FLUCONAZOLE AND FIRE NEEDLE THERAPY TO TREAT CHROMOBLASTOMYCOSIS: A CASE REPORT AND LITERATURE REVIEW

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Abstract. Chromoblastomycosis (CBM), a chronic subcutaneous infection caused by traumatic inoculation of a dematiaceous fungus, may be associated with severe morbidity and is difficult to treat. We report here the case of CBM in a 67-year-old male who presented to our institution with a 4-month history of skin lesions on the dorsum of the right hand. He was treated with a combination of fluconazole and fire needle therapy (acupuncture using red-hot needles) to eradicate lesions. The lesions resolved after 2 months of treatment and he had no further relapses. We also review the treatment of CBM in the literature. Further studies are needed to determine if this combination of fluconazole combined with fire needle therapy may be a possible treatment option for CBM.

Keywords: chromoblastomycosis, fluconazole, fire needle, adjuvant therapy

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INTRODUCTION

Chromoblastomycosis (CBM), or chromomycosis, is a chronic, progressive subcutaneous fungal infection characterized by pigmented muriform cells in the tissue (Queiroz-Telles *et al*, 2017). CBM occurs primarily in tropical and subtropical regions of Africa and Latin America (Queiroz-Telles *et al*, 2009). CBM has been declared a neglected tropical disease (NTD) by the World Health Organization (WHO, 2023). CBM affects mainly low socioeconomic status workers in rural areas, such as farm laborers and gardeners (WHO, 2023). CBM occurs when the causative fungus enters the body through an open wound and is more common on unprotected extremities (Queiroz-Telles *et al*, 2017). CBM lesions are categorized as mild, moderate or severe based on the appearance of the lesions, where mild CBM is characterized by single scales or nodules <5 cm in diameter; moderate CBM is characterized as having single or multiple lesions of tumoral, verrucous or plaque type which may be isolated or conjoined, covering one or two adjacent body areas and having a diameter of <15 cm; severe CBM is defined as having single or multiple lesions of any type covering extensive skin areas that may be adjacent to each other or distant from each other (Krzyściak *et al*, 2014). Untreated, CBM can increase the patient's risk for getting secondary bacterial infections and developing skin fibrosis or even skin cancer (Mohanty *et al*, 2017; Queiroz-Telles *et al*, 2017; Marques *et al*, 2019). Treatment of CBM is not standardized and can be difficult. Itraconazole, terbinafine, posaconazole, amphotericin B, 5-fluorocytosine and fluconazole have all been used, sometimes unsuccessfully, to treat CBM (Pan *et al*, 2022; Logan *et al*, 2023; Guevara *et al*, 2022; Sendrasoa *et al*, 2020). Surgical excision, cryotherapy, electrical cautery, laser vaporization and photodynamic therapy have been used as adjuvants to antifungal therapy (Yang *et al*, 2018; León-Lara *et al*, 2022; Shen *et al*, 2022; Lan *et al*, 2021) to treat CBM. In China, fire needle therapy, a type of acupuncture where the needle is heated until red-hot and then quickly inserted into the affected area, has been used to treat various skin conditions, such as scaly hyperplastic skin lesions and infectious exudative skin lesions (Xing *et al*, 2019; Liu *et al*, 2020; Sterling *et al*, 2014). Fire needle therapy characterized by

"giving equal weight to needling and scorching, stressing warming and unblocking"; "rapid needle insertion and withdrawal" and"needling based on pattern differentiation"; have the double function of acupuncture and moxibustion (Wang, 2017). This technique is thought to regulate immunity, control inflammation, drain pus and reduce swelling, dissipating the nodule (Luo *et al*, 2019).

Fire needle diameters may be thick, average or thin. The thickness of the average needle is 0.8 mm and this is the most commonly used needle for acupuncture (Wang, 2017).

We report here a case of CBM treated using fluconazole and fire needle therapy. We also review the literature regarding the treatment of CBM. To our knowledge, this is the first reported case using a combination of fluconazole and fire needle therapy to treat CBM. This study was approved by the Ethics Committee of the Ninth People's Hospital affiliated with the Shanghai Jiao Tong University School of Medicine (Approval No: SH9H-2022-TK300-1). The patient reported here gave consent to have this case reported.

CASE REPORT

A 67-year-old farmer presented to our institution with a 4-month history of progressively enlarging lesions on the dorsum of his right hand. The skin lesions initially started as a 1×2 cm nodule on the dorsum of his right hand. The nodule was incised and drained at a local clinic but after this the lesion continued to expand to 5×6 cm and developed black discoloration and raised edges, became painful, had an unpleasant odor and caused limited range of motion of the hand. He denied having fever. He was treated with topical fluticasone propionate ointment, moxifloxacin ointment, compound polymyxin B ointment, naproxenone conazole cream and oral clarithromycin and ciprofloxacin, all without improvement. His risk exposure history was significant only for working on a farm.

