Coexisting Chromoblastomycosis and *Mycobacterium fortuitum* Skin and Subcutaneous Infection

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Abstract

We report a diabetic patient with coexisting skin and subcutaneous infection of chromoblastomycosis and *Mycobacterium fortuitum*. Cultures of these skin lesions or discharges frequently fail to demonstrate these organisms. Aggressive skin biopsy revealed finding and diagnosis of chromoblastomycosis and *Mycobacterium fortuitum*. We performed repeat skin biopsies and tissue cultures for this patient. The culture of right arm yielded *Fonsecaea pedrosoi* and the culture of left arm yielded *Mycobacterium fortuitum*. Preferred treatment is usually surgical excision or cryosurgery with liquid nitrogen for small lesions of chromoblastomycosis but we administered itraconazole 200 mg per day for 6 months and the lesions completely recovered with only the sequelae of pigmentation. The *Mycobacterium fortuitum* infection of left arm was cured with 8-month combination therapy of levofloxacin, clarithromycin, and 7-month treatment of amikacin. Duration of treatment depends on the clinical response and achievement of mycologic and histopathological cure. (J Intern Med Taiwan 2008; 19: 365-370)

Key Words: Chromoblastomycosis, *Fonsecaea pedrosoi*, *Mycobacterium fortuitum*
Background

Chromoblastomycosis (chromomycosis) is a chronic localized fungal infection of the skin and the subcutaneous tissue caused by traumatic skin and inoculated with dematiaceous fungi (usually Fonsecaea pedrosoi, Fonsecaea compacta, Phialophora verrucosa or Cladosporium carrionii). The lesions are frequently localized in the feet or legs of outdoor persons associated with farming and woodcutting and warty or cauliflower-like in appearance. This disease is found worldwide and frequently reported from Madagascar and Brazil, rarely reported from North Africa and Asia. We report a diabetic patient with simultaneously coexisting cutaneous infection of chromoblastomycosis, Mycobacterium fortuitum and mucormycosis.

Case

A 74-year-old woman had been a patient of hypertension known for 20 years, diabetes known for 4 years and received regularly medication control from the physicians. Besides, she often complained of low back pain and received some injection drugs to relieve her discomforts. She also frequently helped her son to feed some salt-water fishes which they cultivated near her home.

She had poorly healing wound (4 × 8 square cm) over right lower leg. This wound showed necrotic change and poorly responsive to vancomycin and ceftriaxone infusion in December, 2005. She received above knee amputation on December 21th, 2005. The histopathological examination of the wound showed compatible with mucormycosis (Figure 1). No antifungal regimen was administered for the mucormycosis because of the clean amputation wound.

She was also noted that she had papules and plaque lesions over her right forearm at the same time. But she could not remember how long she had these lesions or any trauma history. The skin biopsy was performed and the haematoxylin and eosin staining of sections showed suppurative granulomatous inflammation and presence of round, yellow-brown, thick-walled sclerotic bodies extracellularly pathognomonic with chromoblastomycosis. (haematoxylin and eosin stain, 10 × 40)

After 2 months of treatment, the right forearm lesions showed progression with ulcerating and necrotic change. Multiple nodular lesions (from 0.1
We performed skin biopsy on both arms again and the histopathological examination of the left arm showed atypical mycobacterial infection with suppurative granulomatous inflammation. Lowenstein Jensen media yielded *Mycobacterium fortuitum* and the isolate was only sensitive to amikacin and kanamycin. The histopathological examination of the right forearm showed chromoblastomycosis and the culture on Sabouraud’s dextrose agar at 37 °C yielded elevated and granular brownish black colonies. *Fonsecaea pedrosoi* identification was confirmed by microscopic colony morphology.

We kept itraconazole 200 mg per day for the patient because she was very thin and old age. The right forearm lesions of chromoblastomycosis improved progressively and completely recovered after 6-month itraconazole treatment with only the sequelae of pigmentation. The left forearm nodular lesions due to *M. fortuitum* infection improved slowly to the combined regimen of levofloxacin 500 mg and clarithromycin 1000 mg per day, even for one-month treatment. Then we added amikacin 300 mg intramuscular injection twice a week. The left forearm lesions had improved and nodular lesions disappeared after 8-month combination therapy of levofloxacin, clarithromycin, and 7-month treatment of amikacin. We stopped these drugs for one month and there is no any more skin lesion noted again.

Because this is a very rare case that several unusual skin and subcutaneous infections including mucormycosis, chromoblastomycosis, and *Mycobacterium fortuitum* coexisted in this patient. We performed several examinations for her to survey the underlying disease except diabetes including white blood cell and differential count, cortisol level, antinuclear antibody, C3, C4, HIV antibody, immunoglobulin A, G, M, protein electrophoresis, and Nitroblue tetrazolium test. These examinations all showed negative finding or the results were within normal level.
Conclusion

Chromoblastomycosis is a chronic fungal infection of the subcutaneous tissues, extend slowly, and may spread along the lymphatic drainage or autoinoculation to neighboring areas of the skin. The infection often results from a traumatic injury and the patient often doesn’t remember how long she or he has had it. Chromoblastomycosis (chromomycosis) is inoculated with dematiaceous fungi (usually Fonsecaea pedrosoi, Fonsecaea compacta, Phialophora verrucosa or Cladosporium carrionii).

