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CT of Central Nervous System Infections in Immunocompromised Patients

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The computed tomographic (CT) scan appearance of parenchymal central nervous system (CNS) infection in 12 immunosuppressed patients was unlike that of the usual bacterial abscess in immunologically intact hosts. The lesions were poorly circumscribed and of low density. Contrast enhancement was minimal and did not assume a "ring" configuration. These CT scan findings heralded a poor prognosis. Compared to the neuropathologic findings, the CT scan generally underestimated the extent of involvement. Three other compromised patients were better able to localize the infection. This successful defense was manifested on their CT scans as the more typical "ring" pattern of contrast enhancement. Patients with this CT scan appearance of their CNS infection had a better prognosis.

CT scanning has facilitated the diagnosis of brain abscess; this combined with accurate localization has altered the prognosis [1–10]. Despite advances in diagnostic techniques and widespread use of antibiotics, the incidence of brain abscess is not decreasing [11, 12]. However, the spectrum of central nervous system (CNS) infections is changing because of an important and relatively new clinical problem—that of CNS infection in the immunosuppressed host [13–22]. With continued advances in cancer therapy and organ transplantation, the frequency of brain abscesses caused by opportunistic organisms in compromised hosts can be expected to increase. The organisms responsible for producing brain abscesses in compromised hosts differ from those that usually cause brain abscess. These more unusual, opportunistic organisms, which are normally of low virulence and pathogenicity in man, include fungi, protozoa, bacteria, and viruses. Because of host immunosuppression, these infections are usually not well localized, and they may not evolve to an encapsulated abscess. Thus, their CT scan appearance can be quite different from the more usual bacterial brain abscess [1–6].

Subjects and Methods

Cranial CT, performed on EMI Mark I and 1005 scanners (160 × 160 matrix), yielded 34 scans in 15 patients (aged 20–62) who were immunocompromised because of their primary disease, drug treatment, or both (table 1). Many disease entities were represented, but most patients were immunosuppressed allograft recipients: cardiac (seven patients) and renal (one) [23]. Three patients had leukemia: two were receiving chronic corticosteroid therapy, one had polycythemia vera (chlorambucil therapy), and one was debilitated by alcohol abuse and renal failure (table 1).

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TABLE 1: **Summary of Clinical Data**

Organism/Case No.	Underlying Disorder	CT Findings	Clinical Outcome
Klebsiella pneumoniae/1	Cardiac transplant	Ring contrast enhancement	Death*
Nocardia asteroides/2	Chronic lymphocytic leukemia	Multiple ring lesions	Living
Toxoplasma gondii:			
3	Cardiac transplant	Ring contrast enhancement	Living
4	Renal transplant	Nonspecific lucency, minimal contrast enhancement	Death
5	Polycythemia vera, diabetes, cirrhosis (chlorambucil)	Nonspecific lucency, no contrast enhancement	Death
Aspergillus fumigatus:			
6	Cardiac transplant	Nonspecific lucency, no contrast enhancement, punctate hemorrhage	Death
7	Cardiac transplant	Nonspecific lucency, no contrast enhancement	Death
8	Cardiac transplant	Nonspecific lucency, marked contrast enhancement	Death
9	Cardiac transplant	Nonspecific lucency, minimal contrast enhancement, punctate hemorrhage	Death
10	Acute myelogenous leukemia	Nonspecific lucency, minimal contrast enhancement	Death
11	Acute lymphocytic leukemia	Multifocal, nonspecific, lucent lesions with faint contrast enhancement	Death
12	Cardiomyopathy (corticosteroid)	Nonspecific lucency, no contrast enhancement	Death
13	Acute renal failure, alcoholism	False negative	Death
Candida albicans/14	Chronic asthma (corticosteroid)	Nonspecific lucency, no contrast enhancement	Death
Herpes zoster/15	Acute renal failure, alcoholism	False negative	Death

Note.—Data on four women and 11 men aged 20–62 years.
* Not due to brain abscess.

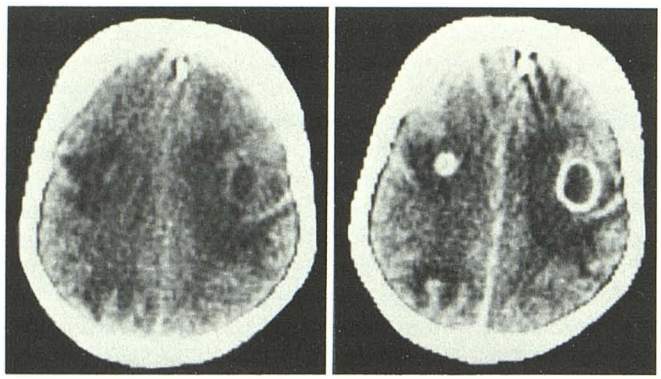

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Fig. 1.—Case 2: chronic lymphocytic leukemia and nocardiosis. Before (left) and after (right) contrast infusion. Three lesions with prominent surrounding edema. The lesion with ring configuration in right hemisphere had well developed abscess capsule at surgery. Lesions resolved completely after appropriate antibiotic therapy.

