CEREBRAL PHAEOHYPHOMYCOSIS DUE TO CLADOPIHALOPHORA BANTIANA

Cladophialophora bantiana a dematiaceous fungus and a member of the family Phaeohyphomycetes, is primarily a neurotropic fungus causing central nervous system (CNS) infection. We report a case of a well preserved, young adult male presenting with a capsuloganglionic abscess caused by C. bantiana, a rare entity. Diagnosis was made based on the mycology and histopathology findings of the aspirate from the abscess through a burr hole. The patient responded clinically to amphotericin B.

Key words: Amphotericin B, dematiaceous fungus, neurotropic, Cladophialophora bantiana

Case Report

A 23-year-old male, a student of botany, presented in September 2005 to the neurology services of the Nizam’s Institute of Medical Sciences, Hyderabad, Andhra Pradesh, India, with complaints of left sided headache since one week, right sided hemiparesis, facial palsy and diplopia since three days prior to admission. The patient did not give any history of symptoms related to raised intracranial tension such as nausea, vomiting, sensory disturbances, or seizures. There was no past history of any other illness including any immunocompromising conditions or travel history.

On clinical examination the patient was a moderately built young man. He was conscious, coherent, oriented and afebrile. The respiratory rate, heart rate, and blood pressure
were all within normal limits. A neurological examination revealed that the patient had features of upper motor neuron facial palsy. There were no meningeal signs or any sensory deficits.

Complete haemogram and blood chemistry were within normal ranges. Patient was seronegative for HIV-1 and 2 by ELISA. A cranial CT (computed tomography) scan revealed a ring enhancing lesion in the left capsuloganglionic region with perilesional oedema and mass oedema. It was interpreted as a cerebral abscess.

With a diagnosis of an intracranial abscess, a left precoronal burr hole aspiration of the abscess was performed. The purulent aspirate and necrotic tissue were submitted for microbiology and histopathology examinations. The seropurulent aspirate was examined by Gram stain, which revealed plenty of pus cells and a few sparsely stained branching fungal filaments. No bacteria were seen. The Ziehl-Neelsen’s smear for acid fast bacilli and a modified 1% acid fast stain were negative. Potassium hydroxide (10% KOH) mount of the aspirate showed branching septate, dematiaceous hyphae with swollen cells (Fig. 1).

Aerobic, anaerobic and mycobacterial cultures of the aspirate were put up. While the latter two were sterile, colonies of a grey mould began to appear on the sheep blood agar plates after five days of incubation at 37º C. The Sabouraud dextrose agar, inhibitory mould agar and brain heart infusion agar at 25º C and 37º C, inoculated with the aspirate, also showed growth of a mould on day five of incubation. The fungal colonies turned grey to black on further incubation. The texture of the colony was powdery to felt-like and the reverse was olive black (Fig. 2). A slide culture of the mould was put up and observed microscopically using the lactophenol cotton blue mount. The morphology of the conidiophores is shown in Fig. 3. They were distinctly pigmented but poorly differentiated and had mostly unbranched conidia with no pigmented hila (these features differentiate the isolate from other Cladosporium spp.). There were 5-10 conidia per chain arranged acropetally. Conidia were one-celled, occasionally 2 celled, pale brown, smooth-walled, ellipsoid to oblong and were 2.3 by 4-7 µm in size.

A thermal tolerance test for growth of the fungus at 42º C was positive. Based on the morphologic and microscopic features, the fungus was identified as Cladophialophora bantiana and thus differentiated from C. carrionii, which has a maximum growth temperature at 35- 36º C.

The isolate was confirmed as C.bantiana by Prof. Arunalok Chakraborthy, Professor In-Charge, Division of Mycology, Department of Medical Microbiology, Postgraduate Institute of Medical Education and Research, Chandigarh, India. It was also sent to Dr. David Denning, Professor of Medicine and Medical Mycology, Faculty of Life Sciences 1.800 Stopford Building, The University of Manchester, Oxford Road Manchester M13 9PT for antifungal susceptibility pattern. As cladophialophora bantiana is classified as a class 3 organism based on biological risk, the isolate was in turn sent to the PHLS mycology reference lab, Bristol, UK for further testing. MICs for selected antifungals were determined by Broth Microdilution susceptibility testing as recommended by the National Committee for Clinical Laboratory Standards. The MICs for Amphotericin B, Itraconazole, Voriconazole and Caspofungin were 2mg/L., 0.25mg/L., 0.5mg/L and 0.5mg/L respectively. The results were interpreted as resistant for Amphotericin B and sensitive for the other three antifungals.

