

A Case of Cutaneous Mucormycosis Occurring after Systemic Steroid Therapy

Soo Hyeon Noh, Jin Kyung Chae, Sang Hyun Park, Kun Park and Eun Jung Kim[†]

Department of Dermatology, Wonkwang University School of Medicine, Iksan, Korea

= Abstract =

Cutaneous mucormycosis is a rare disease caused by zygomycetes such as *Rhizomucor*, *Mucor*, *Absidia*, and *Rhizopus*. The disease usually occurs in immunocompromised individuals, and the organism is rarely pathogenic in an immunocompetent host. Herein, we report a 77-year-old female patient who had multiple erythematous papules and pustules on the left 3rd finger. She had received systemic steroid therapy prior to the occurrence of the skin lesions. The histopathological examination of Periodic Acid Schiff stained section showed chronic granulomatous inflammation and fungal hyphae. *Rhizopus* species was isolated on the fungal culture of the tissue specimen. The patient was finally diagnosed with cutaneous mucormycosis and was treated with itraconazole. [Korean J Med Mycol 2015; 20(3): 70-75]

Key Words: Cutaneous mucormycosis

INTRODUCTION

Mucormycosis is a rare opportunistic infection caused by fungi of the order *Mucorales*, class *Zygomycetes*. Risk factors for mucormycosis include diabetic ketoacidosis, leukemia, lymphoma, cancer, AIDS, hepatitis, liver cirrhosis, anemia, congenital heart disease, burns, severe malnutrition, and iatrogenic immunosuppression¹. According to the site of infection, there are five known types of mucormycosis, i.e., rhinocerebral, pulmonary, gastrointestinal, cutaneous, and disseminated type. The cutaneous mucormycosis is the rarest type and has

the most favorable prognosis amongst the 5 types². Cutaneous mucormycosis involves both epidermis and dermis, and may be caused as a primary cutaneous inoculation or secondary disseminated infection³. Herein, we present a case of cutaneous mucormycosis of the finger caused by *Rhizopus* species.

REPORT OF A CASE

A 77-year-old female presented with gradually progressive asymptomatic multiple erythematous papules and pustules on the left middle finger since 11 months. The patient had undergone systemic

Received: July 3, 2015, Revised: July 13, 2015, Accepted: September 24, 2015

[†]Corresponding author: Eun Jung Kim, Wonkwang University School of Medicine, Dermatology 895 Muwang-Ro, Iksan, Jeolabuk-do, 54538, Korea.

Tel: +82-63-859-1590, Fax: +82-63-842-1895, e-mail: soohvv@hanmail.net

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Fig. 1. (A) Multiple erythematous hard papules with central crust and pustules on left 3rd finger (B) After 2 months of therapy, the lesions were improved with residual hyperkeratosis.

steroid therapy in March 18, 2014, as treatment for gout affecting her right foot. She was started on methylprednisolone 60 mg/day followed by a 6-day taper to 10 mg/day and then, the baseline dose of methylprednisolone was administered for 2

weeks. Thereafter, she was treated with methylprednisolone 5 mg/day for 2 weeks followed by 2.5 mg/day for 1 month. Approximately 1 month after administration of methylprednisolone, multiple papules and pustules with surrounding erythema occurred on the left middle finger. There was no history of trauma. She had a history of atrial fibrillation, hypertension and compression fracture of lumbar vertebrae, and had undergone bilateral subtotal thyroidectomy as treatment for goiter. Dermatological examination revealed well-defined multiple erythematous, hard papules with a central crust, and pustules on the dorsal surface of the finger (Fig. 1A). There were no signs of regional lymphadenopathy. Laboratory investigation showed a leukocyte count of 13,750/ μ l and hemoglobin of 11.2 g/dL. The serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were 40 IU/L and 72 IU/L. The serum creatinine was 0.54 mg/dL; the blood urea nitrogen was 15.5 mg/dL. The C-reactive protein was 0.60 mg/L. Chest radiography revealed non-specific findings. Histopathology of the skin biopsy specimen under low power view showed diffuse inflammatory infiltration and necrosis in the epidermis and deep dermis (Fig. 2A). High power view of the specimen presented chronic granulomatous inflammation with lymphohistiocytes and multinucleated giant cell in the dermis (Fig. 2B). Non-septate fungal hyphae with large and long branches oriented at right angles, were observed on the microscopic examination with Periodic Acid Schiff staining (Fig. 2C). The fungal culture of the tissue specimen on Sabouraud's agar plate revealed rapidly growing whitish cottony colonies that turned dark brown at the surface of the plate (Fig. 3A). On the staining with lactophenol cotton blue stain, the fungus showed brown colored rhizoids and unbranched sporangiospores with sporangia on each end (Fig. 3B). The isolate was

