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Y. Miaux, P. Ribaud, M. Williams, A. Guermazi, E. Gluckman, C. Brocheriou, and M. Laval-Jeantet

PURPOSE: To assess the CT and MR appearance of cerebral aspergillosis in patients who have undergone bone marrow transplantation. **METHODS:** The imaging and clinical data of five patients with cerebral aspergillosis were reviewed retrospectively and compared with autopsy findings. **RESULTS:** Lesions are often located in the basal ganglia and demonstrate an intermediate signal intensity within surrounding high-signal areas on long-repetition-time MR scans. The lesions were multiple in four of the five patients and more numerous on MR images than on CT scans. The lesions (which demonstrate no parenchymal enhancement) are consistent with acute infarcts as confirmed at autopsy. In the large lesions, there is early intravascular and meningeal enhancement, as expected in acute infarcts involving an appreciable portion of the territory of a cerebral artery. **CONCLUSION:** The diagnosis of early cerebral infarction in a patient considered at risk for invasive aspergillosis, even without overt pulmonary disease, is an indication to institute aggressive antifungal therapy.

Index terms: Aspergillosis; Bone marrow transplantation; Brain, magnetic resonance

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Cerebral aspergillosis is a rare condition that affects primarily the immunocompromised host (1–5). Its prevalence has increased with the practice of intensive chemotherapeutic regimens, use of corticosteroids, and transplantation procedures (1–3).

In these patients the common pathway for the fungus to reach the central nervous system (CNS) is hematogenous dissemination from extracranial foci, usually the lungs (4). The mortality rate of cerebral aspergillosis approaches 100% in these immunocompromised patients (6), but there are occasional case reports noting survival with combined aggressive antifungal therapy and surgical resection (6–14). This makes early diagnosis essential. The clinical and laboratory diagnosis of cerebral aspergillosis is difficult, so imaging modalities such as computed tomography (CT) and magnetic resonance (MR) are important. Although there are many reported cases of cerebral aspergillosis in which the CT findings are described (1–3, 6, 8–23), there are less numerous cases with MR findings (7, 8, 11, 12, 14, 16–18, 20, 22–25).

We present five cases of cerebral aspergillosis in immunocompromised patients with CT and MR findings, with autopsy correlation.

Materials and Methods

In one year, five cases of autopsy-documented intracranial aspergillosis were diagnosed. The patients' ages ranged from 28 to 52 years. Three were women and two men. All patients had been treated with bone marrow transplantation for chronic myelocytic leukemia (four patients) and myelodysplastic syndrome (one patient with refractory anemia with excess blasts). All patients had low lymphocyte counts. Unenhanced CT scans were obtained in all five patients.

All patients were examined on a 0.5-T MR machine, using spin-echo sequences. Precontrast T1-weighted 500/20/2 (repetition time/echo time/excitations), proton density–weighted 1940/40/2, and T2-weighted 1940/100/2 images (with flow compensation) were obtained in the axial plane (section thickness, 7 mm; intersection gap, 2 mm; field of view, 25 cm; matrix 224 × 224). T1-weighted images were obtained in the axial and coronal planes after

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TABLE 1: Characteristics of five patients with intracranial aspergillosis

Case	Age, y/Sex	Underlying Condition	Factors Predisposing to Fungal Infection	Interval between Bone Marrow Transplant and Onset of Neurologic Symptoms	Pertinent Clinical Findings	Pulmonary Infiltrate at the Time of CT or MR?	Interval between Onset of Neurologic Symptoms and Death	CSF Protein, mg/100 mL	Granulocyte/Lymphocyte Counts, mm^3
1	52/M	CML	Bone marrow transplantation, corticosteroids	2 mo	Slurred speech, photophobia, mental confusion, fever (38°C), right hemiparesis	No	13 d	200	2150/200
2	28/F	CML	Bone marrow transplantation, corticosteroids	3 mo	Progressive left hemiparesis without fever	Yes, confirmed by chest CT	17 d	88	8600/200
3	44/F	CML	Bone marrow transplantation, corticosteroids	3 mo	Progressive right hemiparesis without fever	No	14 d	100	2300/180
4	41/M	CML	Bone marrow transplantation, corticosteroids	2 mo	Right hemiplegia, fever (38°C)	No	5 d	90	1900/100
5	39/F	RAEB	Bone marrow transplantation, corticosteroids	3.5 mo	Mental confusion	Yes, confirmed by chest CT	8 d	Not done	2500/60

Note.—CML indicates chronic myelocytic leukemia; RAEB, refractory anemia with excess blasts.

intravenous administration of gadopentetate dimeglumine at a dose of 0.1 mmol/kg. All examinations were retrospectively reviewed by two trained neuroradiologists.

Results

Patients' characteristics are described in Table 1. Initial neurologic symptoms included mental confusion (two patients) and hemiparesis or hemiplegia (four patients). Two patients had low-grade fevers (38°C), and three patients were afebrile.

Two patients had pulmonary infiltrates (confirmed by chest CT scans), concomitant with their neurologic symptoms. The interval between the onset of neurologic symptoms and MR imaging ranged from 2 to 8 days (Table 2). The interval between the last MR and death ranged from 3 to 11 days (Table 2).

