All you need to know about fungal CNS infection: 10 years experience of a tertiary hospital.

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Learning objectives

The purpose of our educational exposition is to:

- Illustrate the fungal lesions findings on CT and on MRI and differential diagnoses on the CT and MRI in the 10 years of experience of the Neuroradiology service of the Hospital of Clínicas of Porto Alegre - Rio Grande do Sul - Brazil.
- Describe the CT findings of fungal lesions and differential diagnoses in the series of cases.
- Describe the MRI findings of fungal lesions and differential diagnosis in the case series (T1, T2, Flair and diffusion).
Background

Central nervous system fungal infections are rare, however, with the increasing number of immunocompromised individuals (AIDS, organ transplantation), the central nervous system fungal infections are gaining prominence in the differential diagnosis.

Imaging techniques are sensitive for detecting an abnormality, localizing it, and in many cases categorizing the lesion into infectious/inflammatory disease, neoplastic or vascular disease. The imaging methodologies have had an impact in suggesting infectious/inflammatory conditions because restricted diffusion is characteristic of some stages of some infections.

With the clinical history, physical examination, and the patient's age, the radiologist can more accurately interpret the images and make a probable differential diagnosis.

The central nervous system fungal lesions and differential diagnosis will be described in MRI imaging and CT imaging.
Findings and procedure details

IMAGING FINDINGS AND PROCEDURE DETAILS

Cryptococcosis

Infection with encapsulated yeast Cryptococcus neoformans can result in meningitis or disseminated disease, especially in people with defective cell-mediated immunity. Cryptococcosis is an important fungal infection in patients with severe HIV infection, organ transplantation, reticuloendothelial malignancy, corticosteroid treatment, sarcoidosis and asplenic patients.[1,2]

MRI findings may be normal or demonstrate many abnormalities: dilated Virchow Robin spaces (with gelatinous cysts adjacent to the basal ganglia and the corticomedullary junction, may or may not enhance- fig.5), multiple milliary enhancing parenchymal and leptomeninginal nodules (choroid plexus in the trigone). Cryptococcomas (fig. 1, 2,3,4) presenting as a solid mass or as disseminated lesions, predominantly in the midbrain and basal ganglia. Contrast is needed to detect leptomeninginal nodules. On T2WI/FLAIR, numerous bilateral small foci of high signal intensity that do not enhance can be seen in cryptococcosis, coccidioidomycosis and candidiasis; basal ganglia lesions should also include toxoplasmosis (fig 19) and lymphoma (fig.14) in the differential diagnosis. [3]

Mucormycosis

Mucormycosis is an infection caused by the fungi of the Mucorales order of the class of Zygomycetes.[1] It affects patients with altered cellular immunity: diabetic patients with ketoacidosis, debilitated patients with burns, uremia, malnutrition, HIV patients with a history of drug abuse (basal ganglionic lesions). There are increased risk for mucormycosis in patients undergoing dialysis or taking iron chelating agent deferoxamine. [3]

The CT findings of sinonasal Mucor: sinus opacification, air-fluid concentrations, increased density or calcification, obliteration of the nasopharyngeal tissue planes.[3]

The findings MRI T1WI and T2WI/FLAIR:low intensity may be present in the sinuses . In some cases, bony destruction is present. Orbital extension from the ethmoid sinuses can produce proptosis and chemosis and thrombosis of the superior ophthalmic vein, with extension through the orbital apex and subsequent thrombosis of the cavernous sinus. The lesion can
extend into the infratemporal fossa and pterygopalatine fossa from the maxillary sinus[3] (fig.6,7,8).

