AJNR

# Cerebral aspergillosis: MR imaging and histopathologic correlation.

J Cox, F R Murtagh, A Wilfong and J Brenner

*AJNR Am J Neuroradiol* 1992, 13 (5) 1489-1492
http://www.ajnr.org/content/13/5/1489

# Cerebral Aspergillosis: MR Imaging and Histopathologic Correlation

Joe Cox, F. Reed Murtagh, Adam Wilfong, and Jeff Brenner

**Summary: The authors report a case of intracranial aspergillosis secondary to immunosuppression. Signal intensity changes in the lesion on brain MR are compared with gross and histopathologic findings at autopsy. A peripheral ring of low signal intensity relates to a dense population of Aspergillus hyphal elements and small areas of hemorrhage. CT findings are included for comparison.**

**Index terms: Aspergillosis; Brain, abscess**

Aspergillosis of the central nervous system has increased in prevalence in recent years (1). The practice of iatrogenically induced immunosuppression in transplantation procedures, inflammatory conditions, and cancer treatment, and the widespread use of antibiotics has increased susceptibility to this disease (1–7). Recently, Epstein et al have reported that Aspergillus is second only to Candida as the fungal organism most likely to be responsible for brain abscesses in immunosuppressed patients (8). The angioinvasive nature of this fungus is documented and explains the computed tomography (CT) and magnetic resonance (MR) findings of hemorrhage and infarction seen in pulmonary and cerebral infections (5, 6, 9, 10). We believe this case is unique in that we were able to identify clear boundaries of signal intensity changes and relate them to microscopic sections taken at autopsy. MR, CT, gross, histopathologic, and clinical findings are presented.

## Case Report

This is the case of a 22-year-old white man diagnosed with aplastic anemia in February 1989, who underwent allogenic bone marrow transplantation in October 1990. This was complicated by recurrent graft-versus-host disease, hypertension secondary to cyclosporine, and Candida sepsis. The patient remained pancytopenic after transplantation. For his recurrent graft-versus-host disease, the patient was taking corticosteroids and cyclosporine. He was admitted on March 3, 1991, complaining of left-sided weakness, lethargy, and headaches.

Physical examination revealed a "Cushingoid" young man who was alert and well oriented. He demonstrated right facial weakness, especially upon smiling, and severe left hemiparesis.

Admission CT revealed a large low-attenuation lesion centered in the right basal ganglia with significant mass effect and a large amount of surrounding edema. There was increased attenuation at the periphery of the lesion. Diagnostic considerations included tumor, abscess, and hemorrhagic infarction (considering his hypertension and thrombocytopenia). The following day, an MR and pre- and postcontrast CT were performed. CT demonstrated slightly decreased mass effect and edema but no enhancement (Fig. 1). MR (Fig. 2) demonstrated a large periventricular mass lesion in the right parietal lobe, associated with massive white matter edema, extending to the right parietal, insular and temporal cortices, right basal ganglia, brain stem, and corticospinal tracts. The mass measured approximately 3 × 4 × 4 cm and had a surrounding ring of low signal on the T2-weighted images (Fig. 2B), suggesting a paramagnetic effect.

Two days after admission, the patient had grand mal seizures for which he was treated with diazepam and phenytoin. His mental status rapidly deteriorated; he became unresponsive, and stereotactic brain biopsy and culture on March 6 were positive for Aspergillus. After discussion with the family, medical care was withdrawn, and the patient died on March 8.

Autopsy revealed bilateral cerebral tonsillar herniation with prominent grooving, reflecting its acuteness. Sectioning of the brain (Fig. 3) revealed a 6 × 5 × 5 cm hemorrhagic right frontoparietal infarction extending to the right basal ganglia. There was a moderate midline shift without subfalcian herniation. Numerous punctate hemorrhages were present within the pons. Microscopic sections of the right temporal/parietal region revealed hemorrhage, necrosis, vascular thrombosis, abscess, acute, and chronic inflammation with surrounding gliosis. Numerous acutely branching septate fungal hyphae were present throughout the parenchyma (Fig. 4), with angioinvasion (Fig. 5). Sections were taken in areas of the brain that corresponded to the distinct signal intensity changes seen on MR (Figs. 2A

Received November 19, 1991; accepted and revision requested January 13, 1992; revision received January 30.

