

Neurocryptococcosis: A Pictorial Review

Carlos Roberto Borges Vasconcelos^{1*}, Leandro Tavares Lucato¹, Luis Felipe Sousa Godoy¹, Fernando Frassetto², Cecília Goldman¹, Kátia Nakacima¹, Thamires Baldo Cordeiro³, Mariana Camarço³, Luana Barreto de Almeida Vasconcelos⁴ and Evelin Santiago Andrade Vasconcelos⁵

¹Institute of Radiology, University of São Paulo, Brazil

²Department of Pathology, University of São Paulo, Brazil

³Faculty of Medicine of São José do Rio Preto, Brazil

⁴Department of Dermatology, University of São Paulo, Brazil

⁵Department of Veterinary Medicine, Federal University of Bahia, Brazil

*Correspondence to:

Dr. Carlos Roberto Borges Vasconcelos, M.D
Neuroradiology Fellow
Institute of Radiology, University of Sao Paulo
75 Dr. Ovidio Pires de Campos Avenue
Sao Paulo, 05403-010, Brazil
Tel: 005511954764649
E-mail: betofamed@yahoo.com.br

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Abstract

Cryptococcosis is a pathology caused by a fungus called *Cryptococcus neoformans*. It represents the most common fungal infection of the central nervous system in individuals with acquired immunodeficiency syndrome, affecting 11% of individuals in this group. In immunocompromised patients, the usual neurological impairment is subacute meningitis associated with multifocal dilatation of Virchow-Robin perivascular spaces. Immunocompetent patients are more frequently affected in the parenchyma with formation of fungal abscesses called cryptococcomas. Magnetic resonance imaging is more sensitive in cases of cryptococcal meningitis, but in immunocompromised cases, a normal examination is possible due to a lack of inflammation. Meningeal enhancement is demonstrated on FLAIR and T1-weighted images with contrast. There are four described imaging patterns: cryptococcomas, enlarged perivascular spaces, leptomeningeal and parenchymal nodules, and a mixed pattern. Many other conditions may simulate these radiological findings, making it necessary to be aware of them.

Keywords

Neurocryptococcosis, Radiological findings

Introduction

Cryptococcosis is a pathology caused by a fungus called *Cryptococcus neoformans* [1-3]. The major environmental sources of *C. neoformans* include soil contaminated with pigeon excreta (*C. neoformans* var. *neoformans* and *C. neoformans* var. *grubii*) and eucalyptus trees/decaying wood (*C. neoformans* var. *gattii*). *C. neoformans* var. *gattii* is found mainly in tropical and subtropical regions, whereas *C. neoformans* var. *neoformans* is encountered worldwide. *C. neoformans* var. *neoformans* usually infects immunodeficient individuals, leading to acute diffuse meningitis or meningoencephalitis. In contrast, infection with *C. neoformans* var. *gattii* more typically manifest as a granulomatous inflammatory response in immunocompetent hosts [3] (Figure 1). It represents the most common fungal infection of the central nervous system in individuals with acquired immunodeficiency syndrome, affecting 11% of the individuals in this group.

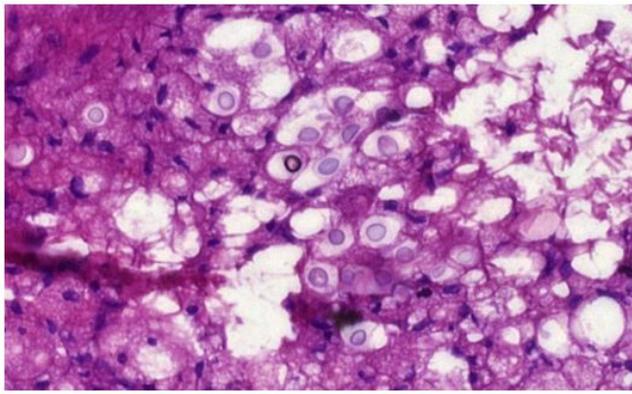


Figure 1: The highlighted oval structures are *Cryptococcus neoformans*. Note some of them with budding.

Immunocompetent patients are also victims of this infection. The infection of the nervous system, even in the absence of immunocompromising, is often caused by hematogenous dissemination from a pulmonary focus. In immunodeficient patients, the usual neurological impairment is subacute meningitis associated with multifocal dilatation of Virchow-Robin perivascular spaces. Immunocompetents are more frequently affected in the parenchyma, with the formation of fungal abscesses, called cryptococcomas that commonly involve the midbrain and basal ganglia [3] (Figures 2 and 3).

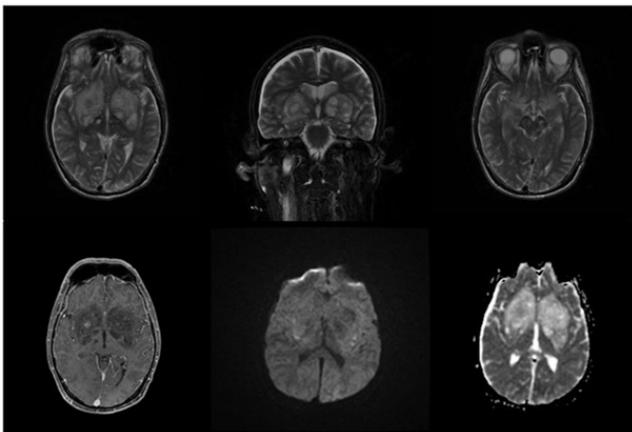


Figure 2: MRI T2, T1 contrast-enhanced, diffusion and apparent diffusion coefficient (ADC) map weighted images, depicting multiple dilated perivascular spaces in the basal ganglia in this immunocompromised patient with cryptococcal meningitis. Radiological signs compatible with gelatinous pseudocysts.

