Cerebral macroabscess caused by *Candida albicans* in an immunocompetent patient: A diagnostic challenge

Sônia M. Figueiredo, Sabrina Campolina, Carlos A. Rosa, Marcus Gontijo, Thelma Tirone, Claudia B. Assunção, Tarcísio F.A. Freire, Paulo P. Christo, Rachel B. Caligiorne

**Abstract**

We describe the history of a 24-year-old immunocompetent man with an expansive lesion in the brainstem that, after many misdiagnoses, was found to be caused by a *Candida albicans* abscess. One year after surgery and 3 months of fluconazole treatment, the patient was asymptomatic and all image and laboratory tests were normal.

**1. Introduction**

Several species of the genus *Candida* are common saprophytes which reside on the skin and mucous membranes in healthy persons. Opportunistic pathogen *Candida* species, such as *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis* and *Candida tropicalis* are opportunistic pathogens which produce mild superficial infection, but occasionally may cause systemic diseases with involvement of the lung, kidney, endocardium, brain, or reticuloendothelial system. In almost all reported cases of disseminated candidiasis, the immune defense mechanisms of the patient were suppressed by predisposing factors such as prior antibiotic therapy [1], systemic adrenocortical steroids [2], indwelling intravascular catheters [2], diabetes mellitus or other serious chronic diseases. In addition, various neoplastic diseases such as lymphoma and Hodgkin’s disease [3] may lead to the development of candidiasis. Therefore, *Candida* species are emerging [4] and are now the fourth leading pathogen of nosocomial bloodstream infection in the United States [5].

Fungi such as opportunistic *Candida* species are not frequently implicated in cerebral infections in healthy persons. Most cases of the central nervous system (CNS) infection caused by *Candida* species occur in premature neonates with adult cases occurring in association with immunosuppression, such as advanced HIV or following neurosurgery.

**2. Case**

A 24-year-old patient, bricklayer, arrived at the hospital complaining of double vision (day 0). The neurological examination showed a right abducent and peripheral facial nerve palsy. The overall patient conditions including his level of consciousness and the rest of the neurological examination were normal.

A cerebral magnetic resonance imaging (MRI) was requested (day +2). It evidenced a complex lesion with hemorrhagic components localized in the brainstem, suggesting a cavernous hemangioma or a ruptured aneurysm (Fig. 1a and b). The arteriography discarded aneurysm. A surgical intervention was made (day +10). In the approach to the lesion, the neurosurgeon...
evidenced a purulent secretion instead of blood. It was drained and a treatment for bacterial abscess with ceftriaxone and metronidazole was started (day +11).

However, the cranial computerized tomography (CT) was done a few days after surgery (day +16), showed that the lesion was the same as before the operation and antibacterial treatment, keeping...
characteristics of abscess. With a new MRI, the lesion extension was confirmed (Fig. 1c–f). The surgeon was convinced that the secretion observed was pus. A spectroscopy was made and confirmed the surgeon’s impression. The lesion was an abscess. A new surgical intervention was performed, after a period without antibiotics (day +27). At this time, direct microscopy presented numerous yeasts. Cultures for fungus and biochemical tests were used for the species identification. The yeast isolate was characterized by standard methods [6] and identified as C. albicans, according to the identification key of Kurtzman and Fell [7] (day +34). The identification was confirmed by nucleotide sequencing of the D1/D2 variable domains of the large subunit of ribosomal DNA. The region was amplified by PCR as described by Lachance et al. [8] using the primers NL-1 (5'-GCATA-TCAATAAGCGGAGGAAAAG-3') and NL-4 (5'-GGTCCGTTTCAAGA-CGG-3'). The amplified DNA was concentrated and cleaned on WizardSV columns (Promega Corporation, USA), and sequenced in a MegaBACE™ 1000 automated sequencing system (Amersham Biosciences, USA). The sequences were edited with the program DNA MAN, version 4.1 (Lynnon Bio-Soft, Vaudreuil, QC, Canada). After alignments with sequences in the EMBL GenBank database, using the Fasta 2.0 program [9], was found to be identical to C. albicans (GenBank accession no. U45776), confirming that this species was the agent of the infection. This strain was deposited in the Collection of Microorganisms and Cells of Universidade Federal de Minas Gerais, under the number UFMG-9003.

A treatment (day +34), with fluconazole was started (400 mg daily for two weeks followed by 200 mg daily for three months) and after three months of follow-up, a new MRI was normal, showing no lesion (Fig. 1g and h). The MRI exams at six month and a year of follow-up also showed no alteration. The patient is asymptomatic.

3. Discussion

C. albicans rarely invades the central nervous system in immunocompetent patients. Therefore, most cases of cerebral candidiasis are unsuspected during life or are diagnosed during the terminal stages of the associated illness [10].

Fungal infections of the CNS are a diagnostic challenge, due to a variety of clinical presentations and the difficulty in confirming the diagnosis in many situations. Despite the approximately 300 species of yeasts from the Candida genus, about only 10 have medical importance. The species C. albicans is the agent for the majority of the cases of systemic candidiasis and, consequently, neurocandidiasis [11].

Encephalitic macroabscesses are rare, but cases have already been reported in patients with severe immunologic deficiency and at lower frequency in normal ones, without immune alteration. To invade the brain parenchyma, blood-borne C. albicans cells must adhere to and traverse the endothelial cell lining of the blood vessels within the central nervous system. Brain endothelial cells are significantly different from those lining systemic blood vessels. For example, they have tight junctions that are not present in the endothelial cells in other vascular beds. Forming the blood-brain barrier, brain endothelial cells restrict the diffusion of large or hydrophilic molecules into the central nervous system, while allowing the diffusion of small hydrophobic molecules [12].

Studies using human umbilical vein endothelial cells (HUVECs) as representative systemic endothelial cells have demonstrated that C. albicans adheres to, invades and damages these cells in vitro [13]. One mechanism by which C. albicans invades these cells is stimulating its own endocytosis, which is induced when the C. albicans invasins bind to receptors such as N-cadherin and HER2 on the endothelial cell surface [14–16]. C. albicans yeast and hyphae can also invade HBMECs by inducing their own endocytosis [16]. However, the mechanism by which this pathogen invades these endothelial cells and infects the brain is poorly understood.

Although infections in the CNS caused by opportunistic pathogen Candida species are prevalent in the immunocompromised patients [17], sometimes we face with this condition in an immunocompetent person for unknown reasons. Thereby, this premise is fundamental in our differential diagnosis to prevent missing the chance to an efficaciously treatment of a potentially lethal condition.

Conflict of interest statement

The authors have no conflict of interest to declare.

Acknowledgements

This work was supported by the National Council for Research and Development—CNPq and Research Foundation of the State of Minas Gerais—FAPEMIG.

References