CASE REPORT

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A Case of Deep Cutaneous *Purpureocillium lilacinum* Fungal Infection in an Immunocompetent Patient

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Purpureocillium is a genus of saprophytic fungi that is commonly found in soil or rotting material. Although rarely a pathogen in humans, it can cause serious infections in immunocompromized patients. An 85-year-old woman presented with a 2-week history of pruritic erythematous plaques with yellowish crusts on her right forearm and dorsal hand. Histopathological analysis identified fungal hyphae and spores in the dermis, and *Purpureocillium lilacinum* was identified through tissue culture, polymerase chain reaction, and DNA sequencing. The skin lesion barely responded to 4 weeks of itraconazole treatment but improved upon the addition of terbinafine. The skin lesion was completely cured after 12 weeks, with no recurrence to date. Here, we report a rare deep cutaneous fungal infection caused by *P. lilacinum* in an immunocompetent patient and postulate that, in this case, the patient's agricultural lifestyle increased the possibility of *P. lilacinum* infection.

Key Words: Deep fungal infection, Immunocompetent host, *Purpureocillium lilacinum*

INTRODUCTION

Purpureocillium species are ubiquitous saprophytic fungi[1,2]. *Purpureocillium lilacinum* was once named *Paecilomyces lilacinus*, but a phylogenetic analysis in 2011 led to its reclassification in the new genus *Purpureocillium*[3]. *Paecilomyces lilacinum* is a rare pathogen in humans[1-6]. Ocular involvement is the most common human manifestation followed by cutaneous infection[7]. Although cutaneous infection by *Purpureocillium* is mostly seen in immunocompromized patients, immunocompetent hosts can be infected[1]. There is no standard treatment, and several systemic antifungal agents, and surgical excision are used[8,9].

We encountered a rare case of cutaneous infection by *P. lilacinum* in an otherwise healthy immunocompetent patient who lived in a rural area. Since greater awareness of cutaneous *P. lilacinum* infection in immunocompetent patients is needed, we report this case with a literature review.

CASE

An 85-year-old woman presented with a 2-week history of erythematous plaques with surface nodularity and eczematoid yellowish crusts on her right forearm and dorsal hand (Fig. 1). She lived alone and farmed in a rural area, and reported no

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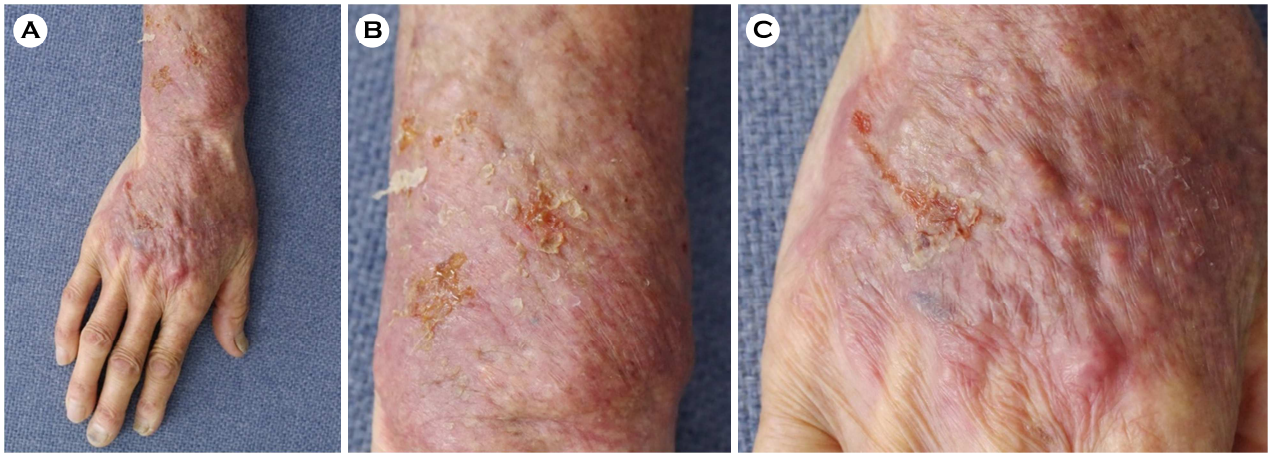

Fig. 1. The skin lesion consisted of erythematous plaques with surface nodularity and eczematoid yellowish crusts on the right forearm and dorsal right hand.