**Aspergillosis**

Aspergillus fumigatus is the human pathogen in the immunocompromised hosts. Primary aspergillosis of the paranasal sinus has been described to be of two kinds: either noninvasive (allergic Aspergillus sinusitis) or invasive, through direct or hematogenous spread. The fungus has a propensity to spread along vessels that serve as direct channels for the seeding of aspergilli and has a tendency for invasion of the walls of both small and large blood vessels (resulting in thrombosis and subsequent infarction or hemorrhage). [5]

CT scanning is not specific for fungal disease, but may be helpful in providing a convenient way to monitor the patient's response to antimicrobial therapy. The CT findings: hyperdense mass lesion in the sinuses along with bony expansion or erosion of sinus walls and/or cranial base, abscesses (ring or homogenous enhancement or not along with mass effect; early hemorrhage or infarction are associated with aspergillosis and should raise suspicion in immunocompromised hosts. [5,6]

The MRI findings: irregular mass having hypointense to isointense signals on T1-weighted images, extremely low signals on T2-weighted images with either bright homogenous enhancement on post-gadolinium T1 weighted images, or ring enhancement pattern[3,5,6] (fig.9,10).

**Histoplasmosis**

Histoplasmosis is caused by the dimorphic fungus Histoplasma capsulatum. Central nervous system (CNS) histoplasmosis is rare and difficult to diagnose (it could be overlooked or mistaken for other pathologies due to its nonspecific symptoms). It may have the following signs: acute and chronic meningitis, stroke due to infected emboli, diffuse encephalitis, ring-enhancing lesions, neurologic deficits, chronic recurrent hydrocephalus, elevated cerebrospinal fluid protein. Histoplasmosis should be considered if the patient is from an endemic area and presents with compatible symptoms.[7]

The MRI findings: single or multiple ring-enhancing lesions in CNS histoplasmosis are nonspecific and may be seen in other diseases like abscess, necrotic tumor, subdural and epidural empyema or toxoplasmosis [7,8](fig. 11).

**Paracoccidioidomycosis**

Paracoccidioidomycosis is caused by the fungus Paracoccidioides brasiliensis and it is the most prevalent systemic mycosis in Latin America in the immunocompetent patients.
The findings clinical depends of the immune response profile according to the tissue and blood released cytokines, resulting in tissue damage. [9]

The T1WI findings: lesions were predominantly hyperintense.

The T2WI findings: hypointense component was present or a perilesional abnormal white matter, a ring-enhancement pattern (fig. 12, 13). Spectroscopy could be showed an increased lipid peak .[10]

CT and MRI are useful for diagnosis, but are not specific because this disease is similar to the granulomatous diseases of the CNS.

The CT findings: hypodense lesions, with annular or nodular enhancing, surrounded by mild edema, after contrast, with multiple mass lesions, or a single mass lesion .[11]

Candidiasis

Neurocandidiasis normally results from systemic candida infection in immunosuppressed patients or to intravascular catheter infections. There are various presentations images that include hydrocephalus leptomeningeal, enhancing nodules with edema (granuloma), calcified granuloma, infarction and abscess formation[12]. The CT findings: it is usually normal. The MRI findings: microabscesses, ring enhancement with a hemorrhagic component. [13]

Nocardiosis

Neuronocardiosis is caused by the Nocardia species. Neuronocardiosis is associated with a state of compromised immunity and steroid therapy.[14] Nocardia is normally sensitive to the sulfonamides. The imaging findings: brain abscess, meningitis is rare, lesions show an enhancing capsule commonly containing multiple loculations. The MRI findings: Flair - multiple lesions, post-contrast a rim enhancement; diffusion-weighted image is positive - proteinaceous material in the abscesses.[3]

Fungal central nervous system infections: Differential diagnosis

CNS Lymphoma

Locations: nuclei of the base, cerebellar hemispheres, thalamus, brain stem, corpus callosum and subependymal region. The findings TC: normally in some cases of steroid use, isolated or multiple areas of expansive effect, with little edema in relation to lesion size, hemorrhagic, Isodense, hyperdense, hypodense, homogeneous
enhancement, or no enhancement - necrotic area. The findings MRI: T1WI - isointense to hypointense, T2WI / FLAIR - variable intensity. DWI - Broadcast restriction (fig.14). [15,16]