CT showed areas of low attenuation with no or minimal mass effect. MR demonstrated intermediate-signal lesions within surrounding high-signal area on proton density– and T2-weighted images and low-signal lesions on T1-weighted images, with contrast enhancement in two cases (cases 4 and 5). In all cases, MR showed more numerous lesions than did CT. These additional lesions were subcortical and smaller (diameter, 1 cm or less) with no contrast enhancement. Multiple lesions were observed in four of the five patients. No hemorrhage was detectable on CT or MR.

All patients died from fungal infections despite aggressive antifungal therapy, 5 to 17 days after the onset of neurologic symptoms. Autopsies were performed within 3 to 11 days after the last MR scans and demonstrated areas of hemorrhagic necrosis containing numerous *Aspergillus* hyphae in all cases. Some arterial vessels within these areas were thrombosed and invaded by fungi, in all patients. The lesions found at autopsy were much larger than expected by radiologic examination; in cases 1 and 4, the largest lesions measured $12 \times 6 \times 5$ cm and $12 \times 7 \times 5$ cm at autopsy, respectively; they measured $3 \times 2 \times 2$ cm and $8 \times 6 \times 5$ cm on the MR scans obtained, respectively, 5 and 3 days before death (Figs 1 and 2).

In two cases (cases 1 and 4) pathologic examination revealed diffuse thickening of the dura mater, whereas MR images obtained 5 and 3 days, respectively, before death showed meningeal enhancement only adjacent to a large parenchyma lesion (case 4). Disseminated vis-

TABLE 2: Radiologic-pathologic correlation

Case	Interval between Onset of Neurologic Symptoms and:		Interval between Last MR Scan and Death	CT Appearance	MR Appearance and Location	Enhancement on MR Imaging	Mass Effect	Hemorrhage?	Pathologic Findings at Autopsy
	CT	MR							
1	1 d	8 d	5 d	1st day: slight low-density lesion in left basal ganglia	Proton density/T2: intermediate-signal lesions within surrounding high-signal	None	Minimal	No	Foci of aspergillosis infection in the kidneys, the liver and the lungs; CNS: thickening and inflammation of dura mater; marked necrosis in left cerebral hemisphere measuring 12 × 6 × 5 cm
	2 d	. . .		2nd day: supplementary lesion in the right frontal area	T1: low-signal intensity in left basal ganglia, right frontal area and left cerebellar hemisphere				Hemorrhagic necrosis in left cerebellar hemisphere, vermis and right frontal lobe; some vessels were thrombosed and invaded by fungi
2	3 d	6 d	11 d	Low-density lesion in right basal ganglia	Proton density/T2: intermediate-signal lesions within surrounding high-signal T1: low-signal intensity in right basal ganglia, right frontal, parietal and occipital lobes	None	None	No	Widespread thoracic and cardiac involvement CNS: areas of focal hemorrhagic necrosis in right basal ganglia (4 cm), right frontal lobe, temporal lobes, parietal lobes, occipital lobes, vermis, and cerebellar tonsils; some vessels were thrombosed and invaded by fungi
3	. . .	6 d	8 d	Low-density lesion in left basal ganglia	Proton density/T2: intermediate-signal lesions within surrounding high-signal T1: low-signal intensity in left basal ganglia, left internal capsule and left cerebral peduncle	None	Minimal	No	Foci of aspergillosis infection in the lungs CNS: areas of hemorrhagic necrosis in left basal ganglia, left cerebral peduncle, left temporal and parietal lobes; some arterial vessels were thrombosed and invaded by fungi
4	1 d	2 d	3 d	Low-density lesion in the territory of the left middle cerebral artery	Proton density/T2: intermediate-signal lesions within high-signal T1: low-signal intensity in the territory of left middle cerebral artery	Intravascular enhancement and meningeal enhancement	Minimal	No	Foci of aspergillosis infection in the lung and in the heart CNS: thickening and inflammation of dura mater; massive hemorrhagic necrosis in left cerebral hemisphere measuring 12 × 7 × 5 cm and in the pons; intraventricular hemorrhage; some arterial vessels were thrombosed and invaded by fungi
5	1 d	3 d	5 d	Low-density lesion in the left frontal area and in the right occipital area	Proton density/T2: intermediate-signal lesions within high-signal T1: low-signal intensity in the territory of right posterior cerebral artery, in the left and right frontal areas and the right parietal area	Intravascular enhancement and meningeal enhancement	Minimal	No	Foci of aspergillosis infection in the lung CNS: areas of hemorrhagic necrosis in frontal lobes, right parietal and occipital lobes; some arterial vessels were thrombosed and invaded by fungi

Fig 1. Axial MR images obtained 8 days after the onset of neurologic symptoms (fever, mental confusion, and right hemiparesis) and 5 days before death (case 1).

A, Proton density–weighted image (1940/40); *B*, T2-weighted image (1940/100). Long-repetition-time images show a high-signal lesion located in the left basal ganglia with little mass effect. This lesion has a central zone of intermediate signal (*arrow*) and measured 3 × 2 × 2 cm. This lesion, which demonstrates no enhancement (not shown), is consistent with an acute infarct. The autopsy performed 5 days after this MR scan showed marked necrosis in the left cerebral hemisphere measuring 12 × 6 × 5 cm. Some arterial vessels were thrombosed and invaded by fungi.

ceral aspergillosis including the lungs was present in all five patients.

