Mycoscience (2010) 51:224–233
DOI 10.1007/s10267-009-0030-2

FULL PAPER

Tiny keratotic brown lesions on the interdigital web between the toes of a healthy man caused by *Curvularia* species infection and a review of cutaneous *Curvularia* infections

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Received: 14 July 2009 / Accepted: 21 December 2009 / Published online: 5 February 2010

Abstract A 74-year-old healthy Japanese man had noticed an itchy lesion with two tiny thick brown scales on the fourth interdigital web of his right foot 3 months earlier. The brown fungus isolated from the scales had demonstrated brown, ellipsoidal, obovoid or clavate, 3-septate conidia. Morphologically, the fungus was identified as *Curvularia* sp., and was differentiated from other human pathogenic species of the genus, such as *C. lunata*, *C. pallescens*, *C. trifolii*, *C. clavata*, and *C. brachyspora*, by molecular analysis based on the DNA sequence data. The fungus grows well on keratotic materials (hairs, nails, and callus), which indicates that it might have the ability to infect the skin surface.

Keywords Phaeohyphomycosis · SEM · Skin infection

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Introduction

Curvularia is an ecologically and economically important genus and is known as an anamorph of *Cochliobolus* Drechs., Pleosporales (class Dothideomycetes, Ascomycota). The approximately 54 species included in the genus are usually known as subtropical and tropical facultative parasites on herbaceous plants (Ellis 1966; Sivanesen 1987) but are extremely rare as an invasive organism in man (Still et al. 1993; de Hong et al. 2000). Skin infections by *Curvularia* species have rarely been reported in either immunocompetent or immunosuppressed patients. Five species are known to cause human skin infections: *C. lunata* (Wakker) Boedijn (Mahgoub 1973), *C. trifolii* (Kauffm.) Boedijn (Kiryu and Suenaga 1985), *C. clavata* Jain (Gugnani et al. 1990), *C. pallescens* Boedijn (Agrawal and Singh 1995; Berg et al. 1995), and *C. brachyspora* Boedijn (Torda and Jones 1997). We present a patient, a healthy elderly man, with itchy brown keratotic lesions caused by *Curvularia* sp. on the fourth interdigital web between the toes. Cultural and morphological characteristics as well as DNA sequence data showed that the causative pathogen was differentiated from the hitherto reported agents of *Curvularia*.

Materials and methods

Case report

A 74-year-old healthy Japanese man consulted our clinic with a 3-month history of an itchy lesion on the fourth interdigital web of the right foot. He lived in the country with his wife, who had not had any similar eruptions. Physical examination demonstrated a red macular lesion with two tiny thick brown scales on the fourth interdigital

web of his right foot (Fig. 1). The scales could not be easily scraped from the skin. The thick brown scales were examined by light microscopy in 10% potassium hydrate solution. Many brown branched geniculate hyphae were demonstrated on the scales (Fig. 2).

Laboratory findings, including blood counts, liver function test, and C-reactive protein (CRP), were all within or almost within the normal ranges. Mantoux reaction was strongly positive. There were no signs of tuberculosis, tumors, or abscesses on computed tomograms of the whole body.

This patient was diagnosed as having phaeohyphomycosis based on the data from the KOH examination and was treated with 1% terbinafine hydrochloride cream. After treatment for 6 weeks, KOH examinations and cultures were negative, but a red macular lesion with fine scales remained at the lesion site. After treatment for 11 weeks, erythema was also seen at the lesion site, so we changed the agent to 1% lanoconazole cream. After 6 weeks treatment with this agent, the skin lesion disappeared.

Cultural and microscopic studies

Scrapings from the tiny thick brown scales on the interdigital web were inoculated onto a slant of Sabouraud dextrose agar (SDA) and incubated at 25°C. After treatment of the lesion with terbinafin cream for 3 weeks, scrapings were obtained again. The isolated brown fungus (KMU 4944) was cultured again on a plate of SDA and potato dextrose agar (PDA) at 25°C. To clarify its invasive ability into keratinized tissues, the isolate KMU 4944 was inoculated on the center of a plain agar, and then epidermal materials (nails and hairs from a healthy man, horny materials from calli on soles) were put around the specimen on the surface of the agar. The materials were treated with gaseous sterilization before examination.

