Brain Cryptococcoma In Immunocompetent Patient. A case report

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ABSTRACT

Background: Cryptococcosis commonly associated with immunosuppressed individuals is an infection caused by Cryptococcus neoformans/var. gattii. This infection has high mortality worldwide. C. neoformans inhabits the lung, later spreading to the Central Nervous System (CNS) which is the most significant site in the clinical manifestation of the disease. However, the prevalence in the CNS is low in immunocompetent individuals. Case presentation: A 42-year-old woman presented only headache, nausea, vomiting and simple partial epileptic seizure. Neuroimaging showed an expansive hypointense frontal lesion and a neurosurgical treatment was proposed, confirmed by histopathological analysis. Discussion: The exposure to C. neoformans among human populations is almost ubiquitous. The immunological status of the patient, the parasitic load and the virulence of the infectious strain are fundamental for the progression of the pathology. The balance of these factors is decisive for the prognosis. Currently, treatment is limited and consists of long term antifungal therapy. Conclusion: In this case, the necessity of differential diagnosis like brain tumors (e.g.: lymphoma and glioblastoma multiforme), resulting in poor prognosis and late treatment is seen. A neurosurgical approach should be instituted as soon as possible when pharmacological treatment is ineffective.

Keywords: Neurocryptococcosis; Cryptococcosis; Fungus; Glioblastoma; Microsurgery

RESUMO

Introdução: A criptocose, comumente associada a indivíduos imunossuprimidos, é uma infecção causada por Cryptococcus neoformans/var. gattii. É uma infecção que apresenta alta mortalidade em todo o mundo. O C. neoformans habita o pulmão e, posteriormente, se espalha para o sistema nervoso central (SNC), que é o local mais significativo na manifestação clínica da doença. No entanto, a prevalência no SNC é baixa em indivíduos imunocompetentes. Relato de caso: Mulher de 42 anos de idade apresentou apenas cefaleia, náuseas, vômitos e crise epiléptica parcial simples. A neuroimagem evidenciou lesão expansiva frontal hipointensa e foi proposto tratamento neurocirúrgico, confirmado pela análise histopatológica. Discussão: A exposição ao C. neoformans entre aspopulações humanas é quase onipresente. O estado imunológico do paciente, a carga parasitária e a virulência da cepa infecciosa são fundamentais para a evolução da patologia. O equilíbrio desses fatores é decisivo para o prognóstico. Atualmente, o tratamento é limitado e consiste em terapia antifúngica de longa duração. Conclusão: Neste caso, observa-se a necessidade de diagnósticos diferenciais como tumores cerebrais (ex.: linfoma e glioblastoma multiforme) resultando em mau prognóstico e tratamento tardio. Uma abordagem neurocirúrgica deve ser instituída o mais rápido possível quando o tratamento farmacológico é ineficaz.

Palavras-chave: Neurocriptococose; Criptococose; Fungo; Glioblastoma; Microcirurgia
INTRODUCTION

Cryptococcosis is an infection commonly associated with immunosuppressed individuals and it is rare in healthy patients. It is caused by the yeasts of Cryptococcus neoformans/Cryptococcus gattii. The most common forms of exposure include a history of exposure to soil and pigeon droppings. Cryptococcal species are fungal pathogens that are morphologically encapsulated yeasts. Diseases such as diabetes, AIDS, chronic liver and kidney disease, long term use of steroids and patients undergoing organ transplantation are often associated with the development of cryptococcal disease. Globally, approximately 1 million cases of cryptococcosis are reported each year, resulting in approximately 625,000 deaths².

After penetrating the host’s tissues, mainly by inhalation, the fungus can cause acute disease or latent infection. First, C. neoformans inhabits the lung and, later, it spreads to the central nervous system, which is the most significant site in the clinical manifestation of the disease. In a small number of cases, granulomatous lesions may appear (cryptococcomas). The current treatment consists of long antifungal therapy with Amphotericin B, fluconazole and 5-flucytosine, since echinocandins have no action against C. neoformans. If pharmacological treatment is not effective against the cryptococcoma, microsurgical resection should be performed to improve the patient’s prognosis, since the high mortality in these cases is worrying1,3.

This paper aimed to present a rare case in which a patient had neurocryptococcosis with no previous history.

CASE PRESENTATION

Female patient, 42 years old, immunocompetent, had just a headache associated with nausea and vomiting for two weeks, and manifested simple partial seizure. Normal neurological examination with no previous history. No significant conditions were identified in her history.

Magnetic resonance imaging (Figure 1) showed an expanding hypointense frontal mass lesion. She underwent microsurgery for resection of the lesion, with macroscopic aspect of a glioblastoma. Wide frontal craniotomy was performed. The lesion was not visualized by the cortex, because of a subcortical lesion. Gross total removal has been achieved. Lesion samples were sent for pathohistological analysis (Figure 2A). The result revealed that the lesion consisted of cryptococcoma (Figure 2B and Figure 2C). After the operation, the patient improved her symptomatic condition.

