

A Rare Case of Onychomycosis Induced by *Cladosporium Cladosporioides*

Dongmei Shi^{1,2}; Guixia Lu¹; Huan Mei¹; Yongnian Shen¹; Ying Qiu²; Weida Liu^{1*}

*Weida Liu

Department of Mycology, Institute of Dermatology, Chinese Academy of Medical Sciences & Peking Union Medical College, Nanjing, Jiangsu, P. R. China.

Tel: +86 25 85470580; Fax: +86 25 85414477. Email: liumyco@hotmail.com

Abstract

The dematiaceous fungus *Cladosporium cladosporioides* (*C. cladosporioides*) is a widely distributed saprophyte that occasionally infects the lung, skin, eye and brain in both immunocompetent or immunosuppressed hosts. We report a rare case of an immunocompetent 56-year-old male patient who presents with a six-year history of onychomycosis caused by *C. cladosporioides* following trauma. The patient achieved complete remission after oral treatment with itraconazole at a daily dose of 400mg for three months.

Keywords

Cladosporium cladosporioides; Onychomycosis

Introduction

The genus *Cladosporium* is one of the most common dematiaceous fungi that inhabits soil environments, certain animal feces, vegetables, rotten wood, nestles, omnivorous animals, mice and decayed fruits and food [1]. *Cladosporium cladosporioides* (*C. cladosporioides*) can cause a wide spectrum of infection clinically in the skin [2-4], cornea [5], brain [6, 7], lung, hair [8], and gingiva [9]. However, onychomycosis (nail infection) induced by *C. cladosporioides* is rare. Here we report a male patient with onychomycosis and its causative agent *C. Cladosporioides* was confirmed by microbiological and molecular analysis.

Case Report

A 56-year-old man presents with a six years history of nail dystrophy, a subungual abscess, and an ecthyma-like crusted lesion involving two fingernails. The patient has a history of injury at his hands when caught the mud crabs (*Scylla serrata*) 6 years ago. Accidentally, a mud crab clutched onto his fingers. The lesions began with small erythematous patches on the periungual areas of his left third finger and right fourth finger. The lesions gradually increased in size and both fingernails were affected and later destroyed in two month period (Fig1A and 1B). By the time when patient visited a local hospital, topical antifungal agent was given intermittently with a poor response. Physical examination in our clinic found no other abnormalities. He did not recall any history of long-term treatment with steroids or any other drugs. He denied fever or weight loss.

Laboratory findings were within normal limits. Serological tests for hepatitis B virus, hepatitis C virus, HIV antibody and anti-nuclear antibodies (e.g., anti-dsDNA antibody, anti-ssDNA antibody, and extractable nuclear antigens antibodies) were all negative. Chest radiography showed unremarkable findings.

For mycological examination, scrapings were collected from the basal layer of two nail plates as well as areas of hyperkeratosis from nails of both fingers. The specimen was subjected to direct microscopic examination in 20% KOH mounts. Fungal elements were seen in the form of thick hyaline septated hyphae with branching (Fig 2A).

A portion of skin biopsies, nail clippings and subungual debris, preserved in sterile saline, were aseptically homogenized and then inoculated onto culture plates containing Sabouraud dextrose agar (SDA) with chloramphenicol and cycloheximide (0.5 mg/ml) and Potato dextrose agar (PDA), respectively. Fungal culture on SDA or PDA manifests as expanding, velvety to powdery, olivaceous green to olivaceous brown Colonies; reverse olivaceous black (Fig 2B-E).

Microscopic examination of a lactophenol cotton blue preparation of the colonies revealed typical morphological features of *Cladosporium* species (Fig 2F). Conidiophores are of variable length, up to 350 µm long and 2-6 µm wide, without swellings, with terminal and lateral ramifications, bearing branched conidial chains, and a pale olivaceous brown. Conidia are ellipsoidal to limoni-form, smooth-walled or slightly verrucose, olivaceous brown, 1-celled, with dark scars, easily liberated. Repeated examination of the nail samples after a week revealed hyaline septated hyphae with dichotomous branching under direct microscopy and yielded *C. cladosporioides* growth again when cultured on SDA. No other fungi were isolated.