**Progressive multifocal leukoencephalopathy**

Progressive multifocal leukoencephalopathy is opportunistic infection caused by DNA virus JC polyomavirus - infects oligodendrocytes and causes demyelination in immunocompromised patients. [17]

The findings imaging: high signal intensity on T2WI/FLAIR in the peripheral white matter, it involves the subcortical U fibers as opposed to HIV or CMV. The findings of the HIV and CMV involve the white matter more centrally or periventricularly. [3] (fig.15,16,17)

**Pyogenic abscess**

Brain abscess development have four stages: first stage- early cerebritis (1 to 4 days), second stage- late cerebritis (4 to 10 days), third stage - early capsule formation (11 to 14 days) , fourth stage- late capsule formation (>14 days). [20]

Brain abscess is a focal infection, which starts as a localized abscess, which is subsequently converted into a collection of pus within a well-vascularized capsule. [18]

The findings CT and MRI: a hypodense lesion with a contrast-enhancing ring. The findings CT: early detection, localization, characterization, determination of number, size, and staging of the abscess. The MRI findings depend on the stage of the infection. Early phase: low T1-weighted images (T1WI) signal and high T2-weighted images (T2WI) signal with patchy enhancement. Later phases: low T1WI signal becomes better demarcated, with high T2WI signal both in the cavity and surrounding parenchyma. MR spectroscopy (1H-MRS) can accurately differentiate between necrotic/cystic tumor and cerebral abscesses. [19](fig.18,19)

**TOXOPLASMOSIS**

Toxoplasma gondii is protozoan parasite normally infecting the CNS of patients with AIDS, with compromised cellular immunity - particularly defects in the lymphocyte-monocyte system. The findings CT: areas of low density with little or no enhancement, gyral enhancement, or isodense nodules that enhance. It is important that a response to appropriate antibiotic therapy can distinguish toxoplasmosis from lymphoma. The findings MRI: multiple lesions of high intensity on T2WI/FLAIR with vasogenic edema and ring or nodular enhancement are seen on T1WI; a low-intensity ring surrounded by high intensity on T2WI/FLAIR with ring enhancement. Hyperintense-necrotizing encephalitis; isointensae- abscess organization. Lesions may present perilesional edema. MR
perfusion: lymphoma (increased perfusion) and toxoplasmosis (decreased perfusion). MRI spectroscopy: toxoplasmosis lesions - elevated lactate and lipid concentrations; and lymphoma shows moderate increased lactate and lipid and markedly increased Cho.[3] (fig. 20)

TUBERCULOSIS

The incidence of tuberculosis has increased with AIDS and the emergence of drug-resistant strains of the bacillus. Intracranial tuberculosis have been showed pathologic processes as tuberculous meningitis and the intracranial tuberculoma. The tuberculoma is a small nodule that can coalesce to form a large lesion. The intracranial tuberculoma produces symptoms from mass effect and associated edema. Imaging depends on the stage of the infection.

The MRI findings- tuberculous meningitis: basal and sylvian cisterns are poorly visualized without contrast because of the dense exudate; FLAIR- the basal cisterns can have increased intensity because of the thick proteinaceous.

The CT findings- tuberculosis meningitis: periventricular low density.

The CT findings- intracranial tuberculoma appears as a nodule that ranges from low to high density.

The MRI findings- T2WI/FLAIR - typical tuberculoma: as a nodule with a small central area (caseous necrosis) of high signal. The high intensity may be observed in the wall of tuberculomas on T1WI and low intensity on T2WI/FLAIR. [3] (figura21)
Images for this section:

**Fig. 1:** A 66-year-old male patient diagnosed with cryptococcal meningitis and cryptococcosis in the left fronto-parietal region. A. Pre-contrast T1-weighted MRI axial image demonstrates isointense lesion in relation to the parenchyma. B. In the T2-weighted axial image of MRI, the same lesion appears hyperintense. C. Axial FLAIR: the lesion is hyperintense. D. There is no restriction on the diffusion of the water molecules (high signal of the ADC MAP).

