

Multiple Cerebral Abscess Caused by *Cladophialophora bantiana*

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ABSTRACT

Multiple cerebral abscess caused by *Cladophialophora bantiana* (*C. bantiana*) is a rare disease. A 36 year-old healthy male, presented with progressive right hemiparesis, seizure and left frontal lobe mass. He failed to respond to empirical treatment with broad spectrum antibiotic. The aspiration of his brain abscess grew *C. bantiana*, so he was treated with antifungal therapy and subsequently with surgical removal of all abscesses. Despite the high mortality rate, he survived with remarkably improved cognition and right side weakness (after four years follow up).

Keywords: Cerebral abscess, *Cladophialophora bantiana*, immunocompetence, antifungal therapy, surgery

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INTRODUCTION

Cerebral abscess is a life threatening condition and has a high morbidity and mortality rate. 96.5% of cases in Suratthani hospital are caused by bacterial infection and less than two percent by fungal infection in immunocompetent patients.¹ Phaeohyphomycosis refers to infection caused by darkly pigmented fungi, which contain melanin in their cell walls. There were 101 cases of culture proven primary cerebral phaeohyphomycosis reported in the English language literature from 1966 to 2002, and 47% of cases were *C. bantiana*.² More than one half of the cases occur in immunocompetent patients. It has a mortality rate of about seventy percent regardless of immune status. The combination treatment with antifungal drugs, such as Amphotericin B and Itraconazole, and a complete excision of abscess will lead to a greater survival outcome.³ This infection has never been reported in Thailand before, although, there was a case with concomitant late soft tissue infection with mycobacterium abscess following a tsunami injury.³

CASE REPORT

A 36 year old healthy farmer presented with 2 days history of progressive right side weakness. He had no significant past medical history, except for an incident where he almost drowned one month ago. His physical examination revealed a well developed male who was alert and oriented, with normal fundi and afebrile. He had right hemi facial paresis, right hemiparesis with motor power grade III, normal deep tendon reflex. The rest of his physical examination was unremarkable. He had a normal complete blood cell count, fasting plasma glucose, electrolytes, renal function, liver function and urine analysis. HIV antibody, toxoplasmosis antigen, Cryptococcal antigen, VDRL and TPHA were all negative. A brain computerized tomographic study (CT brain) revealed a brain abscess 1.7 x 1.9 cm. at his left frontal lobe with increased rim enhancement and florid perilesional edema. (Fig 1A) A provisional diagnosis of left frontal lobe, pyogenic brain abscess was made and the patient was treated with ceftriazone 4 gm/day. His clinical condition went downhill (status - on endotracheal intubation with respirator, semicomatose, seizure, right hemiplegia motor power grade I). A repeated CT brain was done 3 weeks after, which showed multiple brain abscesses, with the largest size being 2 x 1.9 cm. at his left frontoparietal lobe with increased falcine herniation (1.2 cm) (Fig 1B). He received phenytoin, sodium valproate, intravenous mannitol

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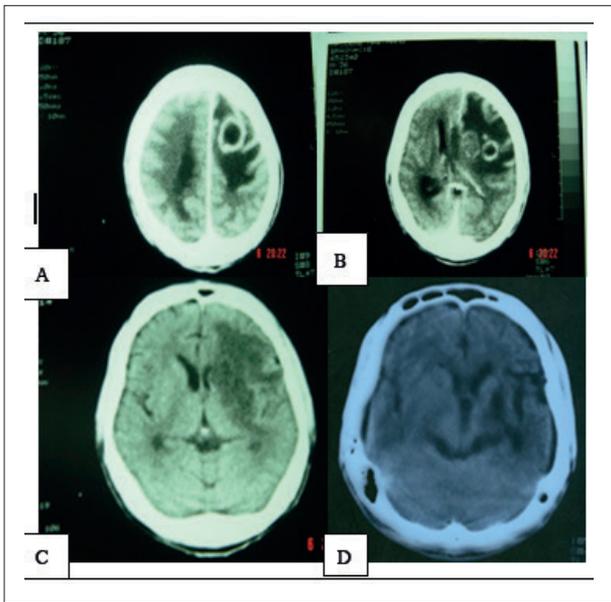