Fonsecaea pedrosoi is the most common dematiaceous fungi causing the chromoblastomycosis. The conidiophores of Fonsecaea pedrosoi are septate, erect and compactly sympodial. Fonsecaea pedrosoi's elongate conidia differ from Rhinocladiella type and are not like the Phialophora's phialides with vase shaped and terminal cuplike collarettes. The conidiophores of Cladosporium are septate and have large primary shield-shaped conidia that produce short branching chains of oval conidia having small dark hila. Fonsecaea pedrosoi identification was confirmed by microscopic colony morphology with these differences. The organisms often gain entry into the human body by direct contact with wood splinters, soil or thorns. The most common appearance is warty, nodular, verrucous or cauliflower-like in appearance. Some lesions may heal spontaneously with scarring. These lesions are not easy to cure and produce complications like squamous cell carcinomatous degeneration, ulceration, lymphedema of the affected limbs, and secondary infection.

Because of the chronic lesions, it is difficult and prolonged time is needed to treat chromoblastomycosis. The preferred treatment is usually surgical excision or cryosurgery with liquid nitrogen for small lesions, residual lesions that are not located in areas of flexion. But for larger lesions more than 15 square cm, itraconazole 200 to 400 mg daily regimen with or without flucytocine is a common treatment choice and have favorably clinical outcome. The duration of treatment is often more than 12 months until the clinical and mycologic cure are achieved without any pathologic evidence of chromoblastomycosis. Terbinafine 500 mg daily or oral pulse itraconazole 400 mg daily, for 7 days each month are another choices of regimens for treatment. In our patient, we had administered itraconazole 200 mg per day for 6 months and her right forearm lesions had improved progressively. No relapsed lesion was observed after 6-month followed up.

*Mycobacterium fortuitum* is a rapidly growing mycobacteria and appears ubiquitously in water and soil. It causes cutaneous infections through trauma or clinical procedures. This patient frequently helped her son to feed some salt-water fishes which they cultivated near her home and had the potential risks of trauma, mucormycosis, chromoblastomycosis and *M. fortuitum* infections. *M. fortuitum* often showed resistance to clarithromycin and this could explain that our patient initially had the poor response to clarithromycin and levofloxacin. We changed to amikacin 300 mg intramuscular injection every 3-day interval and then the left forearm lesions improved dramatically.

This patient had the initial presentation of poorly healing wound over right lower leg and poorly responsive to vancomycin and ceftriaxone infusion. The diagnosis of other infections of fungal or mycobacterial infections should be suspected and challenged. Cultures of these organisms frequently fail to demonstrate these infections because they are not held long enough time to yield or no live organisms are obtained. Skin biopsies and tissue cultures help to identify the real organisms caused these infections and this procedure seems to be more sensitive than using swab wounds.

*Mucormycosis* is caused by ubiquitous fungi of the order Mucorales and can be found in the soil and decaying vegetation or wood. *Rhizopus* species are the most common isolated agents. Cutaneous mu-
Cromycosis is caused by spores introduced into injured skin associated with trauma or wounds. Diabetes mellitus with hyperglycemia impair neutrophil functions as adhesion, chemotaxis, phagocytosis, and impair complement opsonization. In this patient, she has hyperglycemic status, frequently received injection therapy, and the risk factors of easily acquired cutaneous mucormycosis from the environment. The main therapy to treat cutaneous mucormycosis is to do surgical debridement. If the lesions invade the subcutaneous tissue and muscle, extensive debridement, systemically administered amphotericin B (1 mg/kg per day IV) and correct underlying medical conditions are advised. This patient received above knee amputation and no further antifungal regimens was administered because of the clean amputation wound.

Concurrent superinfection of chromoblastomycosis and aspergillosis, actinomycetoma or mycetoma were reported but to the best of our knowledge this is the first reported case of simultaneous coexisting skin and subcutaneous infection of chromoblastomycosis, and *Mycobacterium fortuitum* in the English literature.

References

在一位糖尿病人身上同时存在的產色黴菌病和偶發分枝桿菌的皮膚和皮下感染

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摘  要

這篇是報告在一位糖尿病人身上同時發病的皮膚和皮下產色黴菌病和偶發分枝桿菌感染的個案。光用傷口培養的方式很難去診斷這些感染。必要積極的做皮膚切片才能去發現和診斷產色黴菌病、偶發分枝桿菌所引發的感染。我們為這位病人做了重覆的傷口切片和組織培養，右手的切片培養出產色黴菌而左手的傷口切片培養出偶發分枝桿菌。一般建議的治療方式是外科切除或用液態氫的冷凍療法來治療小範圍的產色黴菌病但我們是用itraconazole 每天200毫克持續六個月的治療，左手傷口偶發分枝桿菌所引發的感染則是用八個月的levofloxacin 和clarithromycin 合併治療及七個月的amikacin 肌肉注射治療，這些傷口最後痊癒而只留下色素沉著的後遺症。治療時間的長短必需依據臨床的反應和黴菌學及組織病理學上的痊癒。