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**Fig. 2:** A- 66-year-old male patient diagnosed with cryptococcal meningitis and cryptococcoma in the left fronto-parietal region (arrow). A. CT axial cut without contrast shows hypodense lesion. B- In contrast-enhanced axial CT scans, the image does not exhibit contrast enhancement(arrow).
**Fig. 3:** Cryptococcomas by Cryptococcus gatti. A. Post-gadolinium sagittal T1: hypointense lesion with peripheral ring enhancement in the bulb (arrow), with signs of adjacent edema. B. Post-Gd axial T1: hypointense lesion with peripheral ring enhancement in the subcortical region (arrow).

**Fig. 4:** Cryptococcosis meningitis. A. T1 axial post-contrast, evidencing the enhancement of the leptomeninges (arrow). B. Axial FLAIR. Hypersignal of the leptomeninges (arrow).
Fig. 5: Axial FLAIR: heterogeneous, predominantly hyperintense lesions in the basal nuclei compatible with gelatinous pseudocysts (arrows), a classic finding of cryptococcosis of the central nervous system. It is also identified choroid plexus (arrows) and leptomeninges hyperintensity.
**Fig. 6:** A 55-year-old patient with mucormycosis in the nasal fossa. A. T1-weighted. Lesion with heterogeneous hyperintense central area in the sphenoid sinus (arrow). B. Axial T2. Central hypointensity and hyperintense peripheral halo. C. ADC map. Restriction (arrow).

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**Fig. 7:** Coronal and sagittal images of the same patient of figure 6. A. T2-weighted coronal image demonstrates hypointense lesion with hyperintense halo (arrow). B. Sagittal T1, heterogeneous lesion, with predominantly central hyperintensity and hypointense peripheral halo (arrow).

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**Fig. 8:** Mucormycosis with orbital and encephalous involvement. A. Axial diffusion. Hypointense lesion with hyperintense halo and diffusion restriction (arrow). B. Axial FLAIR. Hypointense lesion with hyperintense peripheral halo (arrow) and signs of prominent peripheral edema. C. Axial T2. Hyperintense lesion with hypointense peripheral halo (arrow) and signs of prominent peripheral edema. D. T1 coronal contrast. There is an heterogeneous lesion in the left orbital region. Sign of the "phantom nose" (red arrow), characterized by loss of enhancement of the nasal mucosa of the injured side. There is also enhancement in the leptomeninges on the affected side (arrow).

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**Fig. 9:** A. Axial T1 image of a 20-year-old patient with angioinvasive aspergillosis of the central nervous system, demonstrating aspergilloma in the left occipital region (arrow) - hyperintense lesion with hypointense halo. B. Axial T2. Hyperintense lesion (arrow).C. Axial FLAIR. Heterogeneous lesion with hyperintense center (arrow).

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Fig. 10: Axial MR images of invasive CNS aspergillosis, female patient, 13 years with ALL. A and B. DWI and ADC map (arrow); C. Axial SWI (arrow); D. T1 axial post contrast (Gadolinium) (arrow); E. Spectroscopy (TE 35 ms): lesions with diffusion restriction and hypointense material in T2 SWI, slight peripheral enhancement and large lactate peak. Typical findings of fungal lesions by aspergillus.

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**Fig. 11:** Infarcts by vasculitis secondary to Histoplasmosis. 38 years old patient, previously healthy, from Palestine where he lived in caves full of bats. He started with progressive dementia. Biopsy demonstrated CNS histoplasmosis (vasculitis) (arrow). A. Axial post-contrast T1. Lesions in the basal nuclei with peripheral enhancement (arrows). B and C. Axial FLAIR. Hyperintense lesions (arrow).

