab1_951_.. .................................................................... [480]
080812-19_K02_Kwon-ITS4.ab1_929_ .................................................................... [480]

S. brevicaulis_WM_04.498_AJ85377 GTAGTAGATCCTACATCTCGCATCGGGTCCCGGCGAAGGCCAGCCGTCGAACCTTTTATTTCATGGTTTGACCTCGGATC [560]
080911-R2_K01_Oh-ITS1.ab1_951_.. .................................................................... [560]
080812-19_K02_Kwon-ITS4.ab1_929_ .................................................................... [560]

S. brevicaulis_WM_04.498_AJ85377 AGGTAGGGTTACCCGCTGAACTTAA-- [587]
080911-R2_K01_Oh-ITS1.ab1_951_.. .........................GC [587]
080812-19_K02_Kwon-ITS4.ab1_929_ .......---------------------- [587]
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Fig. 4. (Alignment of internal transcribed spacer 1 (ITS1) sequences of the *Scopulariopsis brevicaulis* isolates and *Scopulariopsis brevicaulis* strain WM 04.498 (GenBank accession number: AJ85377). The ITS1 sequences of clinical isolates exhibit a perfect match to that of the reference WM 04.498.

brevicaulis.

The male patient was successfully treated by 3 months administration of oral terbinafine (250 mg daily) and topical 5% amorolfine nail lacquer. At the follow-up, 9 months after the cessation of treatment, clinical and mycological recovery was confirmed. The female patient received oral terbinafine (250 mg daily) and topical 5% amorolfine nail lacquer for 4 weeks. However, this patient did not return for a therapeutic evaluation.

DISCUSSION

Onychomycoses comprising 50% of all onychopathies are caused mainly by dermatophytes and less frequently by non-dermatophytic molds and yeasts[1]. Non-dermatophytes such as *Scopulariopsis* spp., *Aspergillus* spp., *Fusarium* spp., and *Acremonium* spp. are responsible for 1.45～17.6% of fungal nail infections[3-5]. Among the genus *Scopulariopsis*, which are saprophytes found in soil

Table 1. Clinical features of *Scopulariopsis brevicaulis* onychomycosis cases in Korea

Patient number	Age/Sex	Duration	Site	Clinical type	Associated disease	Reference
1	25/M	-	Toenail	DLSO	-	6
2	65/M	-	Fingernail and toenail	DLSO	-	6
3	58/F	-	Toenail	DLSO	-	6
4	20/M	-	Toenail	DLSO	-	6
5	43/F	-	Toenail	DLSO	-	6
6	29/M	-	Toenail	DLSO	-	6
7	43/F	-	Toenail	DLSO	-	6
8	46/M	3 mo	Both great toenails	PSO	Cerebral infarction	7
9	37/M	3 yr	Rt. 1st, 2nd, 4th, 5th & Lt. 4th, 5th toenails	DLSO	None	7
10	42/M	2 yr	Rt. 1st & Lt. 4th, 5th toenails	DLSO	Cerebral contusion	7
11	64/M	2 yr	Rt. 1st, 2nd, 3rd, 5th & Lt. 1st, 2nd, 5th toenails	DLSO	Cerebral hematoma	7
12	48/M	1 yr	Rt. 1st, 2nd, 4th, 5th & Lt. 1st, 5th toenails	DLSO	None	Present case
13	79/F	3 yr	Rt. 1st, 5th & Lt. 1st, 5th toenails	DLSO	None	Present case

M: male, F: female, DLSO: distal and lateral subungual onychomycosis, PSO: proximal subungual onychomycosis, Rt.: right, Lt.: left.

worldwide, *S. brevicaulis*, *S. brumptii*, *S. acremonium*, *S. fusca*, and *S. koningii* are frequently related to human infections[4,8]. Most human infection caused by *S. brevicaulis* is onychomycosis, although there are several reports of other infections including skin infection, endocarditis, and endophthalmitis in patients with impaired immunity, trauma or surgery[2,9,10]. *S. brevicaulis* onychomycosis represents 1～10% of the nondermatophytic onychomycosis cases depending on the population, geographic regions, and the reporters[3-5]. These variations arise due to geographic differences in mold distribution, differences in the criteria used for the diagnosis of onychomycosis, and the use of different methods for fungal culture[3]. In Korea, its prevalence is lower, with reported rates of 1.41%[6] and 1.23%[11]. *S. brevicaulis* onychomycosis is usually found in adults, commonly affecting toenails, because *S. brevicaulis* is a saprophytic mold found in soil[12]. As listed in Table 1, all 13 cases reported in Korea including the two present cases, were adults (mean age, 46.1 years) with higher prevalence in males (nine cases) than in females (four cases). All cases involved toenails, and, in one elderly male, involved both fingernails and toenails[6,7].