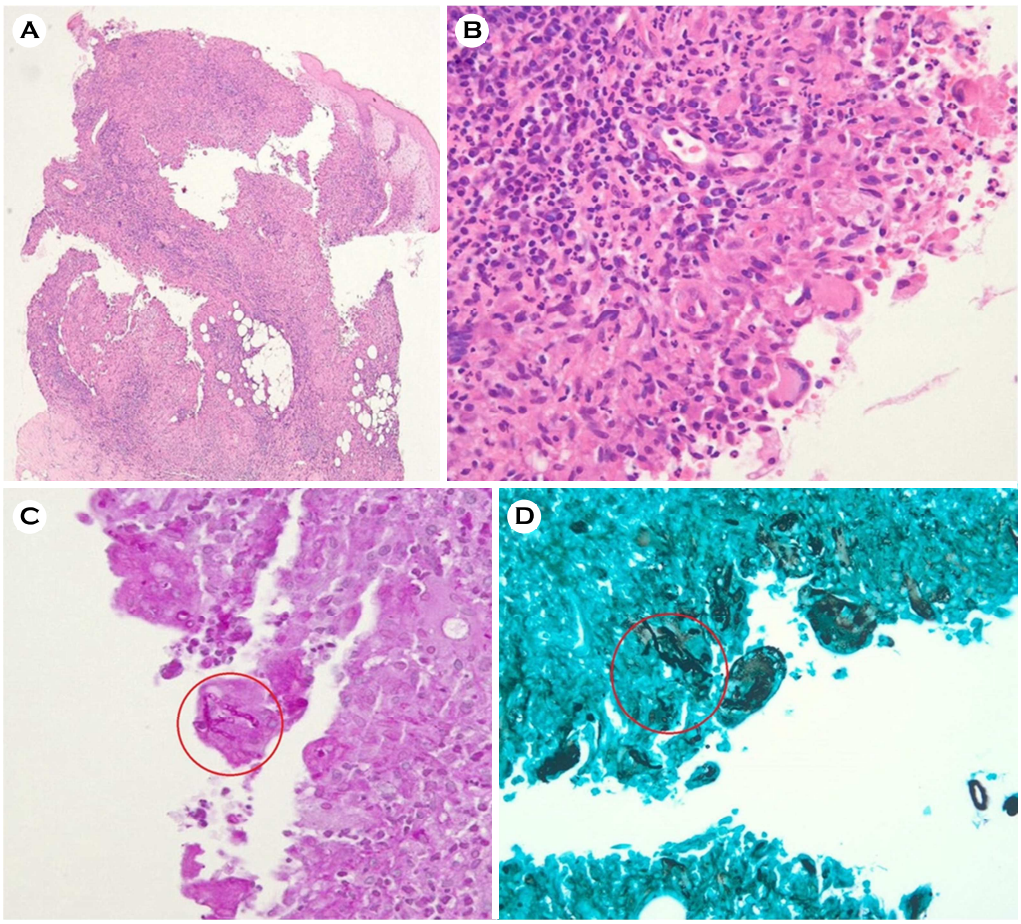

Fig. 2. (A) Histopathological examination revealed dense inflammatory infiltration in the dermis at low power (H&E, ×40). (B) Granulomatous changes, including neutrophils, histiocytes, plasma cells, and giant cells were seen in the dermis (H&E, ×400). (C) Purplish branching fungal hyphae were found among the inflammatory cells upon Periodic acid-Schiff staining (×400). (D) Black fungal hyphae and spores were observed after Gomori-methenamine silver staining (×400).