Fig. 1 Red macular lesion with two tiny thick brown scales (*arrows*) on the fourth interdigital web of the right foot

For microscopic observations, mounts were made in lactophenol from PDA colonies and the slide culture on PDA. For scanning electron microscopy (SEM), the isolate cultured on plates on cornmeal agar (CMA) at 25°C was used; the isolated fungus formed conidia well on this substrate. The specimens were fixed with 2.5% glutaraldehyde and 1% osmic acid, processed through increasing concentrations of ethanol and isoamyl acetate, and then were dried in CO_2 as the transitional fluid-drying gas with a Hitachi critical point dryer (HCP-Auto). The specimens were coated with palladium/platinum with a Hitachi ion sputterer (E105) and examined with a JSM 840 at 15 kV. Furthermore, the specimens developing on the hairs were also examined under low acceleration voltage SEM (Keyence VE-8800) at 1.3 kV without fixation and with coating with gold.

Molecular and phylogenetic analysis

For confirmation of morphological identification, sequences of the internal transcribed spacer (ITS) region of the ribosomal RNA gene and 28S rRNA gene were analyzed for the isolate KMU 4944 (Table 1). The ITS region of the rRNA gene was amplified using the common primer set (ITS1 and ITS2) and procedure (White et al. 1990). The nucleotide sequence of the amplified fragment was determined using the same primers and ABI Prism BigDye Terminator Cycle Sequencing Ready Reaction Kits (http://www.appliedbiosystems.com). A partial sequence of the 28S rRNA gene including the D1–D2 domain was determined by the above-described procedure (White et al. 1990) using the primer set ITS4f (forward primer, 5′-gcat atcaataagcggagga-3′) and LSU2 (reverse primer, 5′-ggtcc

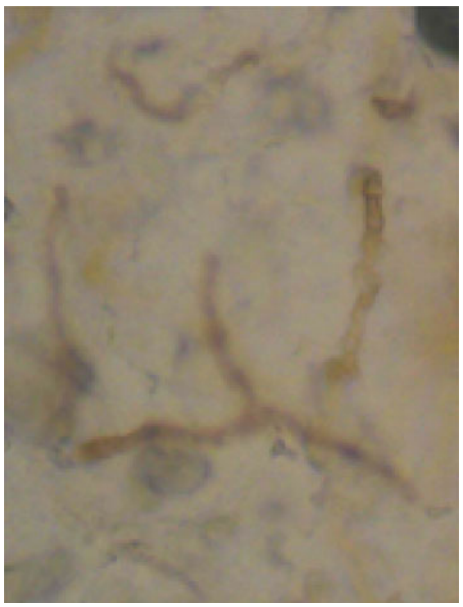

Fig. 2 Brown branched geniculate hyphae in 10% potassium hydrate solution

Table 1 Species and strains used in this study

Species	Species[a]	Strain no.	Origin	ITS sequence	D1–D2 sequence
Curvularia sp.		KMU 4944	Human skin	AB290141	AB290140
Curvularia affinis		KMU 6253	MAFF 425352	AB444656	AB444669
Curvularia akaii	(*Cochliobolus akaii*)	KMU 6003	NBRC 32561	AB288397	AB288214
Curvularia eragrostidis	(*Cochliobolus eragrostidis*)	KMU 6004	NBRC 32563	AB288398	AB288215
Curvularia geniculata	(*Cochliobolus geniculatus*)	KMU 6254	MAFF 235745	AB444657	AB444670
Curvularia geniculata	(*Cochliobolus geniculatus*)	KMU 6005	NBRC 6283	AB288399	AB288216
Curvularia inaequalis		KMU 6255	MAFF 235526	AB444658	AB444671
Curvularia intermedia	(*Cochliobolus intermedius*)	KMU 6256	MAFF 235531	AB444659	AB444672
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6006	ATCC 56691	AB288400	AB288217
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6007	NBRC 6286	AB288401	AB288218
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6008	ATCC 12017	AB288402	AB288219
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6009	NBRC 6382	AB288403	AB288220
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6010	NBRC 6586	AB288404	AB288221
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6011	NBRC 30883	AB288405	AB288222
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6012	NBRC 100164	AB288406	AB288223
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6013	NBRC 100173	AB288407	AB288224
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6285	Leaf (*Oryza sativa*)	AB444668	AB444681
Curvularia lunata	(*Cochliobolus lunatus*)	KMU 6257	MAFF 235532	AB444660	AB444673
Curvularia lunata var. *aeria*		KMU 6001	NBRC 100165	AB288395	AB288212
Curvularia lunata var. *aeria*		KMU 6002	NBRC 100182	AB288396	AB288213
Curvularia pallescens	(*Cochliobolus pallescens*)	KMU 6014	NBRC 100179	AB288408	AB288225
Curvularia pallescens	(*Cochliobolus pallescens*)	KMU 6015	NBRC 100180	AB288409	AB288226
Curvularia prasadii	(*Cochliobolus lunatus*)	KMU 6258	MAFF 305064	AB444661	AB444674
Curvularia prasadii	(*Cochliobolus lunatus*)	KMU 6259	MAFF 425081	AB444662	AB444675
Curvularia protuberata	(*Cochliobolus lunatus*)	KMU 6260	MAFF 425354	AB444663	AB444676
Curvularia senegalensis		KMU 6261	MAFF 235537	AB444664	AB444677
Curvularia trifolii		KMU 6262	MAFF 305097	AB444665	AB444678
Curvularia tuberculata	(*Cochliobolus lunatus*)	KMU 6263	MAFF 425355	AB444666	AB444679
Curvularia verruculosa	(*Cochliobolus verruculosus*)	KMU 6016	NBRC 100175	AB288410	AB288227
Curvularia verruculosa	(*Cochliobolus verruculosus*)	KMU 6264	MAFF 235540	AB444667	AB444680