All authors: Department of Radiology, University of South Florida College of Medicine, 12901 N. 30th Street, Box 17, Tampa, FL 33612. Address reprint requests to F. Reed Murtagh, MD.

AJNR 13: 1489–1492, Sep/Oct 1992 0195-6108/92/1305-1489 

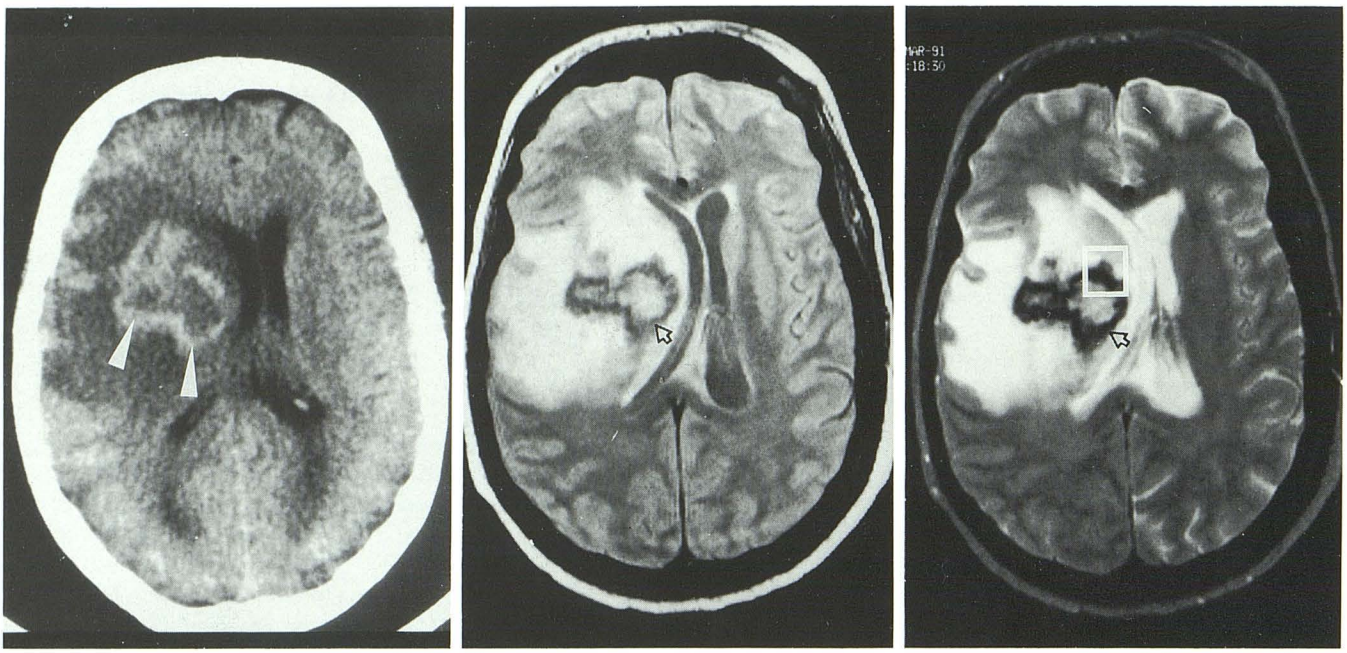


Fig. 1. CT scan (nonenhanced) 1 day after onset of neurologic symptoms shows a large low-density lesion centered in the right basal ganglia. The peripheral area of higher attenuation (*arrowheads*) suggests hemorrhage. There is a large amount of surrounding edema with significant mass effect.