Discussion

Aspergillus fumigatus is the most common human pathogen in the genus *Aspergillus*, but *Aspergillus flavus* and *Aspergillus niger* are also frequently seen. *Aspergillus* organisms grow as mold on decaying vegetable matter (26). They have septate hyphae, which show dichotomous branching, and produces numerous spores. Humans are infected by inhaling these spores, making the lungs the primary site of infection. Some CNS infections have been reported in healthy hosts, but most infections occur in immunocompromised patients (1–5). In these patients, cerebral aspergillosis usually occurs as part of a disseminated infection with an incidence of 10% to 15% (4), and invasive aspergillosis is a major cause of infectious death.

The diagnosis of cerebral aspergillosis is difficult because presenting symptoms are nonspecific (strokelike symptoms or seizures) (1), and fever may be absent (26). Moreover, pulmonary infection may not be present. Cerebrospinal fluid (CSF) findings are usually minimally abnormal, with a slightly elevated protein level. The organism is rarely cultured from the CSF (4, 26). Serologic testing in blood in immunocompromised patients yields inconclusive results (4).

Because the clinical and laboratory diagnosis of aspergillosis is difficult, CT and MR images can be helpful when interpreted with adequate clinical information. The CT and MR appearance observed with intracranial aspergillosis is explainable by the angioinvasive nature of the fungus.

Pathologically (1–3, 21), hyphal elements block intracerebral blood vessels, resulting in infarct, commonly hemorrhagic; this sterile infarct is converted to a septic infarct, when the fungus erodes through the vessel wall into the ischemic brain parenchyma, causing a mixed inflammatory reaction and necrosis (1, 8, 27). However, invasive aspergillosis in the immunocompromised patient is distinguished by its relative lack of inflammatory reaction (2, 28). This erosion of the vessel wall results in fungal vasculitis and maybe mycotic aneurysm (3, 19, 27).

In our retrospective study, the lesions present as low-density lesions with no or little mass effect on CT scans. On MR imaging we saw two different patterns of contrast enhancement.

In cases 1, 2, and 3, the lesions are located in the basal ganglia and present an intermediate signal intensity (isointense to white matter) within a surrounding high-signal area (presumably edema) on proton density– and T2-weighted images (Fig 1). The intermediate signal center of the lesions could represent areas of coagulative fungal necrosis, as demonstrated by the autopsies performed within 3 to 11 days after the last MR scans. On T1-weighted images these lesions show low signal intensity.

All these lesions are consistent with infarcts, and pathologic examinations showed that in these areas some arterial vessels were thrombosed and invaded by fungi. These infarcts exhibit no parenchymal enhancement after intra-

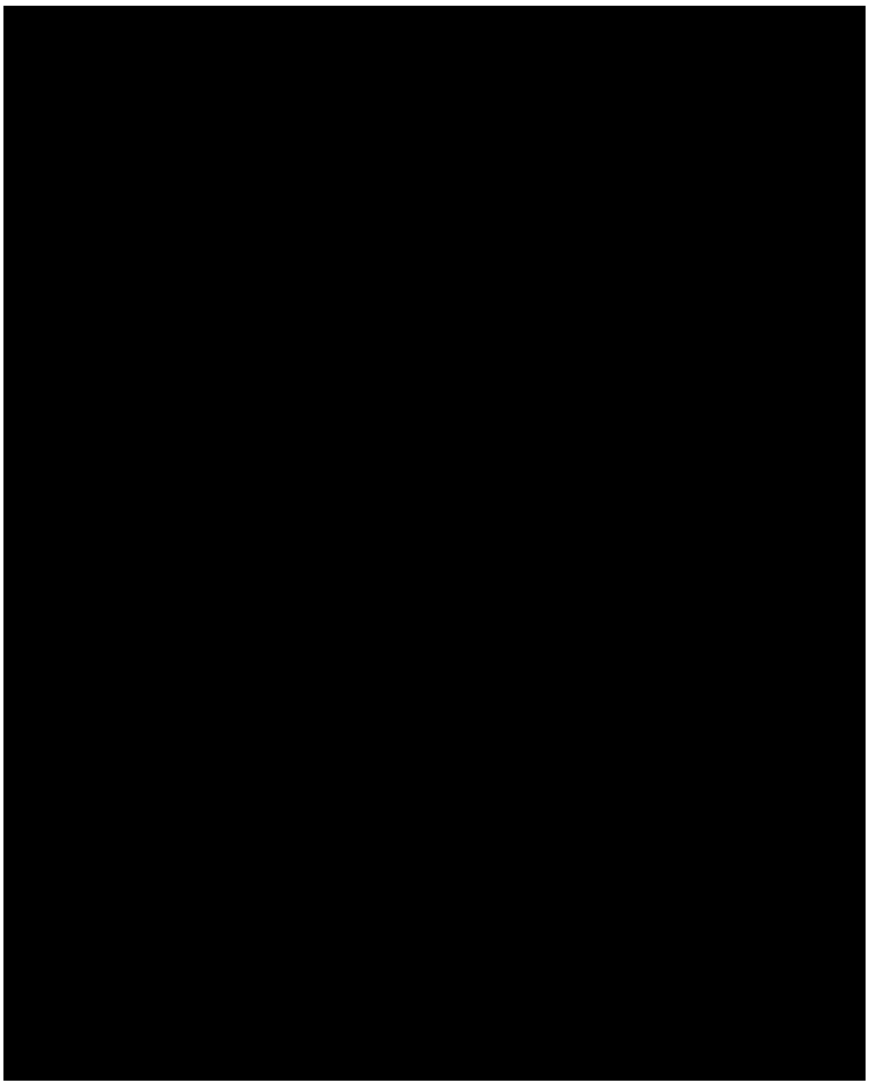


Fig 2. Axial MR images obtained 2 days after the onset of neurologic symptoms (fever and right hemiplegia) and 3 days before death (case 4).