Figure 1. Brain MRI showing right frontal mass lesion hypointense on T1-weighted images and heterogeneously hyperintense on FLAIR T2-weighted images. A, axial FLAIR. B, C, axial and coronal T2. D, axial T2*-weighted image. Surrounding extensive vasogenic edema and irregular ring enhancement (E, F, axial and coronal T1-weighted contrast-enhanced MR images).

Figure 2. A. Cryptococcoma removed from the patient after microsurgery resection. B. Blade overview. C. Magnified view of the cryptococcoma, PAS stained blade, identifying the fungus body in purple magenta and the polysaccharide capsule in pink. It is possible to observe the considerable number of bodies, as well as their capsular limits from the contrast with the light background. The presence of some reproducing cells is also noted.
Cryptococcosis affects immunocompromised and immunocompetent individuals (less frequently). The exposure among human populations is almost universal, since the fungus can be found in different regions of the planet and can infect various populations, such as different species of mammals, insects and plants, although the presentation of the symptoms is relatively rare. The immunological status of the patient, the parasitic burden and the virulence of the infectious strain are fundamental for the progression of the pathology. The balance of these factors is decisive for the prognosis1, 4, 5.

Three possible hypotheses have been proposed to explain the entry into the SNC. The first consists of the binding of cryptococcal cells to the luminal portion of the human blood-brain barrier (BBB) and subsequently their endocytosis by endothelial cells. The second involves paracellular passage from damage to the BBB's narrow junctions. The third, most scientifically supported, is called the “Trojan horse” dissemination. The mechanism is related to the ability to survive in phagocytic cells. Thus, in addition to providing immune avoidance, it also helps in the dissemination within infected phagocytic cells on their way through the body2, 5.

Regarding the virulence mechanisms of C. neoformans, it is possible to mention the presence of specific proteins that act in the adaptation to different pH levels. Furthermore, the production of melanin is necessary for the survival of the fungus, since it allows resistance to multiple stress factors, such as ionizing radiation, heat and free radicals, in addition to protection against macrophages. The synthesis of melanin requires the presence of laccase, an enzyme that has a high amount of precursors of its activity in the brain. This fact may be important for explaining the fungus' predilection for brain colonization. The yeast polysaccharide capsule is its dominant virulence factor and is also important, as it prevents dehydration. Capsular polysaccharides act to inhibit phagocytosis1, 5.

Neurological pathology can be classified into different syndromes: meningitis, encephalitis, meningoencephalitis, ventriculitis, intracranial pressure disorders and space-occupying lesions, such as abscesses, cysts or granulomas. Granulomatous lesions are commonly called cryptococcomas. The clinical manifestations of CNS cryptococcosis include a multitude of signs and symptoms, such as headache, fever, cranial neuropathies, altered lying, lethargy, memory loss and signs of meningeal irritation. Symptoms usually develop over a period of several weeks, but on some occasions, patients present more acute or lack of typical characteristics, such as headache3.

Diagnosis of neurocryptococcosis by imaging tests (CT and MRI) can be extremely difficult, given the considerable similarity between cryptococcoma and some neoplasms, such as glioblastoma multiforme and lymphoma, or cysts2, 3. The shape of the pseudotumor and the diffuse symptoms can sometimes cause confusion. However, in the differential diagnosis, it is interesting to consider the presence of C. neoformans as the cause of the lesion, since the prevalence of the disease is increasing in Latin America, in view of studies in recent years4. Thus, it is necessary to undergo other types of tests to confirm the cryptococcosis.

Treatment is currently limited, and consists of long term antifungal therapy based on Amphotericin, fluconazole and 5-flucytosine, since echinocandins have no action against C. neoformans. Although Amphotericin B has good effect, its toxicity limits its use. Nowadays, there are liposomal drugs that reduce the negative effects of this drug, but its high price makes it difficult to be widely used in developing countries, as Brazil. It is also notable the need to expand research so that the virulence of this fungus is better understood. If the pharmacological treatment is not effective against cryptococcoma, microsurgical resection should be performed to improve the patient's prognosis, since high mortality in these cases is a worrying factor5.

The patient in this study was extensively investigated but did not have an immunosuppressive condition or pulmonary impairment. Since she had a neurological dysfunction that developed quickly, which made the initial diagnosis
favorable to the idea that it was a glioblastoma multiforme, it was decided to perform the surgical removal (Figure 2A). Histopathological analysis (Figure 2B and 2C) confirmed all typical changes related to cryptococcosis and appropriate treatment was quickly instituted.

In this case the necessity of differential diagnosis like brain tumors (e.g.: lymphoma and glioblastoma multiforme), resulting in poor prognosis and late treatment was seen. It constitutes a challenge to the neurosurgeons to diagnose the cryptococcoma. A neurosurgical approach should be instituted as soon as possible when pharmacological treatment is ineffective, since despite the ideal treatment, this is a condition with high mortality.

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