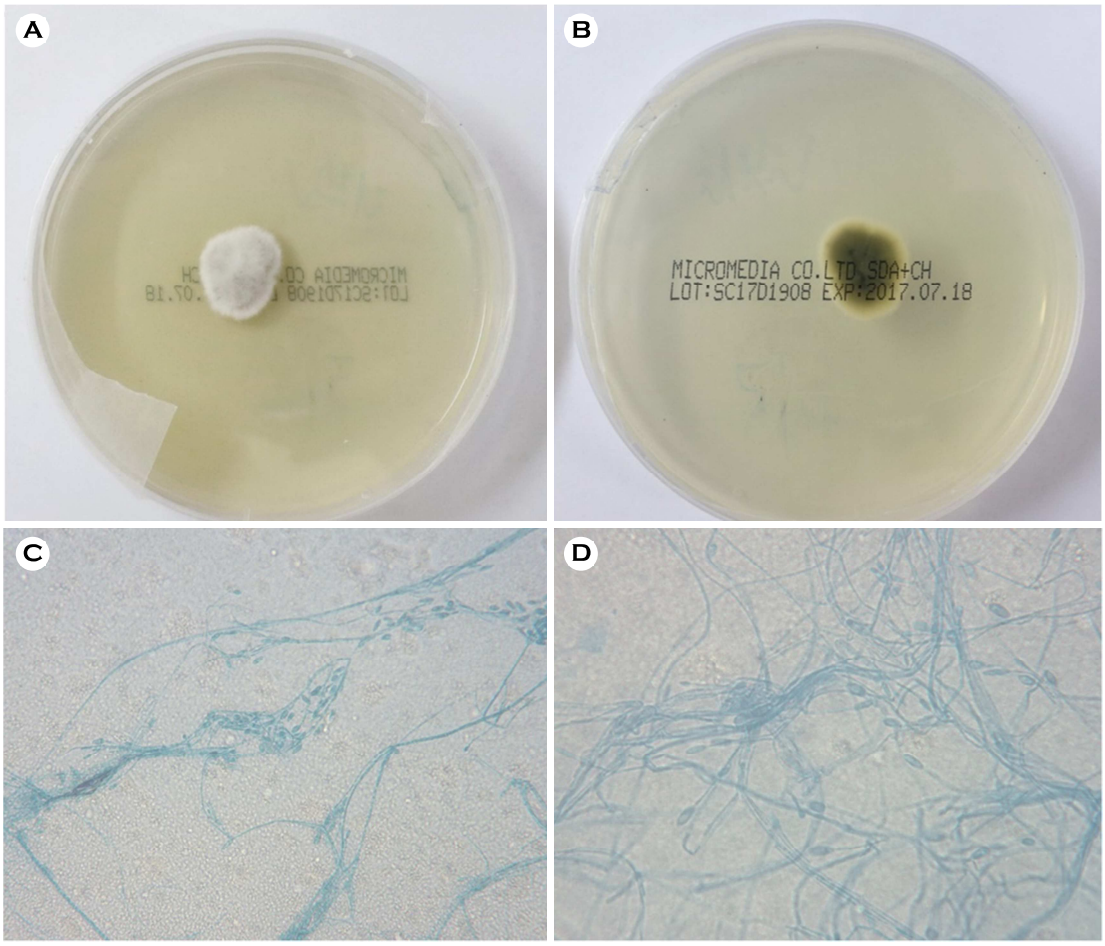

Fig. 3. (A) A whitish dome-shaped floccose colony with shallow radiating furrows grew after a 5-day incubation at 25℃ on Sabouraud dextrose agar. (B) The reverse was dark green. (C, D) Microscopic examination revealed long thin-walled entangled hyphae with single oval conidia after lactophenol cotton blue staining (×100 and ×200, respectively).

noteworthy medical or family history. There was also no trauma or contact history.