Fig 1. CT Brain: (A) A single brain abscess at left frontal lobe. (B) Multiple brain abscesses at left frontoparietal lobe with 1.2 cm. falcine herniation. (C) Post-operation 6 wks showed focal encephalitis left frontoparietal lobe. (D) Four years later show old cerebral infarction at left internal capsule and lentiform nucleus.

and left frontal craniotomy with abscess aspiration performed. Direct gram stained preparation of pus revealed a few white blood cells, a few septate hyphae with single cells in long branch chains, oval conidia, but no bacterial organism was found and no growth on bacterial culture. The sample was further cultured on Sabouroud dextrose agar (SDA) plain, SDA with gentamicin, and SDA with actidion. All tubes showed colonies with an olive grey

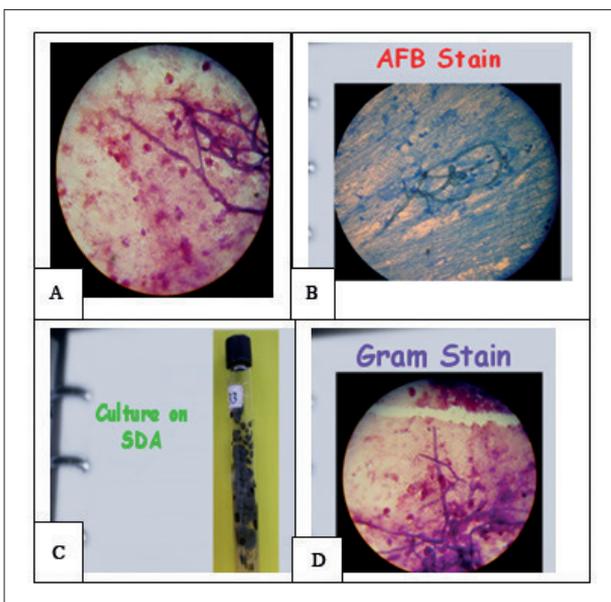


Fig 2. Pus from aspiration of brain abscess: (A) Gram' stain: (B) AFB stain and (D) Gram' stain from culture specimen showed septate hyphae with single cell in long branch chain, oval conidia, no bacterial organism, no AFB. (C) Tube from culture in SDA showed colonies with an olive grey velvety appearance with a black under surface.

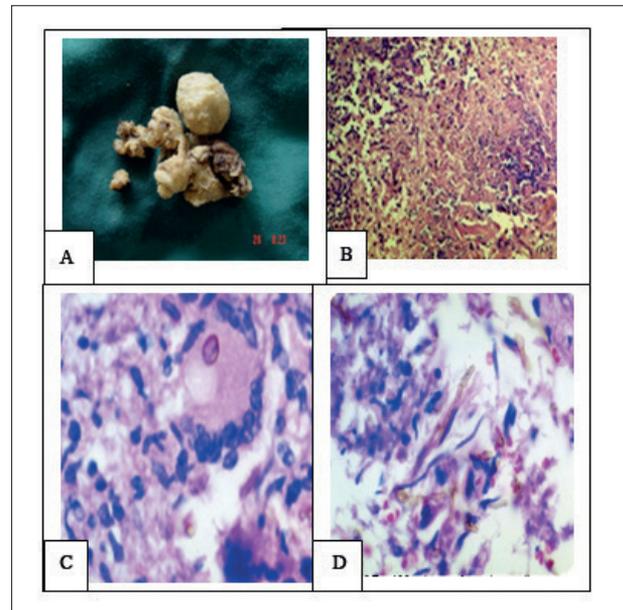


Fig 3. (A) Brain necrotic tissue from surgical removal-yellowish brain tissue with some hemorrhage. (B) H/E x 100 showed caseous granulomatous inflammation. (C) H/E x 400-brown fungus mycelia, phagocytosed by Langhans Giant cell. (D) H/E x 400 showed brown fungus mycelium.