The isolated agent was reconfirmed by sequencing of ITS1 and ITS4 region of rDNA and compared with sequences deposited in GenBank by using the Blast program to find identical or similar sequences. We found that the ITS sequences displayed 99% similarity to the entries of *C. cladosporioides* deposited in GenBank (accession nos. KJ767065.1). The isolated agent was deposited in the Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College in Nanjing, Jiangsu.

The *in vitro* susceptibility of the strain to eight antifungal agents was determined using the microdilution method in accordance with the guidelines of the Clinical and Laboratory Standards Institute (CLSI) M38A. The minimum inhibitory concentrations (MICs) were listed below: itraconazole, 1 µg/ml; ketoconazole, >2 µg/ml; fluconazole, >64 µg/ml; miconazole, 4 µg/ml; voriconazole, 2 µg/ml; anidulafungin, >4 µg/ml; amphotericin B, >4 µg/ml; and terbinafine, 1 µg/ml. The treatment with topical and systemic antifungals was given immediately following MIC assay. The patient was prescribed with oral itraconazole at a daily dose of 400mg in combination with terbinafine cream twice per day. The nails and the periungual lesion healed completely after 3 months (Fig 1C and 1D). To ensure the effectiveness, the itraconazole was then sustained at a daily dose of 200 mg for another 3 months. No recurrence of cutaneous lesions was seen at the 12-month follow-up visit.

Discussion

The saprophytic fungi *Cladosporium* genus commonly inhabits in soil [10]. But some *Cladosporium* spp. can also be isolated from marine environment [11]. Some species, such as *C. sphaerospermum*, *C. oxysporum*, and *C. herbarum*, are often found as culture contaminants and very rarely

as opportunists in humans[12-15].

C. cladosporioides is an opportunistic fungus that causes a variety of clinical infections in immunocompromised and immunocompetent humans and animals. The clinical manifestations vary depending on the immunity of the hosts, as well as entries to the host. For example, its airborne spores are relevant allergens, which may harm patients with asthma. Other types of infection including lung infections (e.g., pulmonary fungus ball), dental granulomas, brain abscesses and eye infections presenting as keratomycosis and corneal ulcer are also documented [16]. However, onychomycosis cases caused by *C. cladosporioides* are quite rare [17]. Up to date, a few cases of onychomycosis caused by *C. cladosporioides* have been reported in Middle East and India [21]. The case we reported here was characterized by complete destruction of the nails in company with painful periungual inflammation at the proximal nail fold.

Onychomycosis is a disorder of nail infection usually caused by dermatophytes, yeasts, and non-dermatophyte molds (NDM). Predisposing factors such as immunosuppression or trauma may allocate the nail plate as a preferred location for invasion by the fungi [18]. It has been suggested that being in contact with water for prolonged period of time may increase the risk of infection by this type of fungus in some adult patients [19]. *C. cladosporioides* has been isolated from the sea. Although we did not test samples from the sea or mud crab for this case; we speculate that trauma, contacting with the sea water or crab that was contaminated by *C. cladosporioides* may cause the infection. To the best of our knowledge, this is the first case of onychomycosis in China that *C. cladosporioides* is solely responsible. Previously, three cases of mycosis caused by *C. cladosporioides* have been reported in China; the first case is phaeohyphomycosis on the face of a panda[22]; the second case is subcutaneous phaeohyphomycosis on the lateral aspect of right buttock in a 49-year-old immunocompetent woman with a history of trauma[2]; and the third one was onychomycosis caused by *C. cladosporioides* in combination with *Trichophyton rubrum* in a patient with psoriasis [17]. In China, trauma and immunosuppression are the key factors of *C. cladosporioides* infection, which is consistent with reports worldwide. However, this case also suggested that trauma may cause skin barrier damage and leads to the intrusion of *C. cladosporioides* in immunocompetent hosts as well.