Predisposing factors for nondermatophytic onychomycosis include footwear, hyperhidrosis, local trauma, family history, psoriasis, peripheral vascular disease, and immune suppression[5]. Among six patients whose history of other ailments was questioned, three cases presented with no underlying diseases, while the other three cases were associated with cerebral infarction, contusion, and hematoma (Table 1). However, the fact that one of two cases involving a 79-year-old female with onychomycosis for 3 years was hospitalized due to herpes zoster suggests that the patient might not have sustained an immunocompetent status.

Onychomycosis is classified into five clinical types: DLSO, proximal subungual onychomycosis (PSO), superficial white onychomycosis, endonyx onychomycosis, and dystrophic onychomycosis[13]. The most common type is DLSO, while PSO is relatively rare[1]. However, Tosti et al.[3] observed 10 cases of PSO and seven cases of DLSO among 17 cases of *S. brevicaulis* onychomycosis. In Korea, DLSO has been the most common, with 12 cases, while one case involved PSO (Table 1)[6,7].

Generally, dermatophytic infections are diagnosed by isolating the dermatophytes from the loci of infection, whereas the isolation of saprophytic *S. brevicaulis* may not necessarily indicate an infection[14]. Therefore, isolation of saprophytic molds and yeasts additionally requires microscopic observation of fungal elements such as hyphae and/or conidia from the lesions. To confirm the diagnosis, isolation and identification of the same species from repetitive cultures can be definitive[15]. In this report of two cases, fungal elements were found by microscopy, and the same fungal species were isolated from the repetitive cultures of toenail specimens. It may not be possible to distinguish the causative agents between *S. brevicaulis* and dermatophytes, which exhibit fragile nails with yellowish brown discoloration. Therefore, KOH examination and culture isolation are necessary for distinction. Thick-walled large conidiophores (4～9 μm) with chains of rough-walled, lemon-shaped conidia may

be confirmed for the presumptive identification. When cultured, the fast-growing colonies are initially white then turn to buff and are powdery at the center. The back of the culture reveals a brownish tan center. When the slide cultures of fungal colonies were presently stained with lactophenol cotton blue, characteristic lemon-shaped conidia with small protrusions were observed in both cases by scanning electron microscopy (Fig. 3); similar observations have been noted[8,10]. Recently, sequencing analysis of the ITS 1 region of ribosomal RNA genes has been considered for the identification of the causative fungus of onychomycosis[16]. The ITS sequences were presently determined from the two isolates and then turned out to be identical to that of *S. brevicaulis* strain WM 04.498 (GenBank accession number AJ85377).

Treatment of onychomycosis has been difficult despite the development of new antifungals. The aims are, of course, the clinical and mycological cure of nails, but more than 25% of all patients reveal an incomplete or no response[17]. In particular, *S. brevicaulis* is difficult to eradicate from onychomycosis and deeper infections[11,18]. Nolting et al.[19] reported that three cases out of six were cured by oral terbinafine (250 mg/day for 48 weeks). Tosti et al.[18] in 1996 treated a case by intermittent itraconazole (400 mg/day for a week each month) for 4 months, but Tosti et al.[3] in 2000 observed a 69.2% cure rate by chemical removal of nails with either topical terbinafine or 8% ciclopirox nail lacquer. De Doncker et al.[20] reported that eight cases out of 10 were clinically and mycologically cured by intermittent administration of itraconazole. In Korea, the cure rates have been quite low: one case out of seven by intermittent itraconazole therapy[6] and none of four cases due to incomplete therapy[7]. In this report of two cases, a male was successfully treated with oral terbinafine (250 mg daily) and topical 5% amorolfine nail lacquer for 3 months, while a female was administered with the same medication for only 4 weeks because she failed to revisit for therapeutic evaluation.

Identification of the causative agent is indispensible to select a proper treatment for onychomycosis, as untreated nondermatophytic molds including *S. brevicaulis* may develop into deeper or disseminated mycosis.

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