Cutaneous scraping for a 10% potassium hydroxide smear identified no fungal elements and histopathological examination of a right forearm biopsy revealed dense inflammatory infiltration in the dermis at low magnification (Fig. 2A) and granulomatous changes with neutrophils, histiocytes, plasma cells, and giant cells in the dermis (Fig. 2B). Purplish branching fungal hyphae were observed among the inflammatory cells after staining with Periodic acid-Schiff (Fig. 2C), and black hyphae and spores were also observed upon Gomori-methenamine silver staining (Fig. 2D).

Culture of a small segment of the biopsied specimen on Sabouraud dextrose agar produced a whitish dome-shaped floccose colony with shallow radiating furrows after 5 days at 25℃ (Fig. 3A). The reverse side was dark green (Fig. 3B). The cultured organism exhibited long thin-walled entangled hyphae with single oval conidia after colonies were stained with lactophenol cotton blue and examined microscopically (Figs. 3C, 3D).

The identity of the organism was confirmed by sequencing the D1-D1 region of its 28S rRNA and the internal transcribed spacer.* Purified DNA from the polymerase chain reaction was sequenced with a BigDye Terminator Cycle sequencing kit (Applied BioSystems, Foster City, CA, USA) and ABI PRISM 3130 genetic analyzer (Applied Biosystems). All sequences were

*Clinical and Laboratory Standards Institute. Interpretive criteria for the identification of bacteria and fungi by DNA target sequencing; Approved guideline. MM18-A. Wayne, PA, USA: CLSI 2008.

compared with those of similar strains using BLAST analysis. The sequence analysis indicated 100.0% homology with *P. lilacinum* ACTT 10114 (GenBank accession no. AY213717.1 and GenBank accession no. AY213665.1). We, therefore, identified our isolate as *P. lilacinum*.

The skin lesion barely responded to 4 weeks of systemic treatment with itraconazole, so terbinafine was added to the therapy, after which improvement was evident. The skin lesion was completely cured after 12 weeks of combination therapy, and there has been no recurrence to date.

DISCUSSION

Purpureocillium is a genus of saprophytic molds that is commonly found in soil or decaying organic material but is a relatively uncommon pathogen of humans[1,2]. It was first described as *Penicillium lilacinum* by Bainer in 1907[10] and then renamed *Paecilomyces lilacinus* by Samson in 1974[3]. Finally, Luangsa-Ard et al. reclassified it in the new genus *Purpureocillium* after a phylogenetic analysis in 2011[11].

Fenech and Mallia first isolated *P. lilacinum* in a human in 1972 from a patient with a pleural effusion[12], and Takayasu et al.[3] reported a cutaneous infection in 1977. Ocular involvement, such as iatrogenic keratitis and endophthalmitis after artificial lens implantation, comprises 51.3% of all reported human infections, followed by cutaneous infection at 35.3%[1]. Other reported sites of infection include the sinuses, endocardium, and lungs[7]. Cutaneous *P. lilacinum* infection occurs primarily in immunocompromized patients with a history of organ transplantation, long-term steroid use, malignancy, or acquired immunodeficiency syndrome, and it is considered rare in immunocompetent patients[1,9,13]. Moreover, 18.6% of the infections seen in immunocompetent patients have no identified trigger factor[1].

Since the first immunocompetent host was described in 1977, there have been 14 cases of cutaneous *P. lilacinum* infection in immunocompetent patients reported worldwide (Table 1)[1,11,14-18]. The patient age distribution was from 7 to 86 (mean 48.2) years with no gender preference was evident.