His past medical history was significant for essential hypertension, type 2 diabetes mellitus, chronic kidney disease, a cerebral hemorrhage and psoriasis, but for psoriasis he was not taking immunosuppressant medication. He had no history of weight loss.

On physical examination the patient's vital signs were normal and he was afebrile. The dorsum of the right hand had a 7×6 cm lesion that was black, firm, minimally mobile and had a foul smell. He was unable to flex the right hand due to stiffness. There were no other skin lesions. He had no lymphadenopathy in the right arm. The rest of the physical examination, including the liver and spleen, was normal (Figs 1A and B).

A complete blood count showed a white blood cell count of 7.4×10^9/l with 68.6% neutrophils, 19.4% lymphocytes and 7.5% monocytes. His erythrocyte sedimentation rate was 49 mm/hour, his c-reactive protein was <0.80 mg/l and his procalcitonin level was 0.16 ng/ml. His estimated glomerular filtration rate was 16 ml/min/1.73 m^2. His liver function testing was normal and coagulation studies were normal.

Fig 1 - Photographs of study subject CBM lesions

A and B: prior to treatment showing well-defined, irregularly shaped plaques on dorsum of the patient's right hand, characterized by a red crust containing black dots and hyperkeratotic plaques; C-E: after 2 months treatment showing a noticeable reduction in scale and plaque is evident; F and G: at one year follow up showing complete resolution of the patient's CBM lesions; H: fire needle treatment of the patient

CBM: chromoblastomycosis

An acid-fast stain of a swab obtained from the skin lesion was negative for acid fast bacilli. He had a negative tuberculin skin test. A fungal culture of the lesion yielded *Candida*, which was assumed to be a commensal organism. A bacterial culture of the lesion yielded both *Klebsiella pneumoniae* and *Enterococcus faecalis*. Metagenomic sequencing of a swab obtained from the lesion identified *Candida, Enterococcus faecalis, Klebsiella pneumoniae* and *Bacteroides fragilis.*

A biopsy of the lesion showed epidermal papillomatous growth with marked hyperkeratosis, focal incomplete coagulation, micro-abscesses and an old hemorrhage. Part of the biopsy specimen had colony-like structures with collagen proliferation, dermal fibrosis, hyperplasia, dilation of the small blood vessels, perivascular infiltration with lymphocytes, plasma cells, scattered neutrophils, isolated eosinophils and occasional multinucleated giant cells. Hematoxylin-eosin staining showed collagen proliferation (Fig 2A), papillomatous growth (Fig 2B), micro-abscesses (Fig 2C), inflammatory cell infiltration (Fig 2D), hyperkeratosis (Fig 2E), fibrosis and multinucleated giant cells. Fungal culture and metagenomic sequencing analysis of the pus did not detect the presence of pathogenic fungi.

The patient was then diagnosed with having chromoblastomycosis with a secondary bacterial infection and the presence of underlying essential hypertension, type 2 diabetes mellitus, chronic kidney disease, a history of cerebral hemorrhage and psoriasis.

The patient was then treated with intravenous fluconazole (200 mg/day), meropenem (1,000 mg/day) and linezolid (600 mg/day) for one month. He was also treated with fire needle therapy (Fig 1H) with the needles placed in the skin lesion to a dept of 0.2-0.3 cm and repeated 20-30 times for each area penetrated. The treatments were spaced 0.5 cm apart (Fig 1H) and given every other day for 1 month.

With this treatment, the inflammation decreased, the odor improved and the lesion decreased in size until the patient was discharged from the hospital. He was continued on treatment as an outpatient with oral fluconazole (200 mg/day), linezolid (600 mg/day) and fire needle therapy (Figs 1C, 1D and 1E) for an additional month. The patient's CBM