[a] Species names in parentheses are the names in the GenBank data

gtgtttcaagacggg). The sequences of ITS and D1–D2 regions were used for molecular identification by the DNA similarity search on BLAST software (http://www.ddbj.nig.ac.jp/search/blast-j.html).

Phylogenetically, a maximum-parsimony tree was constructed based on the ITS sequences of KMU 4944, *C. lunata* isolates, and related fungi (see Table 1) with PAUP v. 4.0b10 (Swofford 2005).

Results

Morphological analysis

Colonies on both media rapidly reached 8 cm in diameter after 2 weeks. These colonies were irregular and floccose, light brown in color on SDA or dark brown on PDA (Fig. 3).

Light microscopic examination of slide culture preparations on PDA revealed hyphae that were pale brown, branched, and septate. Conidiophores were singly erected from the hyphae, straight or flexuous, light brown, smooth walled, and septate. Their upper portions were fertile and geniculate, producing single conidia through distinct pores (Fig. 4). Conidia were ellipsoidal, obovoid or clavate, mostly 3-septate, straight or curved, with the third cell from the base often curved and unequally enlarged, (20–)24–30(–36) μm long, and (10–)12–14(–16) μm thick in the broadest part. Apical and basal cells of the conidia were usually pale brown, and intermediate cells were brown or dark brown (Fig. 4). Hila of the conidia were scarcely or not at all protuberant (Fig. 4b, arrow).

Under scanning electron microscopy, conidia were whorled on the upper portion of the conidiophore (Fig. 5). The conidia were unequally ellipsoidal, and some were slightly curved. The surface of conidia was almost smooth. A shallow punctuation was present at the top surface of the apical cell. Pores were seen on the surface of the bending portion of the conidiophore (Fig. 6, arrows). Conidiogenesis as shown in Fig. 6 was a sympodial proliferation of the conidiogenous cell (upper portion of conidiophore), and a later stage of conidium development demonstrated that the basal portion of the conidium was attached by a hilum to the conidiogenous cell, indicating that it was the basal part of the conidial wall rather than the hilum that protruded. The surface of the basal cell and conidiogenous cell was minutely roughened. The hilum was also visible on the axial center of the conidium in Fig. 7. The tiny dome-shaped protuberances (about 0.2 μm in diameter) were scattered on the surface of the matured conidium (Fig. 7, white arrows).

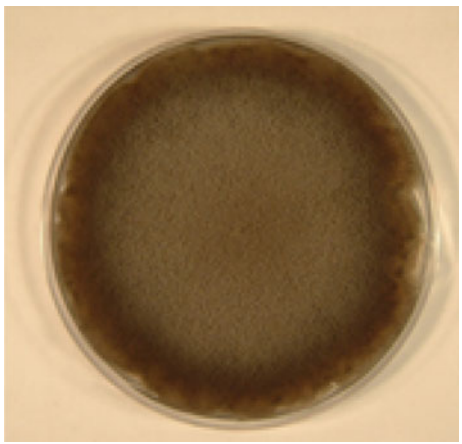

Fig. 3 Colony of *Curvularia* sp. KMU 4944 on potato dextrose agar (PDA) after 2 weeks at 25°C

On the basis of Ellis' key (Ellis 1966), the isolate KMU 4944 was identified as allied species of *C. lunata* var. *aeria* (Bat., J.A. Lima & C.T. Vasconc.) M.B. Ellis, a fungus that has morphologically similar conidia (straight or curved, ellipsoidal, obovoid or clavate, 3-septate, 18–32 × 8–16 μm, the third cell from the base enlarged and the intermediate cells darker than the end cells, with a scarcely protuberant hilum). However, the stromatic structure was never produced in the isolate culture, although large black and cylindrical stromata of *C. lunata* var. *aeria* are commonly produced in CMA and PDA cultures (Ellis 1966; Sivanesen 1987). The isolate superficially resembled *C. pallescens* with respect to the shape and size of the conidia, but the conidia of *C. pallescens* usually have all pale-colored cells.