Table 1. Reported cases of cutaneous *Purpureocillium lilacinum* infection in immunocompetent patients

Case No.	Year (Country)	Age/Sex	Site	Trauma history	Treatment	Clinical course
1	1977 (Japan)	20/Female	Face	Not available	1% clotrimazole cream → griseofulvin	Partial cure
2	1977 (Japan)	50/Male	Face	None	Griseofulvin	Cure
3	1984 (Korea)	19/Female	Face	Not available	Ketoconazole	Cure
4	1997 (USA)	86/Male	Finger	Not available	Itraconazole	Cure
5	1999 (Spain)	36/Male	Leg	None	Itraconazole	Cure
6	2001 (Australia)	59/Female	Leg	Minor trauma	Itraconazole	Cure
7	2004 (USA)	65/Male	Forearm	None	Itraconazole + ketoconazole → fluconazole → excision	Cure
8	2006 (Italy)	59/Male	Leg	Dog bite	Itraconazole	Cure
9	2007 (Korea)	83/Male	Wrist	Not available	Itraconazole	Cure
10	2007 (Iran)	30/Female	Forearm	None	Ketoconazole	Cure
11	2008 (Japan)	7/Male	Face	None	Itraconazole → fluconazole	Cure
12	2013 (Tunisia)	8/Female	Face	None	Itraconazole → voriconazole	Cure
13	2013 (Korea)	72/Male	Shoulder	Not available	Itraconazole → voriconazole	Cure
14	2017 (Korea)	81/Male	Wrist, hand	Not available	Itraconazole	Cure
Our case	2018 (Korea)	85/Female	Forearm, hand	None	Itraconazole → itraconazole + terbinafine	Cure

Of note, all of the infection sites were exposed areas such as the face, arm, or leg, and a preceding trauma was clearly identified in only two cases. Recent cases of immunocompetent farmers developing *P. lilacinum* infection with no specific antecedent event have also been reported[14,15]. It can be inferred that an agricultural lifestyle involving minor trauma and routine contact with soil may be the source of infection in immunocompetent patients. Our patient also lived in a rural area and was in frequent contact with soil, which may have increased the risk of deep cutaneous fungal infection by *P. lilacinum*. Considering the infection site and the patient's rural lifestyle, we postulate that our patient experienced recurrent minor trauma that she did not remember, and was infected by *P. lilacinum* from the soil.

Diagnosis of *P. lilacinum* infection is based on the identification of the fungal organism. Histopathological examination, tissue culture in Sabouraud dextrose agar with lactophenol cotton blue staining, and molecular analysis can help to diagnose deep cutaneous fungal infection by *P. lilacinum* [9,14,15]. Diagnosing *P. lilacinum* accurately is important because each species in the genus *Purpureocillium* exhibits resistance to different antifungal agents[19]. *P. lilacinum* is resistant to conventional antifungal agents, including amphotericin B, fluconazole, and flucytosine, and its *in vitro* susceptibility to itraconazole varies[1,13]. Voriconazole is a promising therapeutic agent[14,20], although there is no established dosage for this antifungal medication and no widely accepted treatment period or protocol for debridement or surgical excision has been established.

In conclusion, a rural or agricultural lifestyle may contribute to an increased risk of *P. lilacinum* infection in immunocompetent individuals. Here we reported a rare case of such an infection and provided a literature review of deep cutaneous fungal infection by *P. lilacinum* in immunocompetent patients.

CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

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PATIENT CONSENT STATEMENT

The patient provided written informed consent for the publication and the use of his or her images.