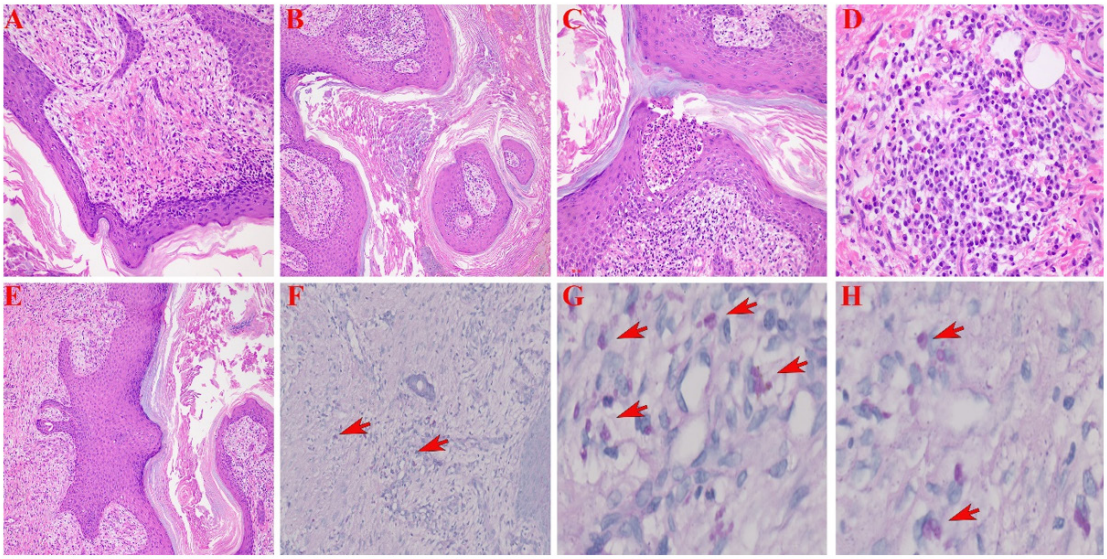

Fig 2 - Pathology of biopsy specimen from study subject

A-E: hematoxylin-eosin stain showing: collagen proliferation (×200) (A), papillomatous growth (×100) (B), micro-abscesses (×200) (C), inflammatory cell infiltration (×400) (D), hyperkeratosis (×100) (E)

F-H: Periodic acid-Schiff stain showing muriform cells (red arrows) within a granulocyte abscess (×200) (F), pigmented muriform cells (red arrows) (×400) (G and H)

CBM: chromoblastomycosis.

lesion resolved completely without evidence of recurrence for one year of follow-up (Figs 1F and 1G). The patient did develop a relapse of his psoriasis during the one year follow up period.

DISCUSSION

CBM treatment duration has been reported to vary from 12 to 48 months (Mouchalouat *et al*, 2011). CBM reported treatment methods consist of antifungal agents, physical methods or their combination (Yang *et al*, 2018; León-Lara *et al*, 2022; Shen *et al*, 2022; Lan *et al*, 2021). However, there is no recommended standardized treatment for CBM due to the lack of high-quality comparative clinical trials. Until such studies occur, we believe treatment should be patient based,

depending on the causative pathogen, lesion severity and infection complications.

Fluconazole has not been commonly reported for the treatment of CBM but it has been used to treat deep mycoses (Diaz *et al*, 1992). In this patient, we decided to treat using fluconazole based on the fungal culture, sequencing results and previous severe CBM cases treated successfully with fluconazole monotherapy (Table 1). However, patients of advanced age, who have diabetes, prolonged CBM disease may not respond well to monotherapy (Yang *et al*, 2013). Given our patient's risk factors we decided to use a combination of fluconazole and fire needle therapy.

In our patient, we used fire needle therapy in addition to fluconazole. Fire needle therapy has been reported to be effective in reducing recurrence rates when used in combination with oral medication to treat skin diseases (Liu *et al*, 2021). The reason for its use against fungal skin disease is the high temperature kills the fungus in thickened keratotic skin lesions (Pan *et al*, 2019). This is especially true with CBM (Lan *et al*, 2021). The fire needle cauterizes the stratum corneum, resulting in necrosis and sloughing of the keratotic lesions eliminating the fungus and reducing recurrence (Zhang *et al*, 2021). CBM is associated with poor local immunity (Logan *et al*, 2023). The inflammatory response caused by the fire needle therapy simulates the immune response and improves blood flow (Luo *et al*, 2019).

The combination of the fire needle therapy with antifungal therapy in this reported patient resulted in a relatively shorter treatment course of 2 months as compared to monotherapy with an antifungal medication to treat CBM which can take up to 12 months with itraconazole or terbinafine (Brito and Bittencourt, 2018) or up to 8 months with fluconazole (Table 1). A shorter treatment course should result in better treatment adherence.

In summary, we successfully treated this patient with dermal CBM using fluconazole and fire needle therapy in a relatively short period without serious complications or recurrence. We conclude this combination may be an effective treatment option. Further studies are needed to determine the efficacy of this combination to treat other CBM patients.

Table 1

Review of previously reported cases of CBM treated with fluconazole monotherapy

Reference	Country		Disease duration	Age in years/sex	Dose and duration of fluconazole treatment	Prognosis
Sharma *et al*, 2010	India	Case 1	8 months	16/male	150 mg/day x 6 months	Improved
		Case 2	19 years	55/male	150 mg/day x 6 months	Improved
Naveen *et al*, 2012	India		15 years	35/female	150 mg/day x continuing treatment	Improved
Yu and Gao, 1994	China		12 years	53/male	200 mg/day x 30 days, then 50 mg/day x 2 years	Cured
Sendrasoa *et al*, 2020	Madagascar		10 years	63/male	100 mg/day x 3 months	Improved
Guerriero *et al*, 1998	Italy		5 years	40/female	NA	Improved

CBM: Chromoblastomycosis; mg: milligram; NA: not available

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CONFLICT OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

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