Fig. 2. MR scan on the same day as the CT scan in Figure 1 (1.5-T machine). *A*, Proton density image (2600/22/1). *B*, T2-weighted image (2600/90/1). The square-shaped insert in *B* roughly corresponds to the histologic section shown in Figure 6 below. Both images show an isointense (to gray matter) center with low signal intensity on the periphery of the lesion (*arrows*). There is large amount of surrounding high-signal edema.

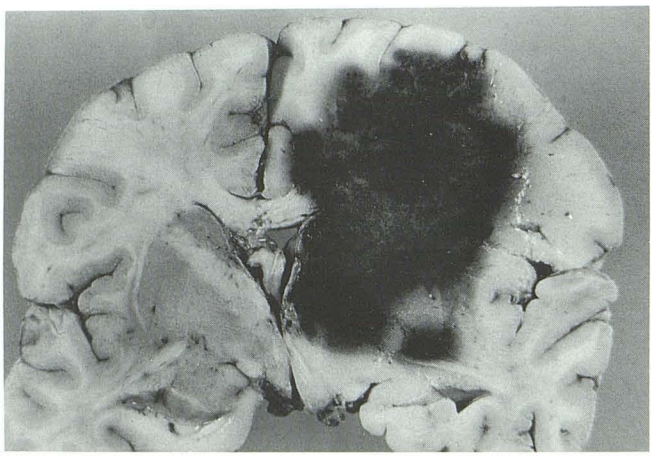

Fig. 3. On coronal section, the lesion appears grossly hemorrhagic. This section might explain the inhomogeneity of the lesion seen on CT and MR.

and 2B). Sectioning of the lungs revealed no gross or microscopic abnormalities.

## Discussion

Aspergillus is a ubiquitous saprophytic fungus, and infection of patients with normal immunity will most often present as sinus mucosal inflammation (11). In immunocompromised patients, Aspergillus most commonly disseminates hematogenously from a pulmonary focus or extends directly through the walls of the paranasal sinuses to involve the brain (1, 2, 4, 8, 9, 12). The mortality rate for cerebral aspergillosis approaches 85% to 100%, depending on the degree of neurologic compromise at presentation (8). Death usually occurs within 1 week of neurologic onset (1).

Our microscopic findings are similar to those of Whelan et al (5) who suggested that mycoses in which the hyphal forms predominate will form patterns consistent with vascular occlusion and secondary abscess formation. The marked inflammatory response leading to edema containing free water is directly related to longer T2 relaxation times and hence the large white areas seen on T2W MR (Fig. 2) (13). The peripheral ring of decreased signal intensity in the proton density and especially the T2-weighted images probably represents a ring of small abscesses interspersed with areas of hemorrhage (Fig. 6). Further examination of the abscesses revealed a