Molecular analysis

The 532 base pairs of the ITS sequence and 541 base pairs of the 28S rRNA sequence were submitted to DDBJ; their accession numbers are AB290141 and AB290140, respectively. The result of the DNA BLAST search with the ITS sequence showed that the most closely related fungus was *C. lunata* [as *Cochliobolus lunatus* Nelson & Haasis (accession no. EF189917)], but there was only 95% similarity, while the result with the 28S rRNA sequence showed 100% similarity with three species: *Cochliobolus sativus* (Ito & Kurib.) Drechsler ex Dastur (DQ678045),

Fig. 4 Slide culture (**a**) of *Curvularia* sp. KMU 4944. Note hila of the conidia (**b**) were barely protuberant (*arrow*)

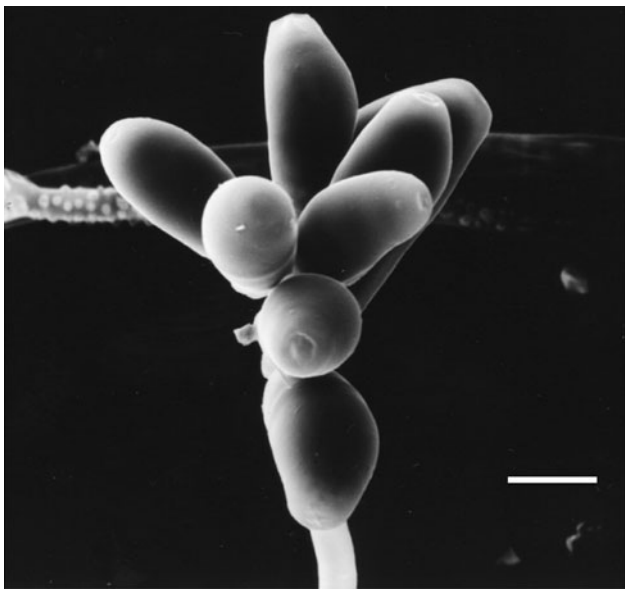

Fig. 5 Scanning electron microscopy (SEM) of fertile apex of conidiophore of *Curvularia* sp. KMU 4944. *Bar* 10 μm

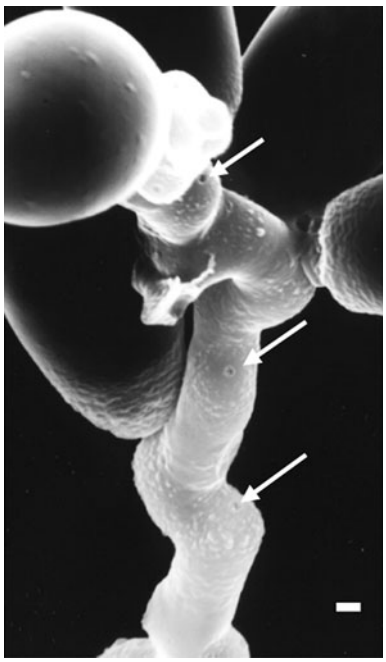

Fig. 6 SEM of conidium formation (*arrows*) of *Curvularia* sp. KMU 4944. *Bar* 1 μm

C. nodulosus Luttr. (AY849940), and *C. heterostrophus* (Drechsler) Drechsler (AY544645).

Phylogenetic analysis

A total of 30 sequences of the ITS region were used to construct a phylogenetic tree of the species of *Curvularia*. *Curvularia verruculosa* NBRC 100175 was used as an outgroup taxon. The data set consisted of 213 characters, of which 12 characters were variable and 35 characters were phylogenetically informative for parsimony analysis. A total of 12 equally parsimonious trees with 97 steps [consistency index (CI) = 0.680, retention index (RI) = 0.792, rescaled consistency (RC) = 0.539) were constructed by the maximum-parsimony (MP) analysis. One of the 12 trees is shown in Fig. 8. Most internal branches were supported in the strict consensus of the 12 trees. A maximum-parsimony tree (Fig. 8) revealed that the isolate clustered with *C. eragrostidis* (Henn.) J.A. Mey., separating the clade including *C. lunata* var. *lunata* and *C. lunata* var. *aeria*.

