Cerebral phaeohyphomycosis: An important differential of tubercular brain abscess

Gurpreet Singh Bhalla, Lavan Singh, Muqtadir Malik, Manbeer Singh Sarao

From Department of Microbiology, Army Hospital (R&R), New Delhi, India

Correspondence to: Dr. Gurpreet Singh Bhalla, Department of Microbiology, Army Hospital (R&R), New Delhi, India. Pnone: +91-8412822489 E-mail: gsbmicrobiology@gmail.com

Received - 26 November 2017 Initial Review - 31 December 2017 Published Online - 14 March 2018

ABSTRACT

Cerebral phaeohyphomycosis (CP), caused by dematiaceous fungi, is a serious form of central nervous system fungal infection. It is a rare disease with male predominance, no specific symptoms or signs and is associated with grim prognosis irrespective of the immune status of the patient. The disease is difficult to diagnose *antemortem*, and many cases are accidentally diagnosed during surgery or autopsy. The early diagnosis and appropriate treatment remain a challenge. The authors report a misinterpreted case of CP in a 53-year-old man without immunodeficiency who showed a favorable outcome after surgical excision and antifungal therapy. Therefore, CP should be an important differential in cases of brain abscess.

Key words: *Brain abscess, Cerebral phaeohyphomycosis, Cladophialophora bantiana*

Dematiaceous fungi have melanin-like pigments in the cell walls and infections caused by them are known as phaeohyphomycosis. Cerebral phaeohyphomycosis (CP) is a rare but generally fatal systemic infection caused by neurotropic fungi belonging to the order *Chaetothyriales* (ascomycete), predominant species being *Cladophialophora bantiana*, *Exophiala dermatitidis,* and *Rhinocladiella mackenziei.* They are environmental fungi and opportunistic pathogens [1]. Although rare, infections caused by dematiaceous fungi are being increasingly recognized in both immunocompromised and immunocompetent humans.

We report a case of CP from north India, in an immunocompetent male, initially diagnosed and managed as cerebral tuberculoma. Correct diagnosis followed microscopy and culture with successful outcome through surgery and antifungal therapy.

CASE REPORT

A 53-year-old immunocompetent male was transferred from a secondary care hospital. There was a history of jerky movements of right upper and lower limbs 18 months back. A magnetic resonance imaging (MRI) brain was done which revealed a well-defined ring-enhancing lesion measuring 2.4 cm × 2.4 cm × 2.5 cm in the left frontal lobe lesion with mass effect. On the basis of radiological appearance, he was diagnosed as a case of tuberculoma brain. He was found to be HIV negative and started on antitubercular therapy along with antiepileptic agents. 7 months later, the patient had a recurrence of the right focal lower limb seizure with secondary generalization and progressive weakness of the right upper and lower limbs. He also developed cognitive symptoms in the form of impaired recent memory and fluency of speech. History was negative for any immune compromise, trauma, or sinusitis. Repeat MRI brain showed increase in the size of the lesion with conglomeration of multiple lesions and surrounding edema. The patient was referred to our center for further management by neurosurgeon. The lesion was excised and thick, purulent, non foul-smelling pus was received for examination and culture. Ziehl–Neelsen stain showed no acid-fast bacilli. Septate fungal hyphae were seen on Gram's stain and KOH mount (Fig. 1), based on which the patient was promptly started on antifungal therapy (liposomal amphotericin B [400 mg IV 24 hourly] and voriconazole [200 mg per oral 12 hourly]). Postsurgery, the power was grade 3/5 in the right upper limb and 2/5 in the right lower limb with the left half of the body being unaffected.

Within 2 weeks, the culture was confirmed to be *C. bantiana.* Olive grey to black velvety growth was seen on Sabouraud's dextrose agar with black pigment on reverse. Lactophenol cotton blue mount showed septate, brown hyphae with unbranched wavy chains of smooth, and brown single-celled conidia (Fig. 2). It was differentiated from other species of *Cladophialophora* by its ability to grow at 42°C.

3 months after surgery, the patient continues to be on liposomal amphotericin B and voriconazole. Clinically, he has improved, with power in both right limbs being 4/5, is ambulatory without support, independent to perform his daily routine and there has been no recurrence, although 3 months is too short a time to comment on recurrence.