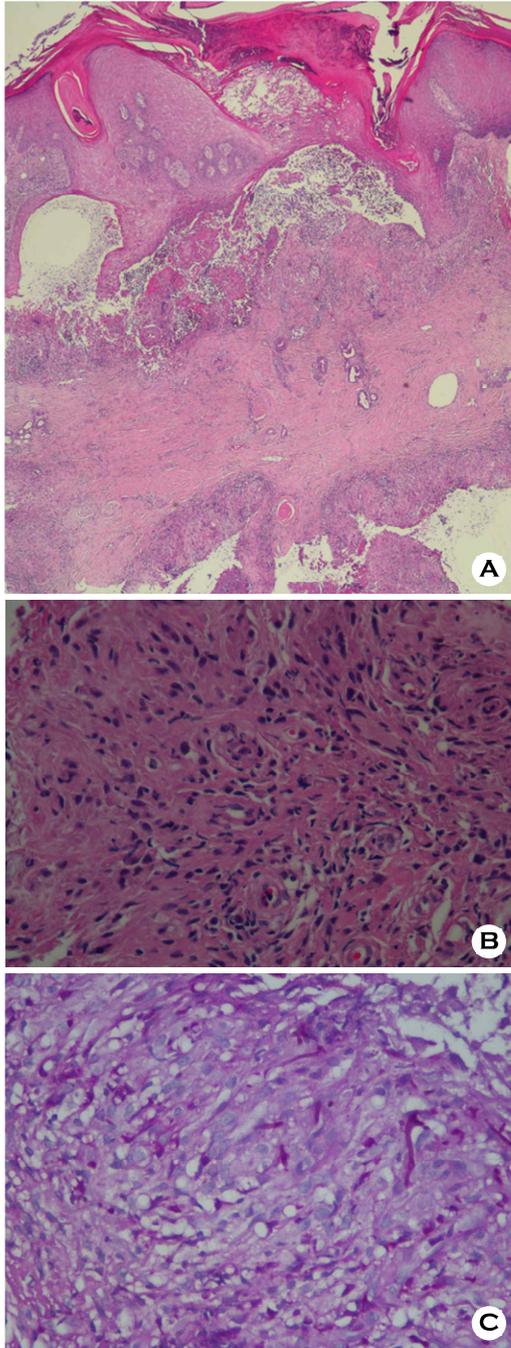


Fig. 2. (A) Diffuse inflammatory infiltration with necrosis in the epidermis and deep dermis (H&E $\times 40$) (B) Chronic granulomatous inflammation including lymphocytes, histiocytes and multi-nucleated giant cell in the dermis (H&E $\times 400$) (C) Multiple non-septated broad hyphae in right angle (PAS $\times 400$)

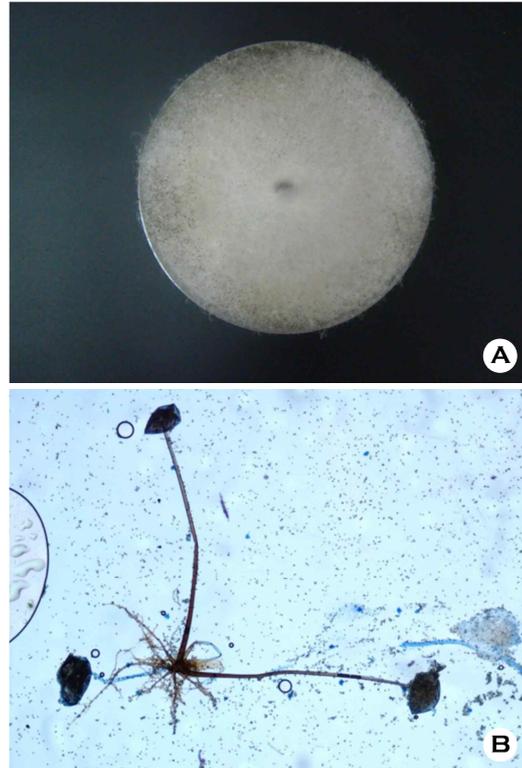


Fig. 3. (A) Rapidly growing whitish to dark brown colony on Sabouraud's dextrose agar at 25°C for 4 days (B) Brown colored rhizoids and unbranched sporangiospores with sporangia on each end in lactophenol cotton blue ($\times 100$)

identified as belonging to *Rhizopus* species of class *Zygomycetes*. Based on the clinical, histopathological and mycological findings, she was diagnosed with cutaneous mucormycosis. After treatment with itraconazole (200 mg/day) for 2 months, the lesions improved with residual hyperkeratosis (Fig. 1B). The patient has been followed up for 5 months without recurrence of symptoms.

DISCUSSION

Mucormycosis is a rare fungal infection that was first reported by Paltauf in 1885⁴. The causative

agent is a ubiquitous saprophytic fungus of the order *Mucorales* and class *Zygomycetes*. Nine genera are included in the order *Mucorales*. *Rhizopus*, *Absidia*, and *Mucor* are the commonly isolated genera from human tissue².