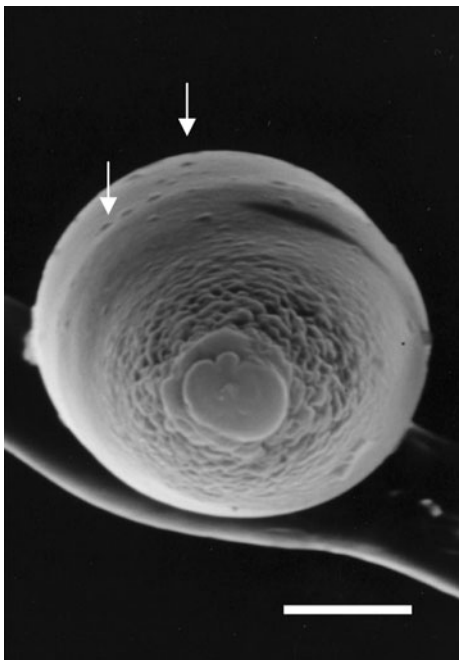

Fig. 7 SEM of conidium (*arrows*) of *Curvularia* sp. KMU 4944. *Bar* 1 μm

These results revealed that the isolate formed a strongly supported clade with species of *Cochliobolus*, but the three species were morphologically different in having *Bipolaris* anamorphs characterized by long slender distoseptate conidia.

Based on a combined ITS and glyceraldehyde-3-phosphate dehydrogenase gene sequences dataset, Berbee et al. (1999) showed that all the *Cochliobolus* species investigated resolved into two main polytomies: clade *Cochliobolus* groups 1 and 2. Group 1 included *Cochliobolus* and *Bipolaris* species that cause serious crop losses, such as *C. sativus*, *C. miyabeanus*, *C. carbonum* Nelson, and *C. heterostrophus*. Group 2 formed a morphologically diverse species of *Cochliobolus* associated with *Curvularia* and *Bipolaris* states. Within clade *Cochliobolus* 2, both *Bipolaris* and *Curvularia* anamorphs were intermingled,

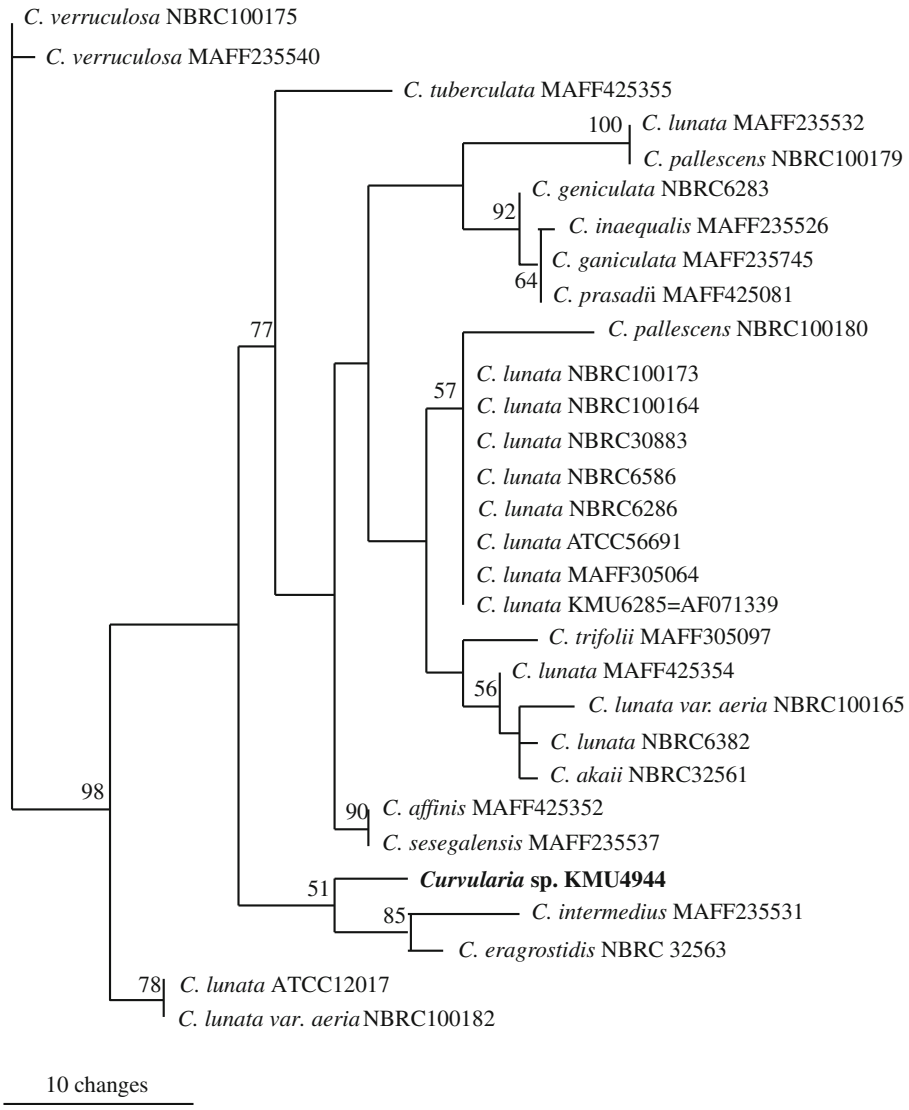

Fig. 8 Phylogenetic relationships of *Curvularia* (*C.*) species inferred from nucleotides sequences of ITS regions of the rRNA gene. A maximum-parsimony tree was constructed using PAUP* (Swofford 2005) with 100 bootstrap replications. Bootstrap values (>50) are shown at the *branches*. ITS regions varied in length from 562 to 619 bases, and gaps were not included in this phylogenetic analysis

