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

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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

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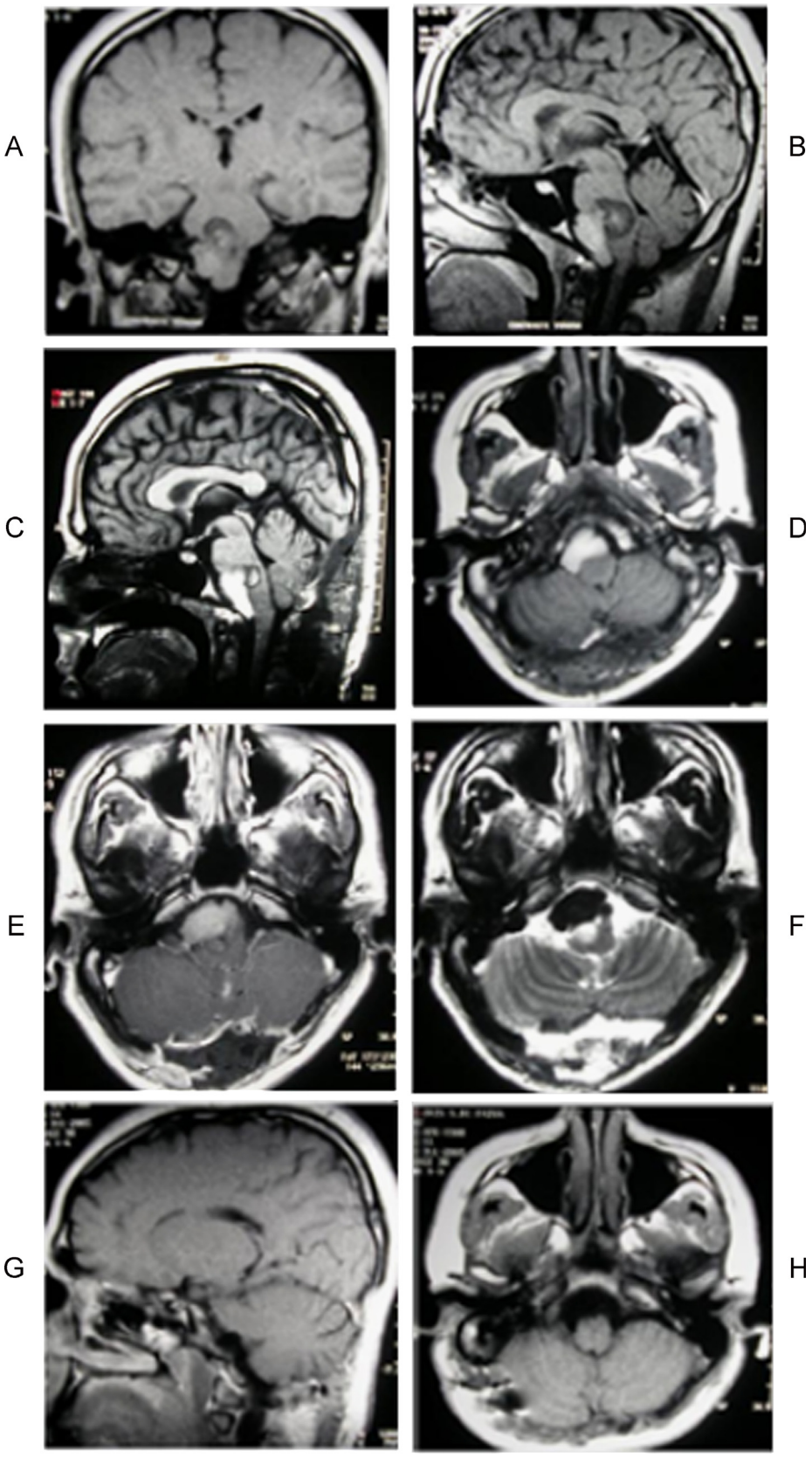

Fig. 1. Magnetic resonance image (MRI) showing the different points of the lesion. A—Coronal FLAIR showing brainstem lesion; B—sagittal T11WI showing hypointense lesions; C—sagittal post-gadolinium T1WI showing gadolinium enhancement; D and E—axial post-gadolinium T1WI showing gadolinium enhancement; F—axial T2-WI showing hypointense lesions and edema; G and H—T1 MRI showing improves of the lesion after treatment.