Onychomycosis is the most difficult type of superficial mycosis to treat. It is a chronic infection that is prone to relapse [22]. Our case responded well to our treatment. Skin and nail lesions were completely cured after 3 months of oral itraconazole. No recurrence of cutaneous lesions was seen at the 12-month follow-up visit. Therefore, it is important to identify the causative agent and ensure that the appropriate treatment is employed.

Acknowledgements

This work was supported in part by grants from the national Natural Science Foundation of China (NM. 81401653) and the National Key Basic Research Program of China (NM 2013CB531605) and was funded by Jiangsu Provincial Special Program of Medical Science (BL2012003).

Figures

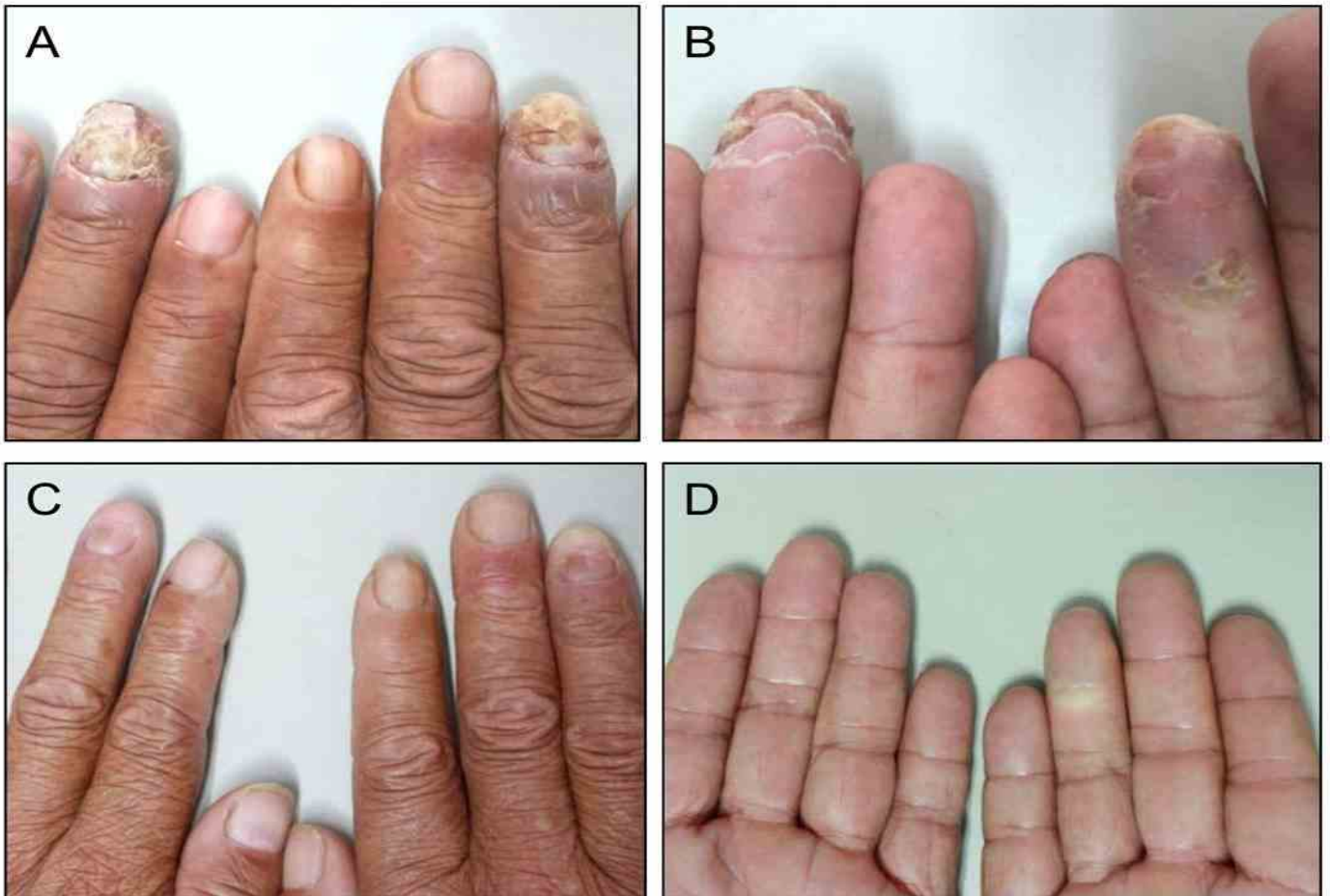


Figure 1: Clinical presentation with inflammation of periungua area and the nail destruction of the left third finger and the right fourth finger (A and B). The skin and nail completely recovered after 3 months of oral treatment with itraconazole (C and D).

