Cladophialophora bantiana

Cladophialophora bantiana is a dematiaceous fungus with a predilection for causing central nervous system (CNS) infection manifesting as brain abscess.

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Immunocompromised individuals with organ transplantations and AIDS are susceptible to acquire the fungal infection, particularly in brain or meninges. However, primary cerebral phaeohyphomycosis caused by C. bantiana appears to be an exception to this rule, occurring more commonly in immunocompetent than in immunocompromised patients ¹⁾.

Epidemiology

It is the most frequently isolated species from cerebral phaeohyphomycosis. It mostly affects adult men in the second and third decade of life ²⁾.

In the Grant Medical College and Sir J. J. Hospital, Mumbai, India, Forty-one (54.70%) abscesses were found to be due to pyogenic organisms, 4% due to Mycobacterium tuberculosis and 1.3% were due to Cladophialophora bantiana ³⁾.

Diagnosis

There is no initial clinical or laboratory feature that makes a preoperative diagnosis possible and relies on microbiological confirmation ⁴⁾.

Treatment

Successful treatment depends on obtaining a complete surgical resection, an accurate microbiological diagnoses for mold identification, and an effective long-term, personalized antifungal treatment. Close radiographic surveillance is necessary to ensure complete eradication ⁵⁾.

C. bantiana tends to be resistant to amphotericin B. Accordingly, Al-Abdely et al. evaluated amphotericin B and three triazoles-posaconazole, itraconazole, and fluconazole-for treatment of C. bantiana infection in mice. In immunosuppressed ICR mice infected intravenously, posaconazole, itraconazole, and amphotericin B prolonged survival. This improvement in survival corresponded with a reduction in brain fungal concentrations for mice which were given itraconazole and posaconazole, but not amphotericin B. In nonimmunosuppressed BALB/c mice infected intracerebrally, posaconazole showed dose-dependent responses in survival and reduction of brain tissue counts. These responses were observed for short, delayed, and prolonged therapy. Although posaconazole prolonged the survival of mice with reductions in brain fungal counts, it did not sterilize brain tissue with continuous therapy for 8 weeks. They concluded that posaconazole shows promise for the treatment of C. bantiana brain infections ⁶.

Outcome

It may carry up to a 70% mortality rate despite advances in surgical resection capabilities and the use of both systemic and intrathecal antifungal treatments ⁷⁾.

The outcome is better in patients with abscess. Excision of the abscess followed by combination antifungal therapy results in better outcome. Close follow-up is required due to high risk of recurrence⁸⁾.

Reviews

Dash C, Kumar A, Doddamani RS. Is complete excision the key to cure for Cladophialophora bantiana brain abscess? A review of literature. Neurol India. 2016 Sep-Oct;64(5):1062-4. doi: 10.4103/0028-3886.190250. PubMed PMID: 27625264. ⁹⁾

Chakrabarti et al. reviewed 124 culture proven C. bantiana brain abscess cases; 103 cases published in English literature during 1952 through 2014 and 21 unpublished cases from the Postgraduate Institute of Medical Education and Research, Chandigarh, India. The majority (57.3%) of the patients was from Asian countries especially from India (62/124, 50%). The diagnosis of the cases was delayed with mean duration 115 days after developing symptoms. The disease was nearly equally distributed in immunocompetent and immunosuppressed hosts but associated with significantly higher mortality (77.1%) in later group. Complete excision of brain lesion in immunocompetent host led to significantly better survival (43.7%). Though all commercially available antifungal drugs have been used in these patients, amphotericin B deoxycholate or lipid preparations were most commonly (62.83%) prescribed agent. None of the drugs used was found to be independently associated with improved outcome. In vitro antifungal susceptibility testing of 13 isolates of our center, demonstrated good activity to voriconazole, posaconazole, and itraconazole, but these triazoles were prescribed in only 29.2% patients. Increased awareness with early suspicion of the disease, and aggressive medical and surgical approach in treating these patients may improve the outcome ¹⁰.

Case series

2017

At the Geisinger Health System, Danville, Pennsylvania, the patients' cases presented with raised intracranial features of headache, visual field cut, and/or memory loss, with a correspondingly wide variety of radiological differential diagnoses. It was the microbiological, histopathological, and genomic identification of C. bantiana that ensured targeted, individualized patient therapies.