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′-GCATATCAATAAGCGGAGGAAAAG-3′) and NL-4 (5′-GGTCCGTGTTTCAAGACGG-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 DNAMAN, 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].

Encephalic 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.

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References

[1] Seelig MS. The role of antibiotics in the pathogenesis of *Candida* infections. Am J Med 1966;40:887–917.
[2] Louria DB, Stiff DP, Bennett B. Disseminated moniliasis in the adult. Medicine (Baltimore) 1962;41:307–37.
[3] Casazza AR, Duvall CP, Carbone PP. Summary of infectious complications occurring in patients with Hodgkin′s disease. Cancer Res. 1966;26:1290–6.
[4] Friedman L. Candidiasis (moniliasis) and aspergillosis. In: Samter M, Alexander HL, editors. Immunological diseases. Boston: Little, Brown; 1965. p. 459–68.
[5] O'Brien D, Stevens NT, Lim CH, O'Brien DF, Smyth E, Fitzpatrick F, et al. Candida infection of the central nervous system following neurosurgery: a 12-year review. Acta Neurochir 2011;153:1347–50.
[6] Yarrow D. Methods for the isolation and identification of yeasts. In: Kurtzman CP, Fell. JW, editors. The yeasts, a taxonomic study. 4th ed.. Amsterdam: Elsevier; 1998. p. 77–100.
[7] Kurtzman CP, Fell JW. The yeasts, a taxonomic study. 4th ed.. Amsterdam: Elsevier; 1998.
[8] Lachance MA, Bowles JM, Starmer WT, Barker JSF. *Kodamaea kakaduensis* and *Candida tolerans*, two new ascomycetous yeast species from Australian Hibiscus flowers. Can J Microbiol 1999;45:172–7.
[9] Altschul S, Thomas L, Madden A, Schäffer JZ, Zheng Z, Webb M, et al. Gapped BLAST and PSI-BLAST: a new generation of protein database searchip programs. Nucleic Acids Res 1997;25:3389–402.
[10] Black JT. Cerebral candidiasis: case report of brain abscess secondary to *Candida albicans*, and review of literature. I. Neurol Neurosurg Psychiat 1970;33:864–70.
[11] Portocarrero SP, Cecilia EP, Corral O, Vivas JR, Picazo JJ. The central nervous system and infection by *Candida* species. Diagn Mycol Infect Dis 2000;37:169–79.
[12] Broadwell RD, Baker-Cairns BJ, Friden PM, Oliver C, Villegas JC. Transcytosis of protein through the mammalian cerebral epithelium and endothelium. III. Receptor-mediated transcytosis through the blood–brain barrier of blood-borne transferrin and antibody against the transferrin receptor. Exp Neurol 1996;142:47–65.
[13] Wächtler B, Citiulo F, Jablonowski N, Förster S, Dalle F, Schaller M, et al. *Candida albicans*—epithelial interactions: dissecting the roles of active penetration, induced endocytosis and host factors on the infection process. PLoS One 2012;7(5):e36952.
[14] Sun JN, Solis NV, Phan QT, Bajwa JS, Kashleva H, et al. Host cell invasion and virulence mediated by *Candida albicans* Ssa1. PLoS Pathog 2010;6:e1001181.
[15] Phan QT, Myers CL, Fu Y, Sheppard DC, Yeaman MR, et al. Als3 is a *Candida albicans* invasin that binds to cadherins and induces endocytosis by host cells. PLoS Biol 2007;5:e 64.
[16] Lossinsky AS, Jong A, Fiala M, Mukhtar M, Buttle KF, et al. The histopathology of *Candida albicans* invasion in neonatal rat tissues and in the human blood–brain barrier in culture revealed by light, scanning, transmission and immunoelectron microscopy. Histol Histopathol 2006;21:1029–41.
[17] Livramento JA, Machado LR, Moreno-Carvalho OA, Lacaz CS, Spina-Franca A. Cerebrospinal fluid in infection of the central nervous system by yeasts of the genus *Candida*: analysis of 11 cases. Arq. Neuropsiquiatr 1989;47(3):332–6.