CASE REPORT:

CLADOPHIALOPHORA BANTIANA AND CANDIDA ALBICANS MIXED INFECTION IN CEREBRAL ABSCESSES OF AN HIV-NEGATIVE PATIENT

Ton Nu Phuong Anh ¹, Pham Van Linh², Truong Quang Anh ¹, Tran Duc Thai ³, Nguyen Thi Hoa ¹

(1) Department of Parasitology, Hue University of Medicine and Pharmacy
(2) Department of Surgery, Hue University of Medicine and Pharmacy
(3) Gamma Knife Center & Neurosurgery Division, HUMP

Abstract:

Cladophialophora bantiana is a black fungus recorded rarely as a cause of brain abscess. We describe the first case seen in Vietnam. A 35-year-old, previously healthy male, HIV negative, came to the hospital with a clinical diagnosis of brain tumor. He underwent surgery to remove the well-delineated circumscribed lesion. Pathology, directed physical examination and mycological examination revealed an abscess due to Cladophialophora bantiana, and Candida albicans. After two weeks of treatment with Fluconazole 400 mg per day intravenously, the clinical response remained unsatisfactory. Therapy was then withheld per the family's request.

Keywords: Cladophialophora bantiana, Candida albicans, fungus, cerebral abscess.

1. INTRODUCTION

Cladophialophora bantiana is a chromogenic filamentous fungus. This dematiaceous fungus is highly neurotropic and has been reported to cause uncommon central nervous system infections [12]. The route for entry of this fungus is unknown but infections have been reported in immune-suppressed and organ transplant individuals [2,7,9]. Only a few cases have been reported in the literature worldwide and treatment has often been unsuccessful [4,6,10,11]. Mark K. Lyons (USA) reported successful treatment with Voriconazole [9]. Cladophialophora bantiana saprophytes are found worldwide in soil, plant, and matter. This fungus is known to cause contamination in laboratories [2]. Cladophialophora bantiana is observed as a golden brown filament; the colour is due to melanin in the cell wall [12].

2. CASE REPORT

The male patient, L.V.T., came from Thanh Hoa province, Vietnam. He was 36 years old, and employed as a fruit worker in a vegetable distributing factory in a Ho Chi Minh City (HCMC) market. The patient did not have a history of immune-suppression or transplantation but had a smoking habit. In 2002, he had a motorbike accident which resulted in head trauma with minor cerebral thrombosis. The patient was treated with medication and returned to normal health. Three months previous to our current examination, he presented at a HCMC district hospital with right extremity weakness, mild loss of function control, and mild convulsions. Right cranial magnetic resonance imaging (MRI) was conducted and resulted in the diagnosis of a right parietal occipital region tumor due to cancer metastasis. The patient was referred to Gamma Knife Center of the

Hue University Hospital for treatment. Upon examination, the patient was lucid with a mild headache, and mild left hemiplegia. The patient tested positively for HbsAg and negatively for HIV. Magnetic resonance imaging (MRI) of the brain revealed a tumor-like image in the right parieto-occipital region (Figure 1). The patient was diagnosed with a primary brain tumor of the right parieto-occipital region. The treatment included surgery to remove the well-delineated, circumscribed lesion. Histopathology, direct examination and culture of the lesion were performed. Pathology revealed central necrosis and granulomatous tissue in the periphery and the presence of fungus hyphae. In the mycological laboratory, direct examination with KOH 30% revealed pigmented hyphae and yeast-like cells (Figure 2).

Figure 1. Brain abscess on MRI image

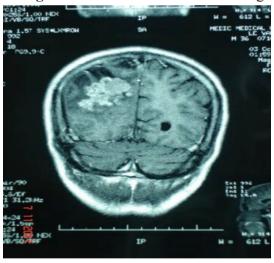
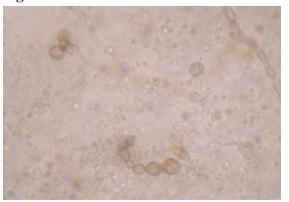


Figure 2. Direct examination with KOH 30%

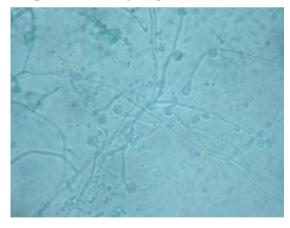


The lesion was routinely cultured on Sabouraud agar with chloramphenicol at room temperature and 370°C. After 48 hours, the yeast colonies grew better at 370°C temperature than at room temperature with milky white colonies. In addition, small black pigment septate hyphal colonies were observed. We prepared a germ tube test with egg yolk, urease test and culture on cornmeal agar to identify the yeast as *Candida albicans* (Figures 3,4) [1,3,5,7,8,13,15].

Figure 3. Germ tube test with egg yolk to identify *C. albicans*



Figure 4. Chlamydospore of *C.albicans*

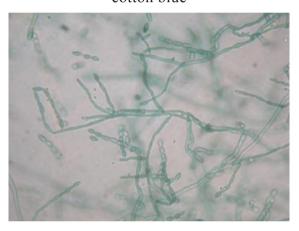


After one week, black pigmented hyphal colonies also grew better at 370°C than at room temperature. Observation of the mature mycelium and microscopy of culture confirmed *Cladophialophora bantiana* (Figures 5,6).