Histopathology features of the tissue on haematoxylin and eosin and Gomori’s silver methenamine stains are shown in Figs. 4 A and B. Branching, septate pigmented hyphae were seen within areas of inflammatory infiltrate and giant cells.
Based on the culture report, the patient was initiated on amphotericin B (AMB) at a dose of 0.5 mg/kg/body weight and the dose was gradually increased to a 3.5 gm (cumulative dose of AMB). During the hospital stay the patient had 2 episodes of right focal seizures without any further progression of the disease. The repeat CT after two months of hospital stay showed mild resolution of the lesion with contrast enhancement. However, the patient responded clinically and was relieved of his presenting symptoms and was discharged with no neurologic deficit.

Discussion

Phaeohyphomycoses encompass a diverse group of dematiaceous fungal infections characterized by pigmented hyphae in the tissues. The term phaeo is derived from the Greek word phios meaning grey and refers to the colour of these fungi in vivo and in vitro. C. bantiana is primarily a neurotropic fungus.

CNS cladosporiosis generally manifests as brain abscess, with a few exceptional presentations such as chronic meningitis. Chronic headache is the commonest symptom. There are no specific clinical or radiological features. CT scan of the cranium often reveals unilateral well circumscribed mass lesion in the frontal lobe.[1,2] In our patient the mass lesion was seen in the capsuloganglionic area.

In a comprehensive review of the phaeohyphomycoses, 48% of the cases were reported to have been caused by C. bantiana with a mortality of 71%. Several of these patients had identifiable risk factors for infection, such as glucocorticoid treatment, diabetes mellitus, lymphoma with neutropenia, eye trauma and intravenous drug abuse.[3] Most infections occur in the second and third decade of life[2] as in our patient. The youngest case reported was a six-day-old child.[4] There is no restriction for race, age or geographic location for Cladophialophora. Typically the infection occurs in young immunocompetent males.[2]

Treatment of established cladosporiosis has been problematic. Although the optimal antifungal therapy is not known, some authors recommend combining amphotericin B with fluconazole and either itraconazole or voriconazole. In vitro data suggests that itraconazole, voriconazole and amphotericin B have activity against C. bantiana, with the azoles having lower MICS than amphotericin B. However, it is difficult to apply this in vitro data to decisions regarding the treatment of human infections.[5] The present patient was treated adequately with amphotericin B with a good clinical response.

References

Prostatic abscess is uncommon and is rarely diagnosed. At the onset, symptoms may mimic several other diseases of the lower urinary tract. Prostatic abscess has undergone a great shift in mortality rate and the types of aetiologic agents since the discovery and use of penicillin. In the 1940s mortality ranged from 6-30% and the major organism was Staphylococcus aureus. Other organisms reported are Enterobacteriaceae family being the most common agents. Among these, Pseudomonas spp. have been reported. More recent data suggests a mortality about 70% of the cases. Other organisms reported are Neisseria, Brucella spp. and fungi like Cladophialophora bantiana. Aspergillus spp. have also been suggestive of diabetic nephropathy. However, to rule out malignancy serum prostatic specific antigen (PSA) levels were performed using the chemiluminescence technique at SRL Ranbaxy laboratories, which was normal (0.8 ng/ mL).

A 50-year-old male, chronic alcoholic and a known case of diabetes mellitus was admitted on 2nd November 2007 with the history of acute urinary retention since three days. The patient was HIV sero negative. As the patient presented with retention of urine, catheterisation was done. Catheter free trial was attempted, which failed, therefore re-catheterisation was done. After six days of catheterisation, the patient developed fever with chills. On clinical examination the patient was febrile, abdominal examination showed grade II fluctuation. There was no history of haematuria, lithuria or symptoms suggestive of acute or chronic renal failure, abdominal swelling or trauma.

Routine urine analysis was done which showed occasional pus cells, no RBCs, no casts. Urine culture was processed by Gram staining and was cultured on blood. Transrectal USG guided 10-12 mL of prostatic abscess pus was aspirated from the non dependent area i.e., near the base of the prostate. Gross examination of the aspirate showed that it was frank pus. The aspirated material was processed for culture and it showed that the causative agent was Cladophialophora bantiana. The patient was febrile, and ultrasonography. The causative agents i.e., Cladophialophora bantiana was isolated from the aspirate and the patient responded to intravenous Ciprofloxacin therapy. No other surgical intervention was required to treat the patient.


Key words: Diabetes; prostatic abscess; Staphylococcus aureus

*V Lakshmi, C Padmasri, P Umabala, C Sundaram, M Panigrahi

*Corresponding author (email <lgorthi@hotmail.com>)

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Departments of Microbiology (VK,CP, PU), Pathology (CS) and Neurosurgery (MP), Nizam’s Institute of Medical Sciences, Pun jagutta, Hyderabad - 500 082, Andhra Pradesh, India

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