A, Proton density–weighted image (1940/40); *B*, T2-weighted image (1940/100). Long-repetition-time images show an infarct in the territory of the left middle cerebral artery.

C, T1-weighted image (500/20); *D*, Postcontrast T1-weighted image (500/20). Note contrast enhancement of distal branches of the left middle cerebral artery (*short arrow*) and adjacent meninges (*long arrow*). These findings correspond to the intravascular enhancement and meningeal enhancement, seen in early cerebral infarction involving an appreciable portion of the territory of a cerebral artery. The autopsy performed 3 days after this MR scan showed a massive hemorrhagic necrosis measuring $12 \times 7 \times 5$ cm. There was thickening and inflammation of intracranial meninges. Some arterial vessels were thrombosed and invaded by fungi.

venous contrast administration. This absence of contrast enhancement may be explained by the absence of inflammatory response related to corticosteroid therapy (corticosteroids can reduce the degree of iodinated contrast enhancement) (2, 3, 29) and to the immunocompromised status (2, 23, 28). In addition, absence of the parenchymal enhancement that usually occurs in infarction may be also explained by the rapidity of evolution of cerebral aspergillosis (5 to 17 days of survival after the onset of neurologic symptoms). The delay between onset of neurologic symptoms and the enhanced MR scans (2 to 8 days) may be too short for the ingrowth of new vessels lacking blood-brain barriers to occur. In the study of Elster and Moody (30) on cerebral infarction, parenchymal enhancement usually occurs 7 to 14 days after infarction.

Cases 4 and 5 present a different pattern of contrast enhancement. In case 4, MR imaging performed 2 days after the onset of symptoms revealed an infarct in the territory of the left middle cerebral artery with contrast enhancement of distal branches of the middle cerebral artery and adjacent meninges (Fig 2). These findings correspond to the intravascular enhancement sign and the meningeal enhancement sign seen on MR images in early cerebral infarction. In the study of Elster and Moody (30), the intravascular enhancement sign is the earliest sign (1 to 3 days), and the meningeal enhancement sign is noted from days 2 to 6. The fifth case presents the same pattern of enhancement in the territory of the right posterior cerebral artery.

In our first three cases, intravascular and meningeal enhancement were not seen in the

small basal ganglia infarcts. The meningeal enhancement sign is seen only with large infarcts that involve an appreciable portion of the territory of a cerebral artery (30). The intravascular enhancement sign was not seen in small infarctions restricted to the basal ganglia (31).

MR imaging detected multiple lesions in four of five patients and CT in two of five (though CT was earlier in each case). These additional lesions were subcortical and smaller (up to 1 cm diameter) with no enhancement. No diffuse meningeal enhancement was seen on MR, whereas pathologic examination revealed diffuse dural thickening in cases 1 and 4. In all cases, autopsy demonstrated that some vessels were thrombosed and invaded by fungi. The lesions found at autopsy were much larger than expected by radiologic examination obtained a few days before: this discrepancy could be caused by failure of radiologic examination to reflect the brain parenchyma destruction or more likely indicates rapid interval increase in the size of invasive cerebral aspergillosis. No hemorrhage was detectable by imaging in the lesions, although there were some areas of hemorrhagic necrosis observed on pathologic examination in all five patients: this discrepancy could also be explained by the rapid evolution of the disease (hemorrhage might not be present at the time of imaging) or could be caused by the lesser sensitivity of the 0.5-T machine in detecting the presence of hemorrhage (susceptibility effects increase with the field strength) (32).

Review of the Literature

To date, there are many reports in the literature about the CT appearance of cerebral aspergillosis in immunocompromised and nonimmunocompromised patients and fewer cases in which MR findings are described. The different neuroimaging patterns reported varied depending on the immune status of the patients and can be divided into infarcts, ring- or nodular-enhancing lesions consistent with abscesses or granulomas, and localized meningitis.

The studies reporting lesions consistent with infarcts on CT (1–3) or on MR imaging (8, 16, 23, 25) concern severely immunocompromised patients (many of whom are transplant recipients) with an aggressive form of cerebral aspergillosis and a rapidly fatal outcome. On CT scans (1–3), these lesions present as poorly defined, low-density lesions with little or no mass effect and faint or no contrast enhancement. On T2-weighted MR images, these lesions demonstrate inhomogeneous high signal intensity (8, 23, 25) with a low-signal peripheral rim in cases of hemorrhagic infarction (16). In the studies with contrast-enhanced MR imaging (8, 23), there is no apparent contrast enhancement in most of the cases. As in our cases, the lack of contrast enhancement could be explained by the rapidity of evolution of the disease: 4 to 17 days of survival after the onset of neurologic or pulmonary symptoms in the study of Grossman et al (3) and 3 to 15 days in the study of Beal et al (1).

In cases with long evolution (less severely immunocompromised patients who recovered [7, 12]), there was contrast enhancement, as expected in infarction. In the case of Van der Knaap et al (12), MR imaging demonstrated the different stages of infarction: high-signal lesions on T2-weighted images in the territory of the middle cerebral artery, with intravascular enhancement of cortical vessels on the first days of infection, and on the next days a stage of intense gyriform enhancement, which gradually subsided. In the patient of Adler et al (7), there was parenchymal enhancement of a basal ganglia lesion on an enhanced MR study obtained 3 weeks after the onset of neurologic symptoms.