Clinical Aspects

Headache and signs of subacute meningeal irritation are the traditional form of clinical presentation in immunocompromised patients. Fever, meningeal irritation, signs of intracranial hypertension and altered level of consciousness may be associated with this condition. Focal signs and seizures are predominate in the presence of cryptococcoma [1].

Imaging

Magnetic resonance imaging (MRI) is more sensitive

in cases of cryptococcal meningitis, but in cases of immunodepression, normal examination is possible because of the scarcity of the inflammatory process. The meningeal enhancement is characterized in the FLAIR and T1-weighted images with contrast.

There are four imaging patterns described: cryptococcomas, enlarged perivascular spaces, leptomeningeal and parenchymal nodules and a mixed pattern. In the presence of Virchow-Robin perivascular spaces, the fungus can proliferate forming colonies rich in mucoid material, structures called “soap bubble-like” gelatinous pseudocysts (Figures 2 and 3).

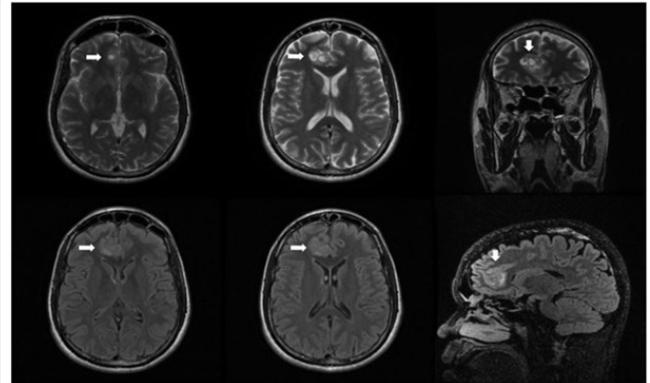


Figure 3: MRI T2-weighted images (upper images) and FLAIR sequences (lower images), depicting a 2.5 cm hypersignal expansive formation (arrow) centered on the cingulate cortex. This is a confirmed case of neurocryptococcoma in immunocompetent patient.

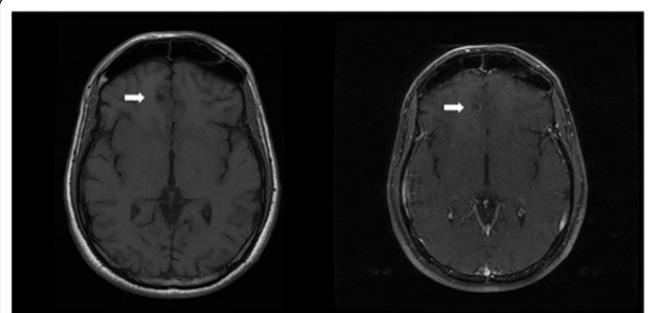


Figure 4: MRI T1-weighted sequences depicting a solid-cystic lesion in the cortical subcortical transition of the right cingulate (arrow) displaying peripheral enhancement to the paramagnetic agent and measuring 2.5 cm in major axial plane axis. The histopathological analysis confirmed neurocryptococcoma.

These structures are manifested in MRI as defined: rounded foci with regular contours, low to intermediate signal in T1, hyperintense signal in T2 and low signal in FLAIR in the predominant topography of the nuclei of the base and brainstem. The enhancement by gadolinium is minimal or absent, as well as perilesional edema [1-4].

Cryptococcomas have a variable size and these are manifested in MRI with hypointense signal in T1 with annular or nodular enhancement, hyperintense in T2 / FLAIR, usually with marked halo of vasogenic edema (Figure 4).

Proton spectroscopy may show a reduction of the peak of the neuronal marker (N-acetyl aspartate - 2.0 ppm), signaling loss and/or neuroaxonal dysfunction, naturally related to the

expansive effect and impairment of the viability of neurons [5]. In the study of perfusion, no area of significant increase in relative cerebral blood volume was observed. The diffusion sequence does not demonstrate restriction areas for the movement of water molecules [3].

Differential Diagnosis

Multiple pathologies may simulate the described radiological findings. Acquired toxoplasmosis usually presents ring-enhancing masses with surrounding edema and involves basal ganglia and cerebral hemispheres. Tuberculosis classic promotes basal meningitis with frequent cranial nerves involvement and parenchymal lesions (tuberculoma). Tuberculomas can be hypointense in T2-weighted images. Primary central nervous system lymphoma often shows increasing lesion(s) along the ependymal surface with T2 hypointensity [6]. Neurosarcoidosis presents leptomeningeal enhancement with or without dural lesions. Expanded perivascular spaces are usually located close to the anterior commissure and follow the cerebrospinal fluid in all MRI sequences, but the differentiation can be difficult [6-10].

Conclusion

Neurocryptococcosis represents a challenging imaging diagnosis. High level of suspicion is important, notably in immunocompromised patients. The identification of specific findings improves the diagnostic accuracy. Several other pathologies may simulate the described radiological findings, making it necessary to be aware of them.

Conflict of Interest

The authors declare no conflict of interest.

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