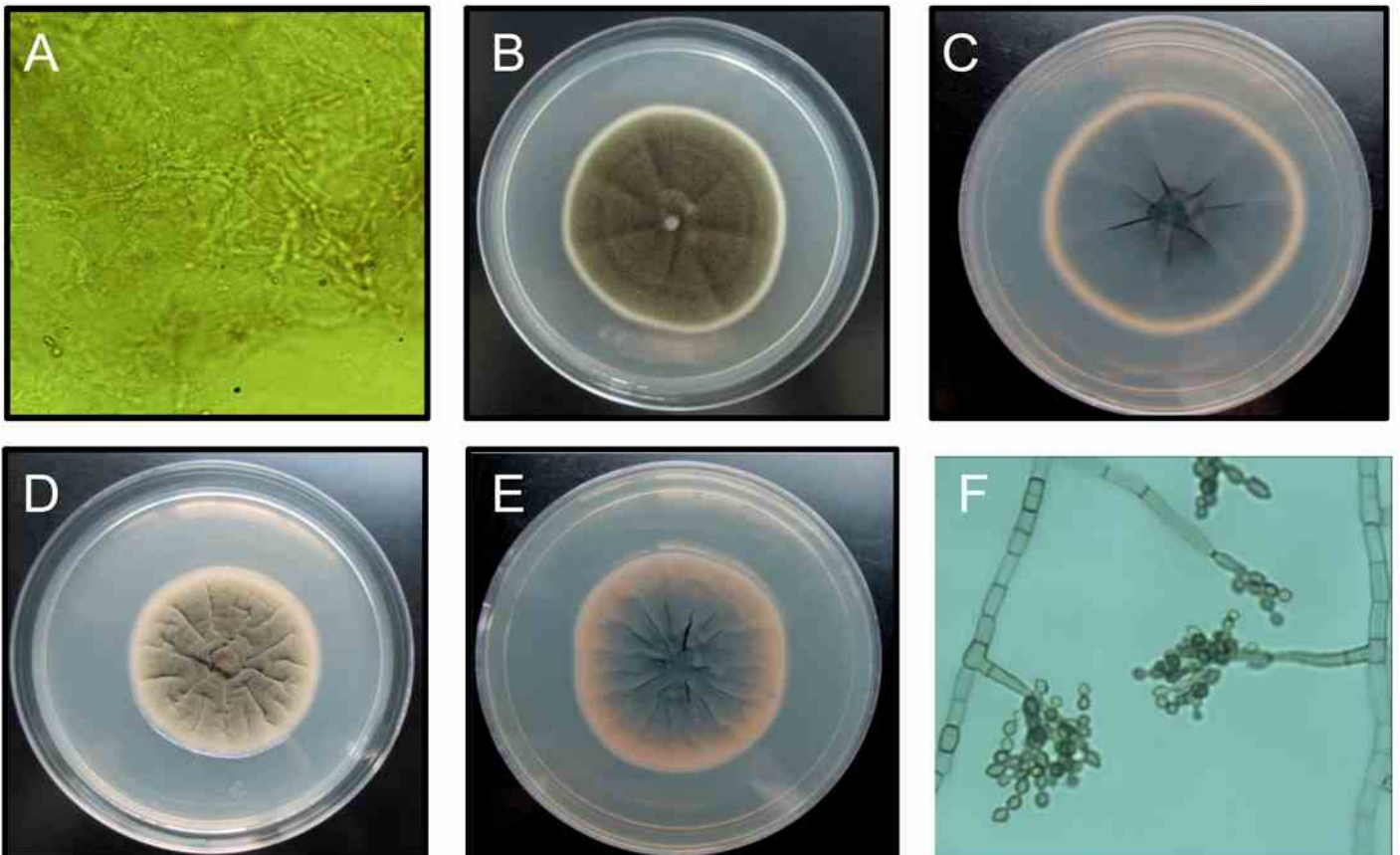


Figure 2: Direct light microscopy of nail clips displaying brown hyphae (original magnification, $\times 400$) (A). Affected skin and nail lesions in culture presenting with olivaceous-green, velvety colonies on Sabouraud's dextrose agar. Reverse greenish-black (B and C). Affected skin and nail lesions in culture presenting with olive brown, velvety colonies on PDA; reverse brownish black (D and E). Light microscopy of lactophenol cotton blue preparation of colonies grown on Sabouraud's dextrose agar presenting with simple or branching, pigmented conidiophores with pigmented, ellipsoidal or cylindrical conidia (original magnification, $\times 400$) (F).

References

1. Bensch K, Groenewald JZ, Dijksterhuis J, Starink-Willemse M, Andersen B, Summerell BA, et al. Species and ecological diversity within the *Cladosporium cladosporioides* complex (*Davidiellaceae, Capnodiales*). *Stud Mycol.* 2010. 67: 1-94.
2. Sang H, Zheng XE, Zhou WQ. A case of subcutaneous phaeohyphomycosis caused by *Cladosporium cladosporioides* and its treatment. *Mycoses.* 2012. 55(2): 195-7.
3. Gugnani HC, Sood N, Singh B, Makkar R. Case report. Subcutaneous phaeohyphomycosis due to *Cladosporium cladosporioides*. *Mycoses.* 2000. 43(1-2): 85-7.
4. Annessi G, Cimitan A, Zambruno G, Di SA. Cutaneous phaeohyphomycosis due to *Cladosporium cladosporioides*. *Mycoses.* 1992. 35(9-10): 243-6.
5. Chew FL, Subrayan V, Chong PP, Goh MC, Ng KP. *Cladosporium cladosporioides* keratomycosis: a case report. *Jpn J Ophthalmol.* 2009. 53(6): 657-9.
6. Kantarcioglu AS, Yucel A, de Hoog GS. Case report. Isolation of *Cladosporium cladosporioides* from cerebrospinal fluid. *Mycoses.* 2002. 45(11-12): 500-3.