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2007

A retrospective study of 10 patients with CNS cladosporiosis managed at National Institute of Mental Health and Neurosciences from 1979 to 2006. It is a descriptive study. The case records were reviewed for clinical presentation, radiological features, management and outcome. Only those patients in whom the fungus could be isolated on culture were included in the study.

The age of the patients ranged from three to 42 years. Nine patients presented with features of space-occupying lesion and one patient with chronic meningitis. There were no specific clinical or radiological features. None of patients had impaired immune status. This infection presented as two pathomorphological forms - diffuse meningoencephalitis and focal abscesses. Burr hole tapping and excision are the surgical options. Both patients with burr hole tapping required excision of abscess subsequently. Two out of seven patients with abscess expired compared to all three patients with diffuse meningoencephalitis who expired. Recurrences occurred in four of the five patients following excision of the abscess. Combination antifungal treatment had better result than monotherapy. The outcome was poor with survival of only 50%.

Thorough microbiological examination is required to diagnose CNS infection caused by C. bantiana. The outcome is better in patients with abscess. Excision of the abscess followed by combination antifungal therapy results in better outcome. Close follow-up is required due to high risk of recurrence ¹²⁾.

Case reports

2017

A 55-year-old diabetic male presented with severe headache, blurred-vision, behavioural abnormalities, eye-pain and ear-discharge. He was undergoing treatment for hypertension, prostatomegaly and obstructive pulmonary disease. He was on steroids for the past six years for uveitis. Haematology reports indicated elevated WBC and platelet count. He was negative for HIV, hepatitis, autoimmune antibodies and tumour markers. CD4 count was within normal limits. Brain magnetic resonance imaging revealed multiple ring-enhancing lesions and oedema in the left tempero-parietal region. Chest X-ray showed irregular consolidations in right paracardiac region and confluence in both lungs. Positron Emission Tomography of whole body revealed multiple lesions in brain, lungs, lymph nodes and C3-vertebrae. Histopathology of the lung lesion showed nontuberculous infectious pathology and brain lesions showed necrosis with occurrence of pigmented hyphal fungi. The pus aspirated during surgical excision of brain lesions grew black mold, identified as C. bantiana. Although patient was started on intravenous Voriconazole, he succumbed to the infection after 7 days. The lesion was initially suspected to be of tuberculous etiology, and the lesions in lungs were also suggestive of malignancy, which was however ruled out by histopathological examination. Such diagnostic dilemmas are common in the infection caused by Cladophialophora, which can cause treatment delay and death. Early diagnosis is therefore mandatory for the rapid treatment and survival of patients ¹³⁾.

2016

Kuan et al. report comprehensive genomic analyses of C. bantiana isolated from the brain abscess of

an immunocompetent man, the first reported case in Malaysia and Southeast Asia. The identity of the fungus was determined using combined morphological analysis and multilocus phylogeny. The draft genome sequence of a neurotrophic fungus, C. bantiana UM 956 was generated using Illumina sequencing technology to dissect its genetic fundamental and basic biology. The assembled 37.1 Mb genome encodes 12,155 putative coding genes, of which, 1.01% are predicted transposable elements. Its genomic features support its saprophytic lifestyle, renowned for its versatility in decomposing hemicellulose and pectin components. The C. bantiana UM 956 was also found to carry some important putative genes that engaged in pathogenicity, iron uptake and homeostasis as well as adaptation to various stresses to enable the organism to survive in hostile microenvironment. This wealth of resource will further catalyse more downstream functional studies to provide better understanding on how this fungus can be a successful and persistent pathogen in human ¹⁴⁾.

A 76-year-old man was admitted with mild motor aphasia and underwent total excision of a mass in the left frontal lobe. With the postoperative diagnosis of brain abscess due to infection with dematiaceous fungi (C. bantiana) associated with hypogammaglobulinemia following gastrectomy, intravenous antifungal drugs including amphotericin B and fluconazole were administered. Regrowth of the abscess with intraventricular rupture was noted at about the 88th day after the initial surgery, and the patient underwent neuroendoscopic aspiration of the pus and placement of a ventricular drain. Following intraventricular administration of miconazole through ventricular drainage or an Ommaya reservoir, neuroradiological findings improved, but general and neurological conditions worsened. Further treatment was discontinued and the patient died 9 months after onset. The poor outcome in this patient is attributed to 1)intractability of dematiaceous fungi, 2)development of ventriculitis and the need for intraventricular administration of antifungal drugs, and 3)untreatable hypogammaglobulinemia following gastrectomy¹⁵.