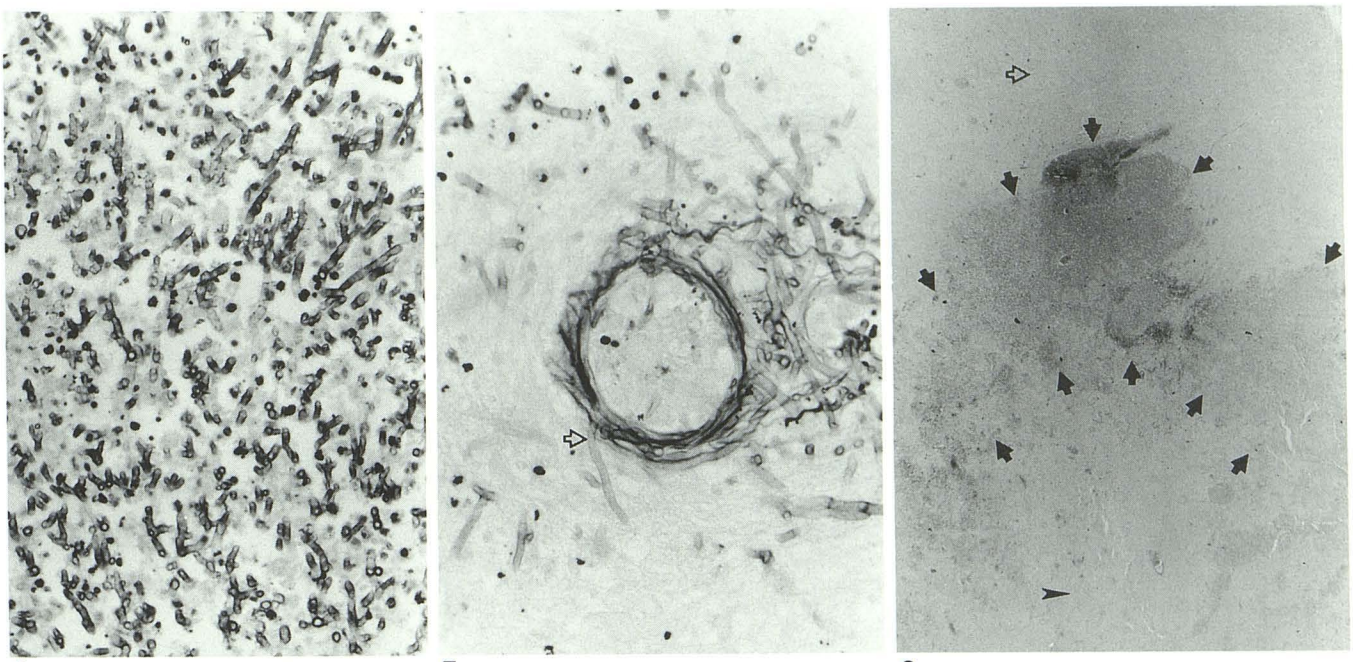

Fig. 4. Grocott-Gomori methenamine silver (GMS) stain of one of the small peripheral abscesses reveals the numerous acutely branching, septate fungal hyphal elements of Aspergillus.

Fig. 5. The angioinvasive nature of Aspergillus is clearly evident in this slide. Hyphal elements (*arrow*) can be seen extending through the wall of a blood vessel.

Fig. 6. Histologic section at the area of the square inset in Figure 2. The *open arrow* indicates the area of edematous brain with intact architecture corresponding to the high signal intensity region seen on MR. The *solid arrows* delineate a narrow portion of a ring of small abscesses interspersed with areas of hemorrhage that were found to correspond with the ring of low signal intensity seen on MR. The central portion of the lesion (*arrowhead*) consists of an area of coagulative fungal necrosis which is isointense to gray matter on MR.

very dense population of branching, septate aspergillus hyphal elements (Fig. 4). In contrast, the center of the lesion demonstrated a relative paucity of hyphal elements. The marked differences in the population density of fungal elements between the periphery and the center of the lesion may be contributing to the distinct signal intensity changes on MR. Earlier MR study of fungal sinus infections (14) noted that low signal intensity on T2-weighted MR images appears to be characteristic of mycetomas. These findings have been attributed of the presence of iron, magnesium, and manganese found in fungal (Aspergillus) concretions (14, 15). These ions are essential to fungal amino acid metabolism (16, 17). The presence of calcium in fungal masses (14), with its paramagnetic effect, may also contribute to the sharp decrease in signal activity seen on T2-weighted images and the peripheral increased attenuation seen on CT scan. Unfortunately, the exact concentrations of the paramagnetic elements mentioned above were not able to be determined.

In addition, the peripheral ring of low signal intensity on MR may be related to the presence of blood breakdown products within the small areas of hemorrhage interspersed between the small abscesses on the periphery. Microscopically, there was no hemorrhage in the center of the lesion. Deoxyhemoglobin may be present in hemorrhage any time from the first 24 hours to 3 to 5 days. Deoxyhemoglobin has 4 unpaired electrons and thus can act as a paramagnet and shorten T2 relaxation times. Methemoglobin will also shorten T2 relaxation times (18, 19) but is usually present between 3 and 7 days after hemorrhage. Furthermore, Herold et al (10) have noted that high osmolality and acidic pH in the inflammatory environment of extravascular blood in a catabolic state are inversely related to T1 and T2 relaxation times.