7. Shimizu T, Seki S, Suyama Y, Fujii H, Takeshita S, Isemura T. An autopsy case of acute myelomonocytic leukemia with spinal cord compression and mycosis of *Cladosporium cladosporioides*. *Rinsho Ketsueki.* 1982. 23(7): 1096-102.
8. Zeller S, Lempert S, Goebeler M, Hamm H, Kolb-Maurer A. *Cladosporium cladosporioides*: a so far unidentified cause of white piedra. *Mycoses.* 2015. 58(5): 315-7.
9. Pepe RR, Bertolotto C. [The first isolation of *Cladosporium cladosporioides* (Fres.) de Vries from dental granulomas]. *Minerva Stomatol.* 1991. 40(12): 781-5.
10. deHoog, G.S., 1983. On the potentially pathogenic dematiaceous *Hyphomycetes*. In: D.H. Howard (ed.): *The Fungi Pathogenic to Humans and Animals*, A: 149-216. Marcel Dekker, New York.
11. Rocha LC, Selegim MH, Comasseto JV, Sette LD, Porto AL. Stereoselective Bioreduction of α -Azido Ketones by Whole Cells of Marine-Derived Fungi. *MarBiotechnol (NY).* 2015;17(6):736-42.
12. Maduri A, Patnayak R, Verma A, Mudgeti N, Kalawat U, Asha T. Subcutaneous infection by *Cladosporium sphaerospermum*-A rare case report. *Indian J PatholMicrobiol.* 2015. 58(3): 406-7.
13. Forster RK, Rebell G, Wilson LA. Dematiaceous fungal keratitis. Clinical isolates and management. *Br J Ophthalmol.* 1975. 59(7): 372-6.
14. Tsai TH, Chen WL, Peng Y, Wang IJ, Hu FR. Dematiaceous fungal keratitis presented as a foreign body-like isolated pigmented corneal plaque: a case report. *Eye (Lond).* 2006. 20(6): 740-1.
15. Zhang L, Muradia G, De Vouge MW, Rode H, Vijay HM. An allergenic polypeptide representing a variable region of hsp 70 cloned from a cDNA library of *Cladosporium herbarum*. *Clin Exp Allergy.* 1996. 26(1): 88-95.
16. Kwon-Chung KJ, Schwartz IS, Rybak BJ. A pulmonary fungus ball produced by *Cladosporium cladosporioides*. *Am J Clin Pathol.* 1975. 64(4): 564-8.