There are few reported cases of patients with ring- or nodular-enhancing lesions (6, 8–11, 13–15, 17, 18, 22). The presence of true ring or nodular enhancement, consistent with abscess or granuloma formation, militates against the aggressive form of cerebral aspergillosis (3) and indicates that the host defense system is able to isolate or encapsulate the offending organisms.

In a case (14) of a bone marrow transplant recipient who survived, there was evolution within several weeks from an infarct to a granuloma, seen as a peripheral rim of low signal intensity on T2-weighted MR images that enhanced after contrast administration.

Ashdown et al (8) reported MR findings in four cases of abscesses in mildly to moderately immunocompromised patients. The lesions presented hypointense rings within surrounding edema on T2-weighted images. There was enhancement of the rings on contrast-enhanced T1-weighted images. Data on the clinical outcome of these patients were not available.

Most of the reported cases of granulomas (6, 11, 13, 15, 17, 22) are the result of initial involvement of the paranasal sinuses and/or the orbits and subsequent contiguous spread to the CNS. These lesions present as low- or intermediate-signal lesions on long-repetition-time MR images (11, 17, 22) with contrast enhancement on CT or MR scans. These cases concern mild to moderate immunocompromised or nonimmunocompromised patients. Most of these patients (6, 11, 13, 15, 17) survived after several weeks or months of evolution.

Localized meningitis has been observed in association with initial involvement of the paranasal sinuses and/or the orbits (5, 8) or the middle ear (24). The radiographic differential diagnosis of low-density lesions on CT with little mass effect and no enhancement, in immunocompromised patients, includes other infectious agents such as *Cryptococcus*, *Candida*, and *Nocardia* organisms, toxoplasmosis, tuberculosis, and progressive multifocal leukoencephalopathy, as well as noninfectious causes including tumors. The MR findings and CSF analysis may help differentiate among these different causes. *Cryptococcus* organisms lead to formation of parenchymal masses called *cryptococcomas*. Cryptococcomas may present as enhancing lesions or as nonenhancing lesions (gelatinous pseudocysts) often located in the basal ganglia (33). These lesions demonstrate a cystic pattern with homogeneous high signal intensity on proton density– and T2-weighted images. In the case of nocardiosis there is ring enhancement of the lesions (2). For *Nocardia* and *Cryptococcus* organisms, cerebrospinal fluid findings may yield the diagnosis. With candidiasis and tuberculosis, meningitis is a common finding, and brain abscesses or granulomas present as enhancing lesions (27). Toxoplasmosis shows a predisposition to involve the basal ganglia (27) and usually presents as enhancing lesions. The MR appearance of intermediate-signal lesions within high-signal areas on T2-weighted images does not favor the diagnosis of progressive multifocal leukoencephalopathy, which presents as high-signal lesions on T2-weighted images; there is no mass effect of the lesions, and cortical gray matter is usually spared (34), in contrast to infarction induced by *Aspergillus* hyphae. Malignant lesions present as enhancing lesions with mass effect.

Conclusion

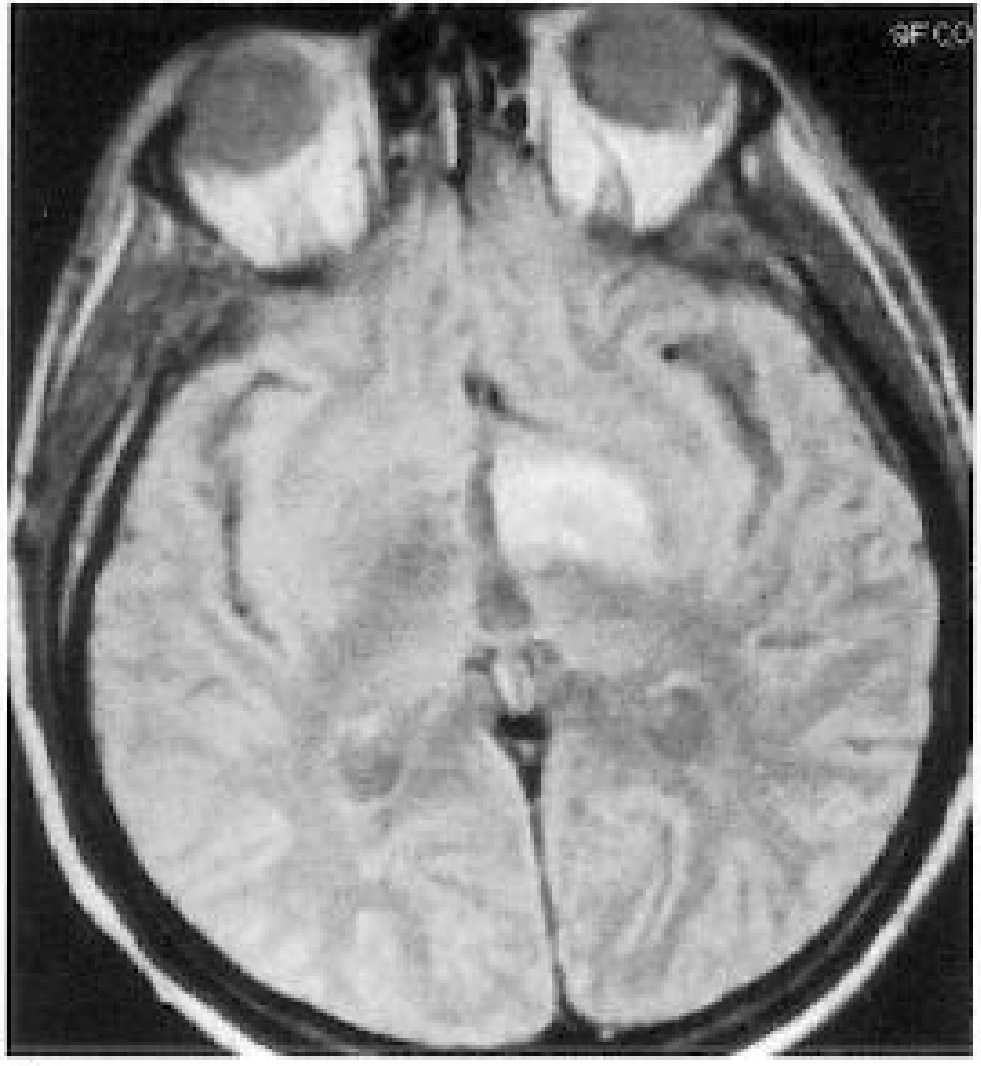
Cerebral aspergillosis indicates a very poor prognosis in the immunocompromised patient, with rapidly lethal evolution in most cases. The literature contains only a few cases of survival (6–14) subsequent to antifungal therapy and surgical intervention. To increase the therapeutic efficiency, high-risk patients, even with seemingly minor cranial symptoms, should be screened with CT and enhanced MR imaging early in the clinical course.