but *C. lunata* (teleomorph, *Cochliobolus lunatus*) and all *Curvularia* species were in group 2.

The analyses generated from 28S rRNA indicated that the isolate rather shared phylogenetic affinities with members of the *Cochliobolus* group 1 and therefore the species identification of the isolate KMU 4944 cannot be ascertained.

Colonization on keratinized materials

The isolate KMU 4944 developed well from each material, with hyaline hyphae present on the conidia at the top. By SEM, hyphae with conidiophores at the top were observed to course along the surface of the hair shafts. Sometimes conidiophores arose from between the cells of the hair cuticle (Fig. 9a,b, white arrows).

Discussion

Curvularia species are most frequently encountered as a parasite or saprophyte of graminaceous plants but are infrequently human pathogens (Berg et al. 1995). Rinaldi et al. (1987) reviewed 24 cases of human infection by *Curvularia* in the literature between 1959 and 1985, including their own 5 cases. The sites of involvement included the lower respiratory system, bone, endocardium, skin and subcutaneous tissue, paranasal sinus, nasal septum, and cornea. The highest incidence of human infections involved the cornea and sinuses. Isolates from the lesions were *C. lunata* (20 cases), *C. geniculata* (2 cases), *C. pallescens* (1 case), and an unidentified *Curvularia* species (1 case). Yvonne et al. (1994) also reviewed 43 cases of *Curvularia* infection in the English-language

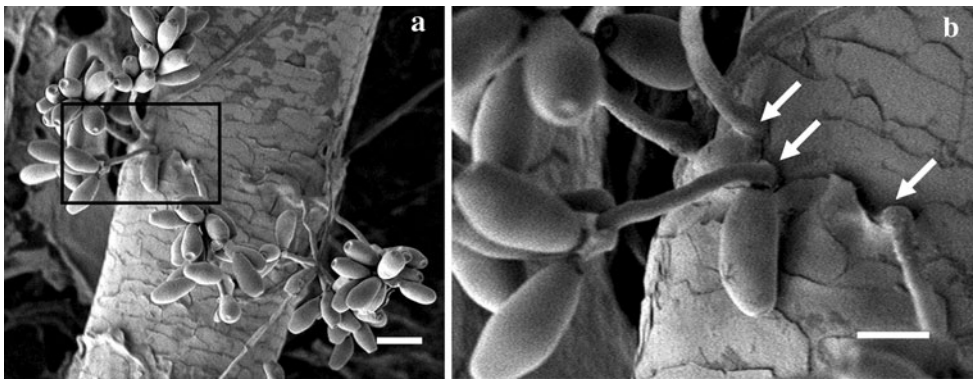

Fig. 9 SEM of growth of *Curvularia* sp. KMU 4944 on the hair shaft. Conidiophores arose from between the cells of the hair cuticle (*arrows*). *Bars* **a** 20 μm, **b** 10 μm

literature between 1959 and 1994, including their 1 case, and reported that *C. lunata* was the species that most commonly caused localized infection (~70%).

Mahgoub (1973) described the first report of cutaneous *Curvularia* infection, caused by *C. lunata*. Thereafter, 25 reports of human skin infection cases in the English and Japanese literature were published (Mahgoub 1973; Rohwedder et al. 1979; Barde and Singh 1983; Kiryu and Suenaga 1985; Duvic et al. 1987; Gugnani et al. 1990; Kamalam et al. 1992; Grieshop et al. 1993; Harris and Downham 1978; Lavoie et al. 1993; Still et al. 1993; Yvonne et al. 1994; Agrawal and Singh 1995; Berg et al. 1995; Torda and Jones 1997; Lopes and Jobim 1998; Fernandez et al. 1999; Bonduel et al. 2001; Tessari et al. 2003; Tamaki et al. 2006; Fan et al. 2008; Garg et al. 2008; Hiromoto et al. 2008), including our patient (Table 2). Five species in the genus *Curvularia* were isolated from the skin lesions. Close to half the cases (10 cases) were cases infected by *C. lunata*. Other cases were infected by *C. pallescens* (3 cases), *C. trifolii* (1 case), *C. brachyspora* (1 case), *C. clavata* (2 cases), and unidentified *Curvularia* species (8 cases).