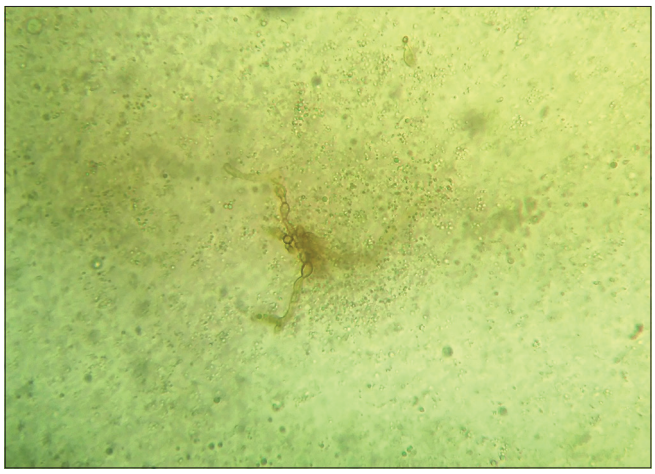

Figure 1: Dark and septate fungal hyphae on KOH mount of the pus (×40)

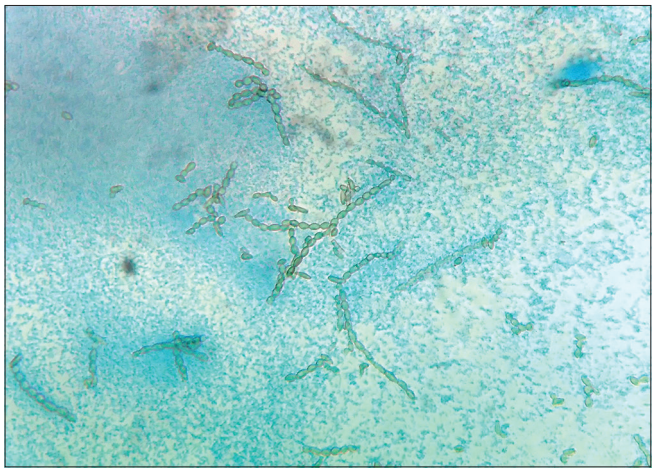

Figure 2: LCB mount from culture: Chains of brown, smooth-walled, single-celled, ellipsoid conidia (×40)

DISCUSSION

C. bantiana is a highly neurotropic fungus with melanin, a known virulence factor, as in other fungi and has been extensively studied in *Cryptococcus neoformans*. It confers a protection from free radicals which are produced by phagocytic cells in their oxidative burst that kills most pathogens [2]. Human melanin (derived from tyrosine) is biochemically different from fungal melanin (derived mostly from acetate) yet sharing the same physicochemical properties. A hypothesis that is used to explain the metastasis of malignant melanoma to the brain can be applied here that, the affinity of melanin to receptors on the blood–brain barrier, allows the fungus to penetrate into the parenchyma. The primary mechanism for dissemination of the fungus is considered hematogenous route, thus majority of reported *C. bantiana* are supratentorial involving the frontal lobes [3].

Various workers in their reviews have reported certain characteristics of CP caused by *C. bantiana*. Most patients are from Asian countries with immunocompetent male hosts with rural origin from India being major contributors. Most common complaints reported in order of their presentation are hemiparesis, seizures, altered sensorium, fever, vomiting, aphasia or dysarthria, and visual disturbances; generally, without any features of meningitis. The majority of the patients had localized brain abscess with a single ring-enhancing lesion; most commonly located in frontal, parietal, and occipital lobes, in order of decreasing frequency [2,4,5]. Our patient had similar features, by being an Indian, middle-aged, immunocompetent male from rural origin. He presented with signs of focal neurological deficit (seizures and hemiparesis), no features of meningitis, and solitary lesion with ring enhancement located in frontal lobe.

Fungal abscesses caused by *C. bantiana* cannot be differentiated with certainty from other bacterial abscesses or central nervous system neoplasia just on the basis of radiologic findings and are also known as "the great mimickers." Irregular heterogeneous lesion with mass effect and surrounding edema is seen on contrast-enhanced images [3]. In particular, differentiating between brain tumors such as high-grade gliomas and metastasis, cerebral tuberculomas, and brain abscesses is often difficult [6]. Due to these difficulties, the diagnosis is often delayed which is the main reason for the high mortality in these cases [4].

Diagnosis is confirmed by microscopic analysis of the lesion along with demonstration of cultural aspects of the causative fungus on which the successful treatment depends [3,5]. Care should be taken to avoid the seeding of CSF or the tract while removal of the lesion or its contents. Samples should be handled in biosafety cabinets because of the known pathogenesis in immunocompetent individuals.