Cerebral aspergillosis lesions are often located in the basal ganglia and demonstrate low attenuation on CT scans and intermediate signal intensity within surrounding high-signal areas on long-repetition-time MR images. The lesions are usually multiple and more numerous on MR than on CT. These lesions, which demonstrate no parenchymal enhancement, are consistent with acute infarcts. In cases of large lesions, there is early intravascular and meningeal enhancement, as expected in acute infarcts involving an appreciable portion of the territory of a cerebral artery. The diagnosis of early cerebral infarction in a patient considered at risk for invasive aspergillosis even without overt pulmonary disease is an indication to institute aggressive antifungal therapy.

References

1. Beal MF, O'Carroll CP, Kleinman GM, Grossman RI. Aspergillosis of the nervous system. *Neurology* 1982;32:473–479
2. Enzmann DR, Brant-Zawadzki M, Britt RH. CT of central nervous system infections in immunocompromised patients. *AJNR Am J Neuroradiol* 1980;1:239–243
3. Grossman RI, Davis KR, Taveras JM, Beal MF, O'Carroll CP. Computed tomography of intracranial aspergillosis. *J Comput Assist Tomogr* 1981;5:646–650
4. Cohen J. Clinical manifestations and management of aspergillosis in the compromised patient. In: Warnock DW, Richardson MD, eds. *Fungal Infection in the Compromised Patient*. Chichester: John Wiley and Sons, 1991:117–151
5. Walsh TJ, Hier DB, Caplan LR. Aspergillosis of the central nervous system: clinicopathological analysis of 17 patients. *Ann Neurol* 1985;18:574–582
6. Epstein NE, Hollingsworth R, Black K, Farmer P. Fungal brain abscesses (aspergillosis/mucormycosis) in two immunosuppressed patients. *Surg Neurol* 1991;35:286–289
7. Adler CH, Stern MB, Brooks ML. Parkinsonism secondary to bilateral striatal fungal abscesses. *Movement Disorders* 1989;4: 333–337
8. Ashdown BC, Tien RD, Felsberg GJ. Aspergillosis of the brain and paranasal sinuses in immunocompromised patients: CT and MR imaging findings. *AJR Am J Roentgenol* 1994;162:155–159