17. Yu J, Wan Z, Lu QY, Chen W, Wang XH. Onychomycosis caused by *Trichophyton rubrum* and *Cladosporium cladosporioides* in psoriasis patient: one case report. Chin J Mycol, 2009, 4(5): 298-300 (in Chinese).
18. Guidelines of care for superficial mycotic infections of the skin: onychomycosis. Guidelines/Outcomes Committee. American Academy of Dermatology. J Am Acad Dermatol. 1996. 34: 116-21.
19. Lohoue PJ, Lando AJ, Kaptue L, Tchinda V, Folefack M. Superficial mycoses and HIV infection in Yaounde. J Eur Acad Dermatol Venereol. 2004. 18: 301-4.
20. Hafidh RR, Abdulmir AS. *Cladosporium* spp. as a causative agent of white superficial onychomycosis. East Mediterr Health J. 2008. 14: 231-3.
21. Ma X, Gu Y, Liu X, Li D, Ling S, Hou J, et al. Phaeohyphomycotic dermatitis in a giant panda (*Ailuropodamelanoleuca*) caused by *Cladosporium cladosporioides*. Med Mycol Case Rep. 2013. 2: 119-21.
22. Vieira MR, Milheiro A, Pacheco FA. Phaeohyphomycosis due to *Cladosporium cladosporioides*. Med Mycol. 2001. 39: 135-7.

Manuscript Information: Received: November 12, 2015; Accepted: January 25, 2016; Published: January 26, 2016

Authors Information: Dongmei Shi^{1,2}; Guixia Lu¹; Huan Mei¹; Yongnian Shen¹; Ying Qiu²; Weida Liu^{1*}

¹Department of Mycology, Institute of Dermatology, Chinese Academy of Medical Sciences & Peking Union Medical College, Nanjing, Jiangsu, P. R. China

²Department of Dermatology, Jining NO.1 People's Hospital, Shandong, P. R. China

Citation: Shi D, Lu G, Mei H, Shen Y, Qiu Y, Liu W. Fetal distress as a presenting symptom of acute leukemia during pregnancy. Open J Clin Med Case Rep. 2016; 1072

Copy right Statement: Content published in the journal follows Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>). © Liu W 2016

Journal: Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.

Visit the journal website at www.jclinmedcasereports.com

For reprints & other information, contact editorial office at info@jclinmedcasereports.com