There is a dearth of literature of antifungal efficacy in human cases of CP and no breakpoints and standardized regimens have been established. The agents used include amphotericin B, 5-fluorocytosine, voriconazole, fluconazole, posaconazole, itraconazole, and ketoconazole [4]. Voriconazole is preferred over itraconazole due to better cerebrospinal fluid penetration and bioavailability [7]. No significant difference in survival was noted with the use of any antifungal agent or combination of antifungal agents [4]. A study conducted by Den *et al*. suggest that a combination of amphotericin B and flucytosine has a promising role in the treatment of primary CP due to neurotropic melanized fungi [1]. Several studies including European society of clinical microbiology and infectious diseases and European confederation of medical mycology joint guidelines have recommended early wide surgical resection followed by targeted treatment is required for the best outcome, especially once the fungus is identified [1,2,7-9].

Relapses are reported after 3 months to more than a year; hence, prolonged follow-ups are advisable. Until complete radiographic resolution occurs or there is evidence of no progression on repeat imaging over prolonged period, therapy should be continued [8]. Only 31 cases have been reported from India (1962 till date) to the best of authors' knowledge. The respective authors have mentioned that, in most of these cases, there was no indication of fungal infection and one even being masqueraded as cerebral tuberculoma [5,10].

It is concluded that CP is a rare disease and of a very grim nature early diagnosis is therefore mandatory for the rapid treatment and survival of patients. Hence, it should be on the list of differential diagnosis of brain abscess.

REFERENCES

1. Deng S, Pan W, Liao W, de Hoog GS, Gerrits van den Ende AH, Vitale RG, *et al.* Combination of amphotericin B and flucytosine against neurotropic species of melanized fungi causing primary cerebral phaeohyphomycosis. Antimicrob Agents Chemother 2016;60:2346-51.
2. Revankar SG, Sutton DA, Rinaldi MG. Primary central nervous system phaeohyphomycosis: A review of 101 cases. Clin Infect Dis 2004;38:206-16.
3. Ahmad M, Jacobs D, Wu HH, Wolk DM, Kazmi SA, Jaramillo C, *et al*. *Cladophialophora bantiana:* A rare intracerebral fungal abscess-case series and review of literature. Surg J (N Y) 2017;3:62-8.
4. Chakrabarti A, Kaur H, Rudramurthy SM, Appannanavar SB, Patel A, Mukherjee KK, *et al.* Brain abscess due to *Cladophialophora bantiana*: A review of 124 cases. Med Mycol 2016;54:111-9.
5. Suri P, Chhina DK, Kaushal V, Kaushal RK, Singh J. Cerebral phaeohyphomycosis due to *Cladophialophora bantiana*-A case report and review of literature from india. J Clin Diagn Res 2014;8:DD01-5.
6. Hakyemez B, Erdogan C, Yildirim N, Parlak M. Glioblastoma multiforme with atypical diffusion-weighted MR findings. Br J Radiol 2005;78:989-92.
7. Garzoni C, Markham L, Bijlenga P, Garbino J. *Cladophialophora bantiana*: A rare cause of fungal brain abscess. Clinical aspects and new therapeutic options. Med Mycol 2008;46:481-6.
8. Aljuboori Z, Hruska R, Yaseen A, Arnold F, Wojda B, Nauta H, *et al.* Fungal brain abscess caused by "Black mold" (*Cladophialophora bantiana*) - A case report of successful treatment with an emphasis on how fungal brain abscess may be different from bacterial brain abscess. Surg Neurol Int 2017;8:46.
9. Chowdhary A, Meis JF, Guarro J, de Hoog GS, Kathuria S, Arendrup MC, *et al.* ESCMID and ECMM joint clinical guidelines for the diagnosis and management of systemic phaeohyphomycosis: Diseases caused by black fungi. Clin Microbiol Infect 2014;20 Suppl 3:47-75.
10. Agrawal A, Shanthi V, Mohan KM, Hegde KV, Reddy U. *Cladophialophora bantiana* brain abscess masquerading cerebral tuberculoma in an immunocompetent host. Rom Neurosurg 2014;2:75-9.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Bhalla G. Cerebral phaeohyphomycosis: An important differential of tubercular brain abscess. Indian J Case Reports. 2018;4(1):7-9.