9. Goodman ML, Coffey RJ. Stereotactic drainage of Aspergillus brain abscess with long-term survival: case report and review. *Neurosurgery* 1989;24:96–99
10. Green M, Wald ER, Tzakis A, Todo S, Starzl TE. Aspergillosis of the CNS in a pediatric liver transplant recipient: case report and review. *Rev Infect Dis* 1991;13:653–657
11. Jinkins JR, Siqueira E, Zuheir Al-Kawi M. Cranial manifestations of aspergillosis. *Neuroradiology* 1987;29:181–185
12. Van der Knaap MS, Valk J, Jansen GH, Kappelle LJ, Van Nieuwenhuizen O. Mycotic encephalitis: predilection for grey matter. *Neuroradiology* 1993;35:567–572
13. Shuper A, Levitsky HI, Cornblath DR. Early invasive CNS aspergillosis. *Neuroradiology* 1991;33:183–185
14. Miaux Y, Singer B, Leder S, Guermazi A, Bourrier P. MR imaging of cerebral aspergillosis: different patterns in the same patient. *AJNR Am J Neuroradiol* 1994;15:1193–1195
15. Coulthard A, Gholkar A, Sengupta RP. Case report: frontal aspergilloma: a complication of paranasal aspergillosis. *Clin Radiol* 1991;44:425–427
16. Cox J, Murtagh FR, Wilfong A, Brenner J. Cerebral aspergillosis: MR imaging and histopathologic correlation. *AJNR Am J Neuroradiol* 1992;13:1489–1492
17. Gupta R, Singh AK, Bishnu P, Malhotra V. Intracranial *Aspergillus* granuloma simulating meningioma on MR imaging. *J Comput Assist Tomogr* 1990;14:467–469
18. Mikhael MA, Rushovich AM, Ciric I. Magnetic resonance imaging of cerebral aspergillosis. *Comput Radiol* 1985;9:85–89
19. Sharma RR, Gurusinghe NT, Lynch PG. Cerebral infarction due to *Aspergillus* arteritis following glioma surgery. *Br J Neurosurg* 1992;6:485–490
20. Sparano JA, Gucalp R, Llena JF, Moser FG, Wiernik PH. Cerebral infection complicating systemic aspergillosis in acute leukemia: clinical and radiographic presentation. *J Neurooncol* 1992;13: 91–100
21. Whelan MA, Stern J, De Napoli RA. The computed tomographic spectrum of intracranial mycosis: correlation with histopathology. *Radiology* 1981;141:703–707
22. Wilms G, Lammens M, Dom R, et al. MR imaging of intracranial aspergilloma extending from the sphenoid sinus in an immunocompromised patient with multiple myeloma. *J Belge Radiol* 1992;75:29–32
23. Yuh WTC, Nguyen HD, Gao F, et al. Brain parenchymal infection in bone marrow transplantation patients: CT and MR findings. *AJR Am J Roentgenol* 1994;162:425–430
24. Murai H, Kira J, Kobayashi T, Goto I, Inoue H, Hasuo K. Hypertrophic cranial pachymeningitis due to *Aspergillus flavus*. *Clin Neurol Neurosurg* 1992;94:247–250
25. Parker SL, Laszewski MJ, Trigg ME, Smith WL. Spinal cord aspergillosis in immunosuppressed patients. *Pediatr Radiol* 1990; 20:351–352
26. Lyons RW, Andriole VT. Fungal infections of the CNS. *Neurol Clin* 1986;4:159–170
27. Sze G, Zimmerman RD. The magnetic resonance imaging of infections and inflammatory diseases. *Radiol Clin North Am* 1988;26:839–859
28. Young RC, Bennett JE, Vogel CL, Carbone PP, De Vita VT. Aspergillosis: the spectrum of the disease in 98 patients. *Medicine (Baltimore)* 1970;49:147–173
29. Crocker EF, Zimmerman RA, Phelps ME, Kuhl DE. The effect of steroids on the extravascular distribution of radiographic contrast material and technetium pertechnetate in brain tumors as determined by computed tomography. *Radiology* 1976;119: 471–474
30. Elster AD, Moody DM. Early cerebral infarction: gadopentetate dimeglumine enhancement. *Radiology* 1990;177:627–632
31. Sato A, Takahashi S, Soma Y, et al. Cerebral infarction: early detection by means of contrast-enhanced cerebral arteries at MR imaging. *Radiology* 1991;178:433–439
32. Gomori JM, Grossman RI, Yu-Ip C, et al. NMR relaxation times of blood: dependence on field strength, oxidation state, and cell integrity. *J Comput Assist Tomogr* 1987;11:684–690
33. Popovich MJ, Arthur RH, Helmer E. CT of intracranial cryptococcosis. *AJNR Am J Neuroradiol* 1990;11:139–142
34. Sartor K. Infections and inflammations. In: Sartor K, ed. *MR Imaging of the Skull and Brain*. Berlin: Springer Verlag, 1992: 617–692



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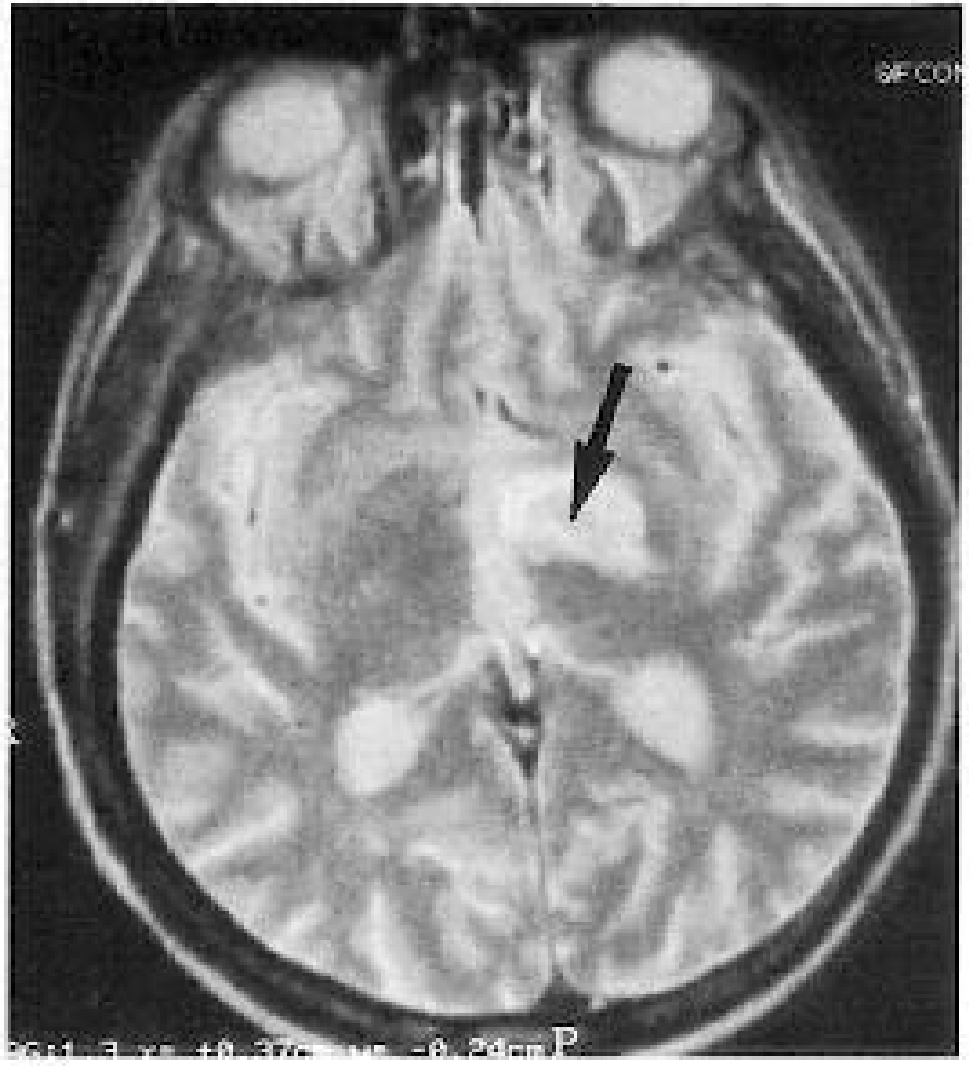