REFERENCES

1. Pastor FJ, Guarro J. Clinical manifestations, treatment and outcome of *Paecilomyces lilacinus* infections. Clin Microbiol Infect 2006;12:948-960
2. Castro LG, Salebian A, Sotto MN. Hyalohyphomycosis by *Paecilomyces lilacinus* in a renal transplant patient and a review of human *Paecilomyces* species infections. J Med Vet Mycol 1990;28:15-26
3. Samson RA. *Paecilomyces* and some allied hyphomycetes. Stud Mycol 1974;6:58
4. Polat M, Kara SS, Tapisiz A, Demirtas Z, Sari S, Kalkanci A, et al. Successful treatment of *Paecilomyces variotii* peritonitis in a liver transplant patient. Mycopathologia 2015;179:317-320
5. Steiner B, Aquino VR, Paz AA, Silla LM, Szvascki A, Goldani LZ. *Paecilomyces variotii* as an emergent pathogenic agent of pneumonia. Case Rep Infect Dis 2013;2013:273848
6. Vasudevan B, Hazra N, Verma R, Srinivas V, Vijendran P, Badad A. First reported case of subcutaneous hyalohyphomycosis caused by *Paecilomyces variotii*. Int J Dermatol 2013;52:711-713
7. Marchese SM, Smoller BR. Cutaneous *Paecilomyces lilacinus* infection in a hospitalized patient taking corticosteroids. Int J Dermatol 1998;37:438-441
8. Hall VC, Goyal S, Davis MD, Walsh JS. Cutaneous hyalohyphomycosis caused by *Paecilomyces lilacinus*: report of three cases and review of the literature. Int J Dermatol 2004;43:648-653
9. Itin PH, Frei R, Lautenschlager S, Buechner SA, Surber C, Gratwohl A, et al. Cutaneous manifestations of *Paecilomyces lilacinus* infection induced by a contaminated skin lotion in patients who are severely immunosuppressed. J Am Acad Dermatol 1998;39:401-409
10. Bainer G. Mycotheque de l'edole de pharmacie IX. *Paecilomyces*, genre nouveau de mucedinees. Bull Soc Mycol Fr 1907;23:26-27, Cited from Kwon-Chung KJ, Bennett JE. Medical mycology. Philadelphia: Lea & Febiger, 1992:

747-750
11. Luangsa-Ard J, Houbraken J, van Doorn T, Hong SB, Borman AM, Hywel-Jones NL, et al. *Purpureocillium*, a new genus for the medically important *Paecilomyces lilacinus*. FEMS Microbiol Lett 2011;321:141-149
12. Fenech FF, Millia CP. Pleural effusion caused by *Penicillium lilacinus*. Br J Dis Chest 1972;66:284-290
13. Blackwell V, Ahmed K, O'Docherty C, Hay RJ. Cutaneous hyalohyphomycosis caused by *Paecilomyces lilacinus* in a renal transplant patient. Br J Dermatol 2000;143:873-875
14. Jung MY, Park HJ, Lee JH, Lee JH, Yang JM, Lee DY. A localized cutaneous *Paecilomyces lilacinus* infection treated with voriconazole. Korean J Dermatol 2013;51:833-836
15. Kwak H, Park SK, Yun SK, Kim HU, Park J. A case of localized skin infection due to *Purpureocillium lilacinum*. Korean J Med Mycol 2017;22:42-49
16. Saghrouni F, Saidi W, Ben Said Z, Gheith S, Ben Said M, Ranque S, et al. Cutaneous hyalohyphomycosis caused by *Purpureocillium lilacinum* in an immunocompetent patient: case report and review. Med Mycol 2013;51:664-668
17. Ko WT, Kim SH, Suh MK, Ha GY, Kim JR. A case of localized skin infection due to *Paecilomyces lilacinus*. Korean J dermatol 2007;45:930-933
18. Nagamoto E, Fujisawa A, Yoshino Y, Yoshitsugu K, Odo M, Watanabe H, et al. Case of *Paecilomyces lilacinus* infection occurring in necrotizing fasciitis-associated skin ulcers on the face and surrounding a tracheotomy stoma. Med Mycol J 2014;55:E21-27
19. Aguilar C, Pujol I, Sala J, Guarro J. Antifungal susceptibilities of *Paecilomyces* species. Antimicrob Agents Chemother 1998;42:1601-1604
20. Castelli MV, Alastruey-Izquierdo A, Cuesta I, Monzon A, Mellado E, Rodriguez-Tudela JL, et al. Susceptibility testing and molecular classification *of Paecilomyces* spp. Antimicrob Agents Chemother 2008;52:2926-2928