Histologically, the center of the lesion consisted of areas of coagulative fungal necrosis where Aspergillus hyphal elements were sparsely present. On MR, these areas are roughly isointense to gray matter (Fig. 2B). The center of this lesion is

analogous histologically to the center of the target-like appearing lesions seen on a previously reported MR study of invasive pulmonary aspergillosis (10). In this study, the centers of the Aspergillus lesions were believed to represent coagulative fungal necrosis, and the periphery of the lesions corresponded to subacute hemorrhage or hemorrhagic infarction.

## References


1. Beal MF, O'Carroll CP, Kleinman GM, Grossman RI. Aspergillosis of the nervous system. *Neurology* 1982;32:473–479
2. Grossman RI, Davis KR, Taveras JM, O'Carroll CP. Computed tomography of intracranial aspergillosis. *J Comput Assist Tomogr* 1981;5:646–650
3. Tully RJ, Watts C. Commuted tomography and intracranial aspergillosis. *Neuroradiology* 1989;17:111–113
4. Jinkins JR, Siqueira E, Zuheir Al-kawi. Cranial manifestations of aspergillosis. *Neuroradiology* 1987;29:181–185
5. Whelan MA, Stern J, de Napoli RA. The computed tomographic spectrum of intracranial mycosis: Correlation with histopathology. *Radiology* 1981;141:703–707
6. Potente G. CT findings in fungal opportunistic pneumonias: body and brain involvement. *Comput Med Imaging Graphics* 1989;13: 423–428
7. Danziger A, Price H. Computed axial tomography in intracranial aspergillosis. *S Afr Med J* 1978;54:706–708
8. Epstein NE, Hollingsworth R, Black K, Farmer P. Fungal brain abscesses (aspergillosis/mucomycosis) in two immunosuppressed patients. *Surg Neurol* 1991;35:286–289
9. Mikhael MA, Rushovich AM, Ciric I. Magnetic resonance imaging of cerebral aspergillosis. *Comput Radiol* 1985;9:85–89
10. Herold CJ, Kramer J, Sertl K, et al. Invasive pulmonary aspergillosis: evaluation with MR imaging. *Radiology* 1989;173:717–721
11. Brandt-Zawadski M, Norman D. *Magnetic resonance imaging of the central nervous system.* New York: Raven Press, 1980:252–254
12. Nov AA, Cromwell LD. Computed tomography of neuraxis aspergillosis. *J Comput Assist Tomogr* 1984;8:413–415
13. Swensen SJ, Keller PL, Berquist TH, McLeod RA, Stephens DH. Magnetic resonance imaging of hemorrhage. *AJR* 1985;145: 921–927
14. Zinreich SJ, Kennedy DW, Malat J, et al. Fungal sinusitis: diagnosis with CT and MR imaging. *Radiology* 1988;169:439–444
15. Gupta R, Singh AK, Bishnu P, Malhotra V. Intracranial aspergillus granuloma simulating meningioma on MR imaging. *J Comput Assist Tomogr* 1990;14:467–469
16. Van de Heide S, Kauffman MF, Devries K. Cultivation of fungi in synthesis and semi-synthetic liquid medium. *Allergy* 1985;40: 592–598
17. Kubicek CP, Rohr M. Metabolic effects of manganese deficiency in *Aspergillus niger*: evidence of increased protein degradation. *Arch Microbiol* 1985;141:266–268
18. Gomori JM, Grossman RI. Mechanisms responsible for the MR appearance and evolution of intracranial hemorrhage. *Radiographics* 1988;8:427–440
19. Grossman RI, Gomori JM, Goldberg HI, et al. MR imaging of hemorrhagic conditions of the head and neck. *Radiographics* 1988;8: 441–454