Cutaneous mucormycosis is categorized into two types according to the mode of infection: primary implantation of spore into the skin or secondary hematogenous dissemination from another source, especially pulmonary⁵. Primary cutaneous mucormycosis was first described by Sutherland-Campbell⁶ in 1929, and is of two types⁷. The subacute superficial type is characterized by vesicles or pustules that may progress to eschar. The biopsy specimen does not show characteristic vascular

invasion in this type. The gangrenous type is the more typical form and is characterized by rapidly progressive ulceration and dissemination in immunocompromised patients⁷.

In the present case, the patient's skin lesions were limited to one finger and consisted of multiple papules and pustules, with no systemic signs and symptoms. Based on the findings, the following differential diagnoses were considered: deep fungal infection, dermal tuberculoid granuloma, vasculitis, and herpetic whitlow. On the skin biopsy, both epidermis and deep dermis showed chronic granulomatous inflammation and fungal hyphae. There were no unusual findings on radiological and laboratory investigation. Since *Rhizopus* was isol-

Table 1. Reported cases of primary cutaneous mucormycosis in Korean literatures

Author (Year)	Age/Sex	Site	Duration	Skin lesion	Treatment
Lee et al ¹¹ (1989)	M/54	Chest	10 days	Black crusted plaque	Amphotericin B for 2 weeks
Choi et al ¹² (1991)	M/34	Knee	Non described	Extensive necrosis with eschar	Amphotericin B for 40 days
Jo et al ¹³ (1995)	M/58	Thigh	1 week	Erythematous plaque with eschar	Amphotericin B for 38 days
Kim et al ¹⁴ (1998)	F/32	Wrist	6 months	Angular ulceration	Ketoconazole for 3 weeks and amphotericin B for 2 weeks
Lee et al ¹⁵ (1999)	F/53	Leg	4 days	Black necrosis with bullae	Amphotericin B for 8 days
Song et al ¹⁶ (2000)	F/68	Shin	10 days	Erythematous plaque	Amphotericin B for 23 days
Seo et al ¹⁷ (2006)	F/69	Wrist	10 months	Angular ulceration	Amphotericin B with itraconazole for 40 days
Jun et al ¹⁸ (2008)	M/24	Face	17 years	Extensive crusted plaque	Itraconazole for 10 days and ketoconazole for 4 months with amphotericin B ointment for 1 months
Yang et al ² (2010)	F/77	Wrist	6 months	Erythematous plaque	Non described
Our case (2015)	F/77	Finger	11 months	Erythematous papulopustule	Itraconazole for 2 months

ated on the fungal culture, she was diagnosed with the subacute superficial type of primary cutaneous mucormycosis.

Spores cause fungal infection only after overcoming the host immune response. When *Rhizopus* is inoculated into healthy animals, it does not induce disease because oxidative metabolites of phagocytic cells are fungicidal for *Rhizopus* hyphae. Besides, cationic proteins called defensins also have a fungicidal effect on *Rhizopus* spores and hyphae⁸. The tissue-invasive hyphae are too large to be engulfed completely by phagocytes while neutrophils have been demonstrated experimentally to impair or kill hyphae⁹. In a study involving animals with diabetes and those administered steroids, inhaled spores were shown to have invaded the lung and entered into the bloodstream. Although steroids are thought to influence the host immune system, the precise mechanism has remained largely unknown⁸.

Our patient was administered systemic steroid therapy with methylprednisolone. Her treatment regimen is thought to have induced immunosuppression and the consequent infection.

Most of the reported cases of cutaneous mucormycosis are of the life-threatening gangrenous type with amphotericin B being the treatment of choice. Liposomal amphotericin B is relatively safe at higher doses due to less nephrotoxicity¹⁰. There are reported nine cases in Korean literatures (Table 1). But treatment duration and dosage still remain unclear¹⁷. And amphotericin B cannot be taken orally. Since our patient refused parenteral therapy, an orally administered alternative was chosen. One study reported successful treatment with oral itraconazole, 200 mg/day for 2 months and the patient became culturally negative¹⁹. However, another study found itraconazole as being unreliable against mucormycosis¹⁰. Since this was

a case of subacute superficial cutaneous mucormycosis, which is less severe than the gangrenous type, we treated her with itraconazole monotherapy (200 mg/day). After 2 months of treatment, the skin lesions had improved with residual hyperkeratosis.

In conclusion, this case suggests that treatment with steroids or immunosuppressants can cause deep fungal infection, although its incidence has decreased with the improved infection control measures and hygienic practices for care of immunocompromised patients. In addition, the rare subacute superficial type of cutaneous mucormycosis with milder symptoms than that of the gangrenous type, is amenable to cure with itraconazole monotherapy.

Conflict of interest

The authors declare that they have no conflicts of interest in the research.

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