velvety appearance with a black undersurface. (Fig 2C, 2D) The identification of *C. bantiana* was unavailable at this hospital. The culture specimen was finally identified by the Department of Medical Science in Bangkok, Thailand. The patient received intravenous amphotericin B and oral itraconazole 400 mg/d. His condition worsened (progressive motor weakness from grade I to zero on the right side and from grade IV to III on the left side, with high fever). CT. brain showed more abscesses in the left frontoparietal lobe (diameter of 1.5, 2-2.5 cm.) with midline shift of 1.2 cm. (Fig 1B) The patient underwent a second craniotomy and total abscess excision 18 days after the first.

The histopathological finding showed multiple pieces of necrotic brain tissue with black pigment in some areas. (Fig 3A) Microscopic examination showed caseous granulomatous inflammatory response with fungal mycelium in his brain tissue. (Fig 3B, 3C, 3D) The pathological diagnosis was fungal granulomatous brain abscess. There were no apparent sources of fungus in his body, and he had a normal echocardiogram. He received a total cumulative dose of intravenous amphotericin B 2.9 gm, plus four weeks of 400 mg/d of itraconazole orally. His hospital course was complicated by postoperative *Klebsiella pneumoniae*, which was treated with antimicrobial drug. He gradually recovered with few neurological deficits (no fever, good consciousness, right hemiparesis gr.II) and CT brain showed left frontoparietal lobe encephalitis (Fig 1C).

Four years later, the patient was on oral phenytoin. CT brain demonstrated a focal left hypodense area at his left high parietal lobe, at the craniotomy site, unchanged from the old infarct in his left internal capsule and lentiform nucleus. (Fig 1D) Currently he is doing well, except for mild right hemiparesis.

DISCUSSION

Cerebral phaeohyphomycosis is a term used to describe the dark pigmented fungal infection which involves the cerebrum. *Cladophialophora bantiana* is the most frequently isolated species, because of its affinity to glial tissue which is a soil based neurotrophic fungus.² This organism is found in soil, wood, and decaying vegetable matter throughout the world. Most of the cases occur in rural areas where there is occupational exposure to them. *C. bantiana* infection is common in subtropical non-arid climate zones. 44% of cases have a history of occupational exposure. *C. bantiana* can cause a disseminated fatal infection, as well as pulmonary, cutaneous, subcutaneous, cerebral abscess and myelitis. Pathogenicity is due to melanin which can scavenge free radicals produced by phagocytic cells. The most possible source of infection in this patient was water or soil at the shrimp farm which he aspirated at the time of his near drowning accident. In a prior report, this is a common fungal brain abscess in immunocompromised patients and those receiving organ transplantation,^{5,6} but now it is frequently found in immunocompetent hosts. The clinical presentation of *C. bantiana* brain abscess is only 4% presented with classical triad of brain abscess.^{2,7} This patient had presented with right side hemiparesis. The most important determination for cure is resectability of the lesion.^{3,8,9} Antifungal therapy alone is not associated with improved survival rate. The current recommendation is a combination of total surgical removal of brain abscess follow by systemic antifungal therapy² such as amphotericin B, liposomal amphotericin B which has increased potency and reduced toxicity especially nephrotoxicity.¹⁰ The newer azoles, itraconazole, voriconazole, have been found more effective in treatment because of they have good penetration to cerebrospinal fluid and brain tissue.^{11,12} The mortality rate varies from 34-73%, regardless of the immune status.² This patient was immunocompetent and underwent total surgical removal of his brain abscesses followed by systemic amphotericin B and oral itraconazole. Fortunately he was cured with minimal disability. However, he continues taking anti-epileptic drug.

In conclusion, we successfully treated a case of *C. bantiana* brain abscess, with the combination of total surgical removal of the lesions and antifungal agents. This is probably the first reported case of multiple cerebral abscesses caused by *Cladophialophora bantiana* in Thailand.

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