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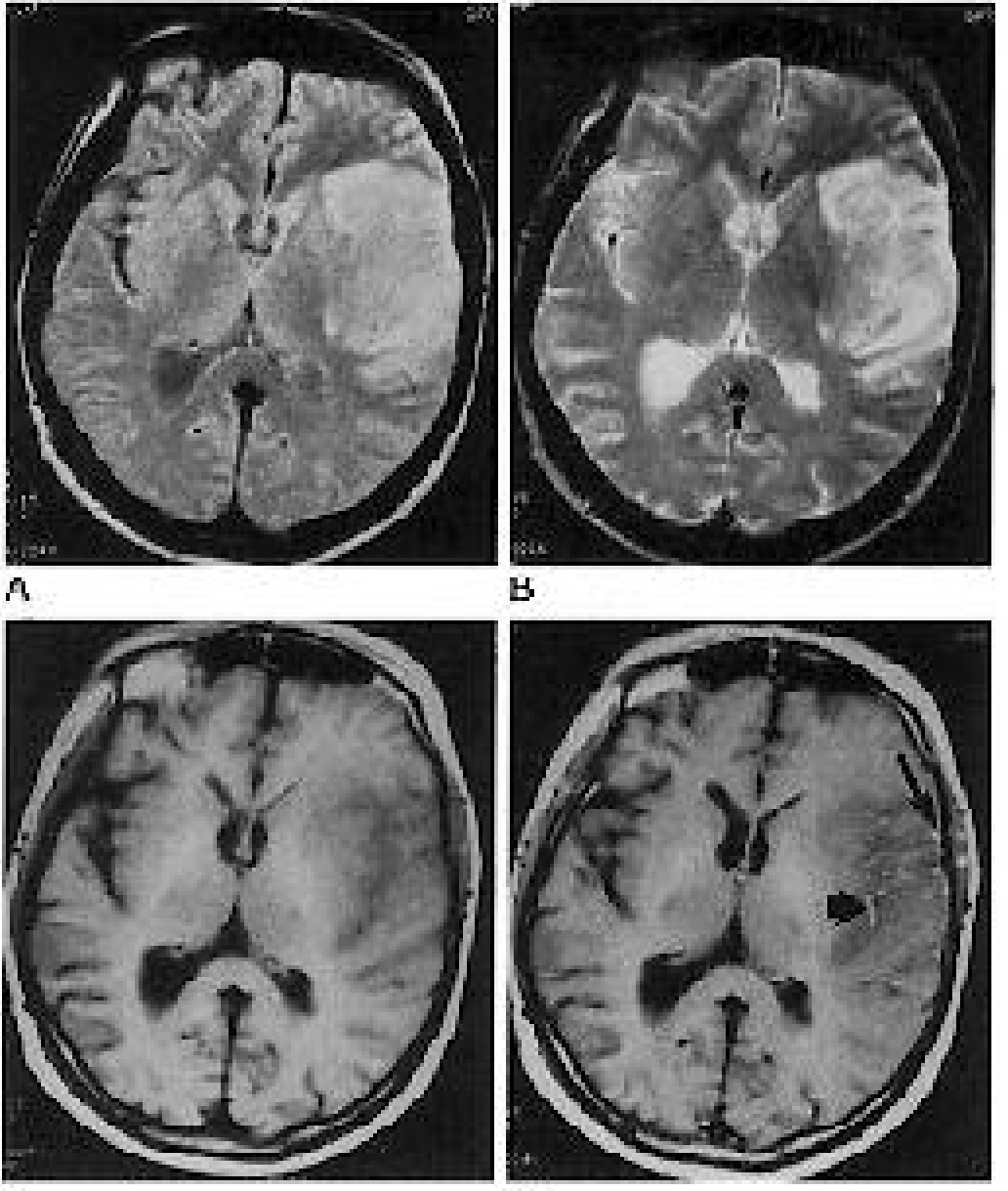
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