Features of skin lesions caused by *Curvularia* infections are variable. Those lesions were divided into two groups: the deep mycosis type and the superficial infected type. In the deep mycosis type, 16 cases were reported: abscess (mycetomas) (Mahgoub 1973), ulcer (Rohwedder et al. 1979; Berg et al. 1995, Torda and Jones 1997; Hiromoto et al. 2008), ecthyma gangrenosum-like lesion (Bonduel et al. 2001), firm tender nodules and nodes (Tessari et al. 2003; Garg et al. 2008), papules (Kiryu and Suenaga 1985; Duvic et al. 1987), macular lesion with central necrosis (Fernandez et al. 1999), hemorrhagic bullous lesion (Lavoie et al. 1993), and others [burn wound (Grieshop et al. 1993; Still et al. 1993), elevated hyperpigmented scaly lesion (Harris and Downham 1978), and surgical wound (Yvonne et al. 1994)]. In the superficial infected type, 7 cases were reported: pigmented macules (Gugnani et al. 1990; Agrawal and Singh 1995), scaling lesion (Lopes and Jobim 1998), and brown thick scales (present case) on the web between the toes and onychomycosis (Barde and Singh 1983; Kamalam et al. 1992). Similar to our case, a 50-year-old Caucasian woman with a scaling lesion on the interdigital web between the toes caused by *C. lunata* was reported from Brazil (Lopes and Jobim 1998). In 24 cases of *Curvularia* infection, all patients had skin lesions involving the upper or lower extremities, except for 1 case of fungal sternal wound infection in a neonate with congenital heart disease. Six cases involved subjects who worked or played outdoors (Mahgoub 1973; Harris and Downham 1978; Rohwedder et al. 1979; Barde and Singh 1983; Agrawal and Singh 1995; Torda and Jones 1997; Garg et al. 2008; Hiromoto et al. 2008).

Eight (Harris and Downham 1978; Duvic et al. 1987; Grieshop et al. 1993; Still et al. 1993; Yvonne et al. 1994; Torda and Jones 1997; Tessari et al. 2003; Garg et al. 2008) of 16 cases of deep mycosis and 5 cases (Gugnani et al. 1990; Kamalam et al. 1992; Agrawal and Singh 1995), including our case, of 7 cases of superficial infection showed pigmented brown to black lesions; 2 cases showed seborrheic keratosis-like lesions (Duvic et al. 1987; Torda and Jones 1997). One patient (Torda and Jones 1997) first underwent cryotherapy for the pigmented lesion on the thigh, and the other patient (Duvic et al. 1987), with acquired immunodeficiency syndrome (AIDS), demonstrated tiny brown spotty lesions on the scrotum. Some papules resembled small follicular seborrheic keratosis. In 2 cases of mycetoma, black grains were discharged from the sinus (Mahgoub 1973; Garg et al. 2008).

Twelve cases were patients with immunosuppressive conditions such as patients receiving immunosuppressive therapy systemically (Barde and Singh 1983; Berg et al. 1995; Tessari et al. 2003) or locally (Kiryu and Suenaga 1985), patients (Grieshop et al. 1993; Still et al. 1993) with severe burn, a neonate (Yvonne et al. 1994), a premature baby (Fernandez et al. 1999), an overdosage cocaine user (Lavoie et al. 1993), a patient (Bonduel et al. 2001) with anaplastic anemia undergoing bone marrow transplantation (BMT), a homosexual (Duvic et al. 1987) with AIDS, and an immunocompetent man (Fan et al. 2008). Three cases