Figure 5. Cladophialophora bantiana and Candida albicans cultured on Sabouraud chloramphenicol medium



Figure 6. Cladophialophora bantiana in microscopic preparation stained with cotton blue



The final diagnosis was brain abscess caused by *Candida albicans* and *Cladophialophora bantiana*. The patient was treated with 400 mg intravenous fluconazole per day. After two weeks of treatment, the clinical response to antifungal therapy remained unsatisfactory, and MRI image showed increased mass size. Therapy was then suspended per the family's request.

3. DISCUSSION

Though the route of entry for *Cladophialophora bantiana* was not clear, the most widely accepted portal of entry was inhalation of spores followed by brain involvement via the hematogenous pathway [7,11]. Our patient had a brain trauma and

worked in an environment that could be contaminated with *Cladophialophorabantiana* spores. Though the patient had no history of immune-suppression or transplantation, he did present a brain abscess infected with *Candida albicans* and *Cladophialophora bantiana*. These fungi could be found in external ear canals. We highlighted these factors in order to supply more data for hypothesising the possible infectious route.

Cladophialophora bantiana is an uncommon cause of central nervous system infections. The symptoms of infection are headache and localized nervous signs. The disease is more frequent in males than in females with a ratio of 3:1. The age of patients ranges from 6 to 77 years old. Brain abscesses can be single or multiple lesions which are easy to see on MRI images. Histopathology often shows central necrosis and granulomatous tissue in the periphery [7,12]. In this case, direct examination of the pus with KOH 30% revealed the golden brown septate hyphae fungus with swollen cells at irregular intervals and branching of conidial chains. Giemsa staining showed similar morphology. Culturing the sample on Sabouraud agar with chloramphenicol at both room temperature and at 370°C allowed the identification of black fungal colonies suggestive of Cladophialophora bantiana (Figure 6).

The optimal treatment for fungal *Cladophialophora bantiana* remains unclear. Surgical excision followed by appropriate antifungal drugs has not yielded encouraging results as 15 of 20 patients have died despite aggressive surgical treatment and intensive chemotherapy. All patients showed recurrence and died within 3 to 11 months following surgery [11].

Lyon reported the following minimum inhibitory concentrations (MICs) of *Cladophialophora bantiana*: Amphotericin B

0.5 μg/ml, Fluconazole 16μg/ml, Itraconazole 0.015μg/ml, and Voriconazole 0.03μg/ml [9]. He also reported the first successful case of treatment of *Cladophialophora bantiana* cerebral abscesses with the relatively new antifungal agent voriconazole. However, Tüker referred to a successful treatment case with Fluconazole 400 mg/day over 3 months [14]. In another case reported by Roche, *Cladophialophora bantiana* was sensitive in vitro to Amphotericin B, Itraconazole and Flucytocin, but the patient in this case was

treated with Amphotericin B and Flucytocin unsuccessfully [13].

Our patient received surgery and was treated with Fluconazole 400 mg per day for 3 months. After 2 weeks, the lesion on the MRI image had spread and clinical staging was unsatisfactory. At the same time the family asked for discontinuation of treatment and the patient was sent home. This confirmed the difficulty of treatment of this type of infection when expensive antimycotic drugs were not easily available.

REFERENCES

- 1. Badillet G, Bievre CD, Gueho E (1986) Champignons contaminant des cultures. Champignons opportunistes. Atlas clinique et biologie. Tome 1. Varia, Paris, pp.80-85.
- 2. Bioforma (2002), Les moisissures d'intérêt médical, Cahier de Formation, N.25. Bioforma, pp.114-115.
- 3. Drouhet E (1987) Coures de Mycologie médicale. Biologie des Candida et autres levures d'interet medical. Institut Pasteur, Paris, pp.1-8.
- Freitas A et al. (1997) Cladophialophora bantiana (Previously Cladosporium trichoides): First Report of a Case in Brazil. Braz J Infect Dis 1(6):313-316.
- 5. Gentilini M (1993) Médecine tropicale, Flammarion Médicine Science, pp.272-275.
- Goel A, Satoskar A, Desai AP, Pandya SK (1992) Brain abscess caused by Cladosporium trichoides. Br J Neurosurg 6:591-3.
- Hoog de GS (1995) Atlas of clinical fungi. Central bureau voor Schimmel cultures/ Universitat Rovirai Virgilli, pp.89, 144, 222-223.
- 8. Koenig H (1995) Guide de Mycologie médicale, Ellipses, pp.13-82.
- 9. Lyon MK, Blair JE, Leslie KO (2005) Successful

- treatment with voriconazole of fungal cerebral abscess due to Cladophialophora bantiana. Clin Neuro Neurosurg 107: 532-4.
- Nadkani TD, Goel A, Shenoy A, Karapurkar AP (1993) Cladosporium bantianum (Trichoides) infection of the brain. J Postgad Med 39: 43-44.
- 11.Staib P and Morschhauser J (1999) Chlamydospore formation on Staib agar as a species-specific characteristic of Candida dubliniensis. Mycose 42:521-524.
- 12.Raut A, Muzumda D, Narlawar R, Nagar A, Ahmed N, Hira P (2003) Cerebral abscess caused by Cladosporium bantiana infection. Neurol Med Chir (Tokyo) 43: 413-415.
- 13.Roche M, Redmond RM, O'Neill S, Smyth E, A case of multiple cerebral abscesses due to infection with Cladophialophora bantiana. J Infect.2005; 51: 285-8.
- 14. Türker A, Altinors N, Aciduman A, Demiralp O, Uluoglu U (1995) MRI findings and encouraging fluconazole treatment results of intracranial Cladosporium trichoides infection. Infection. 234:60-2.
- 15. Walker TS (1998) Microbiology. W. B. Saunders Company, pp.290-317.