Neurocryptococcosis: A Pictorial Review

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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.
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).

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).

These structures are manifested in MRI as described: 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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