

Primary Cutaneous Cryptococcosis Successfully Treated With Fluconazole

Jun-Hyoung Park, M.D., Young-Wook Ryoo, M.D., Kyu-Suk Lee, M.D.

Department of Dermatology, College of Medicine, Keimyung University, Taegu, Korea

We report a case of primary cutaneous cryptococcosis on Rt. forehead and perioral area of 57 year old woman with non-insulin dependent diabetes mellitus and Lt. cerebral infarction. She had large ulcers with yellowish purulent exudates on Rt. forehead and perioral area for 2months. A histopathological examination from the lesion showed numerous encapsulated, round spores and the organisms were identified as *Cryptococcus neoformans* in a series of fungal studies. The patient received a 5-week course of IV and oral fluconazole with resolution of her skin lesion. The patient is free of any lesion several months after completing therapy. This experience supports the use of fluconazole as initial and single therapy in primary cutaneous cryptococcosis. (*Ann Dermatol* 12(2) 148~151, 2000).

Key Words : Primary cutaneous cryptococcosis, Fluconazole

Primary cutaneous cryptococcosis is an opportunistic infection caused by direct inoculation of *Cryptococcus neoformans* into skin^{1,2}. To diagnose primary cutaneous cryptococcosis, the lesions limited in skin and there must be no evidence of systemic infection at least for 4weeks of follow up. A series of antifungal agents such as amphotericin B, 5-fluorocytosine, itraconazole and fluconazole in single or combination therapy have been used for the treatment of primary cutaneous cryptococcosis^{3,4,5}. The most chosen treatment was amphotericin B and 5-fluorocytosine but due to serious toxicity the new, better tolerated drugs such as itraconazole and fluconazole have recently been used with good result^{6,7}.

CASE REPORT

A 57-year-old woman was first seen in the derma-

tology department with a chief complaint of large ulcers on Rt. forehead and perioral area for 2months. Initial erythematous macule with erosion developed on Rt. forehead without trauma and then similar lesions developed in a sporotrichoid pattern along the Rt. face and they progressed into large ulcers. In her past history she has been given hypoglycemics irregularly for 7years and suffered from Lt. cerebral infarction 2years ago. A clinical examination showed 4 × 5 cm sized well marginated ulcer with a yellowish purulent exudate and similar lesions sized 2 × 2 cm and 1 × 1 cm were seen on Rt. perioral area (Fig.1). Routine laboratory evaluations revealed elevated glucose level as high as 160mg/dl and chest X-ray revealed no pathological finding. Lumbar puncture for cerebrospinal fluid analysis revealed no abnormality in cell count and chemistry and no organism on Gram stain, potassium hydroxide smear, AFB stain, India ink stain and fungal cultures. Brain CT disclosed multiple ischemic lesions at the both basal ganglia, brain atrophy and hydrocephalus. Skin biopsy specimen from the ulcer of Rt. forehead showed epidermal necrosis and granulomatous infiltration of inflammatory cell throughout the dermis and lots of spores observed in upper dermis(Fig. 2A). On PAS and mucicarmine staining the spores stained red(Fig. 2B). On Gomori methenamine silver stain these are stained black in color. Because 5µm

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Reprint request to : Joo Won Kim, M.D., Department of Dermatology, Korea University Guro Hospital 80 Guro-Dong, Guro-Gu, Seoul, Korea (152-703)

Tel : 02) 818-6161, Fax : 02) 838-2359

E-mail : kughdm@elim.net

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urea agar. After 5 days we could find moist, smooth surfaced and mucoid cream colored colonies on Sabouraud dextrose agar at 37°C. The culture on caffeic acid agar showed dark brown colored colonies at 28°C (Fig. 3) and on urea agar purple colored discoloration due to hydrolysis of urea by the organism. India ink stains from the colonies showed thick encapsulated budding round spores (Fig. 4). For the identification of the yeast we performed API20 test (bio M rieux, france) to identify *Cryptococcus neoformans*. The patient was given IV fluconazole 400mg at first day and then prescribed IV fluconazole 200mg daily for 3 weeks. This treatment led to complete resolution of ulcers without adverse effect attributable to drug. After that, she was given oral fluconazole 100mg a day for last 2 weeks when we performed potassium hydroxide smear and fungal cultures three times but no organism was detected (Fig. 5). The patient is free of any lesion several months after completing therapy.

DISCUSSION

Cryptococcosis is an opportunistic infection caused by *Cryptococcus neoformans* which is found in the excreta of birds, mainly pigeons and

Fig. 1. A 4×5 cm sized well marginated ulcer with a yellowish purulent exudate and similar lesions sized 2×2 cm and 1×1 cm on Rt. perioral area.

sized spore like organisms were detected on potassium hydroxide smear of the specimen from the lesions, multiple fungal cultures performed on Sabouraud dextrose agar, caffeic acid agar, and

Fig. 2. A. Epidermal necrosis and granulomatous infiltration of inflammatory cell throughout the dermis and lots of spores observed in upper dermis (H&E stain, ×200). B. On PAS staining the spores stained red.

Fig. 3. Dark brown colored colonies on caffeic acid agar at 28 °C.

Fig. 5. Complete resolution of ulcers with slight erythema and scar after 5-week course of fluconazole therapy.

chickens and in soil contaminated by the organism^{8,9}. The organism enters the body through the respiratory tract and spreads into central nervous system, eye and prostate hematogenously. Predisposing factors for cryptococcosis are AIDS, hematopoietic malignancies, sarcoidosis and corticosteroid therapy⁹. Our patient has been given hypoglycemics irregularly for 7 years and suffered from Lt. cerebral infarction 2 years ago.

The cutaneous involvement as a secondary spread occurs in 10% to 15% of cases of systemic

Fig. 4. Thick encapsulated budding round spores on India ink stains.

cryptococcosis¹⁰. Skin lesions may appear as papules, nodules, acneiform pustules or abscess. Most often the eruption is superficial but progresses to necrosis and ulceration with time⁸. Primary cutaneous cryptococcosis which is caused by direct inoculation of *Cryptococcus neoformans* into skin is extremely rare^{1,2,11,13}. Clinically primary cutaneous cryptococcosis is manifested as erythematous papule, nodule or ulcerated and indurated plaque in normal person with previous trauma history or immunosuppressed patient^{1,4,11,13}. To diagnose primary cutaneous cryptococcosis, the lesions limited in skin and there must be no evidence of systemic infection at least for 4 weeks of follow up.

Our case was a 57 year old woman with a chief complaint of large ulcers on Rt. forehead and perioral area for 2 months. Clinically we suspected secondary infected herpes simplex, impetigo, sporotrichosis and blastomycosis etc. but a series of laboratory, radiographic, fungal and histopathological evaluation disclosed primary cutaneous cryptococcosis in patient with NIDDM and Lt. cerebral infarction.

The patient received a 5-week course of IV and oral fluconazole with resolution of her skin lesion. The patient is free of any lesion several months after completing therapy. Even though itraconazole and fluconazole have proved to be effective against cryptococcosis recently any clinical trial with fluconazole single therapy for primary cutaneous cryptococcosis is reported in Korea. So this experience supports the use of fluconazole as initial and single therapy in primary cutaneous cryptococcosis.

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