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**Fig. 12:** MRI axial images of a 53-year-old male patient, alcoholic, from the countryside, used to chew grass. MRI demonstrated paracomas in the CNS. A. T2-weighted image showing lesions with heterogeneous low signal in the cerebellum (arrow). B. Post-contrast T1 image exhibiting hypointense lesions with peripheral ring enhancement in the cerebellum (arrow).

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**Fig. 13:** a. AXI T1 pre-contrast; B.-AXI T2 gradient; C.T2 coronal; D. AXI FLAIR; E.Axial T1 post-contrast; F. AXI T2. Right parietal lobe expansive lesion hypointense in T2 and iso/hyperintense in T1 and peripheral enhancement. T2 weighted images shows an onion-like image.

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**Fig. 14:** T2 images. Hypointense lesion. DWI. Restricted water diffusion. T1 post-Gd. Homogeneous enhancement. High cellularity lesion. Primary central nervous system lymphoma.

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**Fig. 15:** Signal hyperintensity in T2 (A) and FLAIR (B) involving juxtacortical white matter (U-fibers), with no mass effect (arrows), assimetric.

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**Fig. 16:** c. Intralesional T2-weighted microcyst in the right frontal region (green arrows). d. Hypersignal areas in T2 involving the juxtacortical white matter (U-fibers) and involving fibers of the cortico-spinal tract (red arrow).
Fig. 17: e, f: AXIAL FLAIR: hyperintensity in white matter of right frontal lobe. DWI restricted periphery

Fig. 18: A 58-year-old male, renal TX with multiple pyogenic abscesses bilaterally; Axial FLAIR exhibits hyperintense lesions with edema. B., C: diffusion restriction.
Fig. 19: a. AXI FLAIR; B. AXI T2; C. AXI T1 post gd; D. DADC; and. Diffusion, f. SAG T1 post-contrast; g. SAG Flair. T2 / FLAIR hyperintense lesion peripheral T2 hypointensity. Ring enhancement. Central DWI restriction.

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**Fig. 20:** Patient with CNS toxoplasmosis. A. Axial FLAIR exhibiting hypointense lesion in the nuclei of the base with hyperintense peripheral halo (arrow). B. Axial T1 exhibiting the same hypointense lesion with peripheral ring enhancement. Mural nodule (eccentric target signal).

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**Fig. 21:** Patient with CNS tuberculosis. A. T2-weighted image exhibiting hypointense subcortical lesions (arrows). B. T1-weighted post Gd. Ring enhancement (arrows).

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Conclusion

Radiologists play a central role in the diagnosis of major central nervous system infections. The most notable lesions in this study are those caused by fungal infections and differential diagnoses in the central nervous system (CNS). The most used imaging resources in this study were magnetic resonance imaging and computed tomography. In this experiment, it was observed that computed tomography (CT) was more used in situations of urgency - acute cases, in the search for focal lesions and some complications such as hemorrhages, mass effect. Magnetic Resonance Imaging (MRI) played an important role in the elucidation of differential diagnoses because it had greater sensitivity in the specific characterization of each lesion. It is concluded that in some cases, correlation with clinical data, laboratory data and biopsy is necessary for the final diagnosis.
References

1-Qazzafi,Z.; Thiruchunapalli,D; Birkenhead,D; D. Bell; Sandoe ,J.A.T. Invasive Cryptococcus neoformans infection in an asplenic patient. 2007 The British Infection Society. Volume 55, Issue 6, Pages 566-568


10-Reis F.; Collier P.P.; Souza T.F; Lopes, G.P.; Bronzatto E; Silva J.N.A; Pereira, R.M; Appenzeller, S. Neuroparacoccidioidomycosis (NPCM): magnetic resonance imaging (MRI) findings. Mycopathologia. 2013 Feb; 175(1-2): 181-6