2014

A 34 year old immunocompetent woman who presented with convulsions. She was initially treated with antituberculous drug. During 15 days of treatment, she deteriorated. Hence she underwent craniotomy, which revealed brain abscesses due to C. bantiana. Subsequently she was treated with fluconazole, but eventually succumbed to the infection on the 7th day of treatment. Mortality remains high with this rare mycosis, even in immunocompetent patients. The case illustrates the clinical and radiological similarities between tuberculoma and other etiologies of brain abscesses. This emphasizes the need to perform histological and microbiological studies prior to the initiation of any form of therapy ¹⁶.

A 27 year-old male patient presenting without any chronic disease was admitted to the emergency department of our hospital with the complaints of persistent headache and diplopia. Magnetic resonance imaging (MRI) showed a space-occupying lesion in the right parietal lobe and left frontal lobe. Brain abscess was diagnosed in the patient who was referred to the neurosurgery department. Treatment was initiated with ceftriaxone and metronidazole. The abscess material sent for direct microscopic examination in the mycology laboratory was stained with Gram and Giemsa and cultured in the Sabouraud dextrose agar medium (SDA) with and without antibiotics (cycloheximide and chloramphenicol). Then, it was incubated at 37°C and 25°C. Direct examination and staining revealed a septate hyphae. The patient who received liposomal amphotericin B was referred to the infectious diseases department. Surface colors of all media including SDA with cycloheximide were olive-gray to

black and contained velvety colonies. Lemon-like very long and integrated chains of conidium with poor branching in cornmeal Tween 80 agar, as well as growth at 42°C in passages, positive urease test result and cycloheximide resistance suggested C.bantiana. The isolate was confirmed as C. bantiana based on its DNA sequence analysis. Minimum inhibitor concentration (MIC) values for amphotericin B, voriconazole, caspofungin, and posaconazole were 2 μ g/ml, 0.03 μ g/ml, 0.03 μ g/ml and 0.03 μ g/ml, respectively. Liposomal amphotericin B was replaced with voriconazole due to the antifungal susceptibility profile. The patient who was symptom-free was discharged at 24 days after hospitalization with oral voriconazole treatment. In conclusion, cerebral phaeohyphomycosis should be considered in immunocompetent individuals. Given the fact that early diagnosis saves lives, such specimens should promptly be sent for mycological analysis ¹⁷⁾.

A case of multiple brain abscesses caused by C. bantiana in an immune competent patient. The diagnosis was based on CT scan of head, direct examination and culture of the aspirate from the abscess. Despite complete surgical resection of the abscesses and antifungal therapy with amphotericin B and voriconazole the patient could not be saved. All the cases of cerebral phaeohyphomycosis due to this rare neurotropic fungus reported from India between 1962 and 2009 have also been reviewed ¹⁸⁾.

2008

A 20-yr-old male presented with multiple brain abscess which was subsequently proven microbiologically to be due to Cladophialophora Bantiana. In spite of near total excision and appropriate antifungal agents succumbed to his illness.

George et al. report this case to highlight its rarity and high mortality in an immunocompetent host. There is no initial clinical or laboratory feature that makes a preoperative diagnosis possible and relies on microbiological confirmation ¹⁹.

A 53-year-old male who presented with headache, tremor and memory disturbance. Radiological evaluation was suggestive of brain abscess. He underwent gross total excision of the cerebral abscess. The histopathological examination and pus culture was suggestive of brain abscess caused by Cladophialophora bantiana. Authors report a rare case of biopsy and culture proven Cladophialophora bantiana brain abscess in an immunocompetent host. The authors review the relevant literature and current treatment options while emphasizing the need for a cost-effective novel antifungal drug to salvage a subset of patients suffering from this rare but increasingly frequent condition ²⁰.

2006

Cerebral phaeiohyphomycosis due to Cladophialophora bantiana²¹⁾.

2005

Lyons et al.report the first successfully treated case of Cladophialophora bantiana cerebral abscess with the relatively new antifungal agent voriconazole. Infection with this organism is often fatal. A 64year-old man presented to our institution with progressive neurologic symptoms due to a brain abscess. A stereotactic brain biopsy confirmed the pathogen as C. bantiana. We discuss the successful treatment of this patient, and review the pharmacological actions of voriconazole and the literature on the treatment of this organism. Previously considered a rare cause of cerebral abscess, C. bantiana fungal infections have become more common in recent years. Aggressive and continuous treatment with voriconazole may offer an improved chance of survival in these patients²²⁾.

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