Table 2 Cutaneous *Curvularia* infections

Isolate	Clinical features	Site(s) of lesions	Occupation or condition of patient	Author
C. lunata	Mycetomas (right foot)	Leg	Farmer	Mahgoub
	Chronic leg ulcers	All nails of toes and fingers	Football player	Rohwedder
	Dystrophic nails	Left thumb	Cowboy with leprosy[a]	Barde
	Black discoloration of thumb nail	Right arm and chest	Elderly housewife	Kamalam
	Brown skin lesion with scales	Breast and right foot	Burn involving 65% of the total body	Grieshop
	Slightly black sternal wound	Surgical sternal wound	Neonate with congenital heart disease	Yvonne
	Scaling lesion	Fourth interdigital web of right foot	Housewife	Lopes
	Macular lesion with central necrosis	Chest, back and upper and lower extremities	Premature baby (24 weeks gestation)	Fernandez
	Deep brown firm tender nodules	Upper right arm	Heart transplant recipient	Tessari
	Gross swelling with multiple discharging sinuses	Right foot	Farmer	Garg
C. pallescens	Black irregularly margined lesion	Both feet and right thigh	Male farmer	Agrawal
	Black irregularly margined lesion	Left thumb	Male farmer	Agrawal
	Leg ulcer	Right leg	Elderly woman with rheumatoid arthritis[b]	Berg
C. trifolii	Hard military papules	Right forearm	Actinic reticuloid[c]	Kiryu
C. clavata	Dark irregular patch	Right side of waist and left thigh	Female student from Nigeria	Gugnani
	Unknown	Left foot	Immunocompetent man	Fan
C. brachyspora	Ulcers	Both thighs	Male who enjoyed gardening	Torda
Curvularia species	Elevated pigmented scaly lesion	Right leg	Football player	Harris
	Small round black lesions	Arms and legs	Burn involving 44% of the total body	Still
	Hemorrhagic bullous lesions	Arms and legs	Cocaine user	Lavoie
	Ecthyma gangrenosum-like lesion	Arms and limbs	Anaplastic anemia patient who underwent BMT	Bonduel
	Tiny, flat, rough papules	Scrotum	Homosexual with AIDS	Duvic
	Ulcer	Forearm	Elderly man	Tamaki
	Round, ulcerative, and crusted lesion	Left forearm	Pricked and injured by a fallen tree	Hiromoto
	Brown scales		Elderly man	Present report

BMT bone marrow transplantation

[a] Receiving immunosuppressive drugs

[b] Treated with aspirin, predonisone, and methotrexate

[c] The lesion occurred in areas treated with corticosteroid cream

(Harris and Downham 1978; Rohwedder et al. 1979; Tessari et al. 2003) developed dissemination. One was a heart transplant recipient who was infected by *C. lunata* (Tessari et al. 2003), and the others were immunocompetent patients (both football players) infected by *C. lunata* (Rohwedder et al. 1979) and an unidentified *Curvularia* species (Harris and Downham 1978). The patient with a sternal wound infection caused by *C. lunata* was a neonate with congenital

heart disease, who developed multiorgan failure and died (Yvonne et al. 1994).

Topical application of imidasol was successful for treatment of superficial skin infection by *Curvularia* (Gugnani et al. 1990; Kamalam et al. 1992; Lopes and Jobim 1998).

Amphotericin B with or without surgery is the drug of choice for the treatment of deep skin infections and disseminated infections and is usually successful for deep skin infections, except in disseminated cases. Early surgery is important (Rohwedder et al. 1979).

Pathogenesis of skin surface infection with the isolate KMU 4944 was not clear. All but one (Barde and Singh 1983) of the six patients (Barde and Singh 1983; Gugnani et al. 1990; Kamalam et al. 1992; Agrawal and Singh 1995; Lopes and Jobim 1998) with superficial infection by *Curvularia* were healthy women or men. The lesions involved the extremity and were brown to black in color. Brown hyphae were seen in KOH specimens from the scales of the lesion in four cases. In our case, brown hyphae were also seen in the KOH specimen. It was reported that *C. penniseti* (Mitra) Boedijn (Muhsin and Salih 2000), *C. tuberculata* B.L. Jain (Muhsin and Salih 2000), *C. lunata* (Anbu et al. 2006), and *C. brachyspora* (Marcondes et al. 2008) have keratinolytic activity (Anbu et al. 2006). The isolate KMU 4944 could grow well on the keratinized materials (hairs, nails, and calli) on plain agar. Sometimes, conidiophores arose from between the cells of the hair cuticle. This finding suggested that the isolate KMU 4944 could grow in the hair shafts. The isolate KMU 4944 might also have keratinolytic activity, which indicates that it might have the ability to infect the skin surface.

The brown fungus isolated from the tiny thick scales on the interdigital web of the right foot is classifiable in the genus *Curvularia* because of the formation of dark sympoidal conidiophores that bear curved, multicelled, brown poroconidia with paler end cells. The fungus is morphologically similar to *C. lunata* var. *aeria* in having ellipsoidal, obovoid or clavate, straight or curved, 3-septate, the third cell being larger, and smooth-walled conidia with a scarcely protuberant hilum. However, our molecular approach for the confirmation of definitive species identification indicated that the isolate KMU 4944 was found to be unrelated to *C. lunata* var. *lunata* and *C. lunata* var. *aeria* as well as the other reported *Curvularia* taxa as human pathogens. Therefore, the fungus seems to be a hitherto unknown species of *Curvularia*. Further studies based on the sequences analysis of more genes are needed to assess if the isolate can be considered a new species of *Curvularia*.

Acknowledgment We thank Dr. M. Tuda (Professor Emeritus, Kyoto University, Japan) for his valuable comments on the morphological identification.

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