Results

The CT features of CNS parenchymal infection in these patients can be divided into two major groups. One group of three patients (cases 1–3) was characterized by the typical ring contrast enhancement described for the more usual bacterial abscess (fig. 1). Three different organisms were represented: *Toxoplasma gondii, Nocardia asteroides*, and *Klebsiella pneumoniae* (table 1). These patients were able to localize and encapsulate the infection; two survived the infection. Necrotizing bronchopneumonia and sepsis (staphylococcal) was the cause of death in the other (case 1). Aspiration of the abscess in cases 2 and 3 revealed an abscess capsule in both. Neuropathologic examination demonstrated an abscess capsule in case 1. In each patient the offending organism was identified and treated with the appropriate antibiotic(s).

The second group was 12 patients (cases 4–15) with CT scans prior to contrast infusion that demonstrated poorly defined, low density lesions which were usually small, deep, and initially often solitary (fig. 2). Early in the disease course, abnormalities were subtle. Most frequently, they were located in the basal ganglia or in the centrum semiovale and resembled deep cerebral infarcts. In two patients (cases 6 and 9), both with asperigillosis, small hemorrhages were present within the low density lesion (fig. 3). Contrast enhancement was minimal, often consisting of vague, patchy enhancement at the edges of the lesion. Prominent but poorly circumscribed contrast enhancement occurred in only one patient as the infection became widespread (case 8, fig. 4). One patient (case 15, *herpes zoster* meningoencephalitis) exhibited prominent contrast enhancement of the subarachnoid space and tentorium, but no parenchymal lesions were detectable on the CT scan. One probable false-negative examination occurred with widespread CNS aspergillosis (case 13); a CT scan 10 days before death was

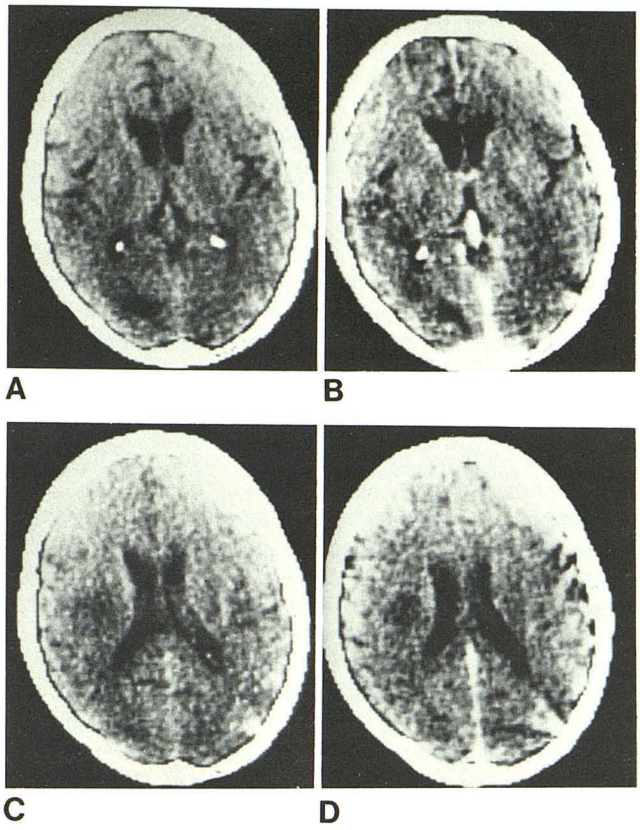

Fig. 2.—Case 6: cardiac transplant with aspergillosis. Before (left column) and after (right column) contrast infusion. Noncontrast scans revealed two poorly defined areas of low density; one in the right occipital lobe, the other in the right centrum semiovale; neither enhanced with contrast. Neuropathologic examination identified aspergillosis in each of these lesions.

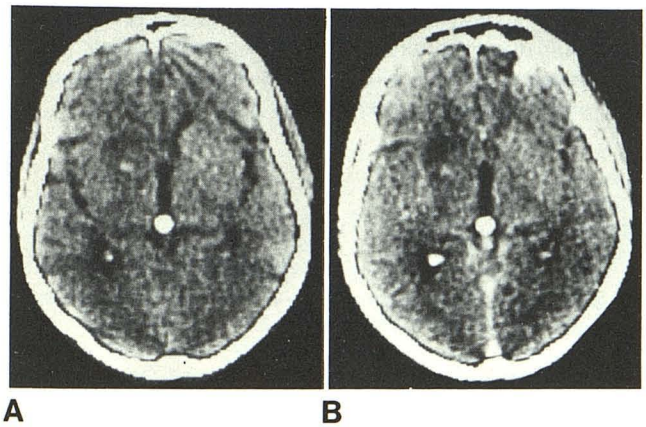

Fig. 3.—Case 9: cardiac transplant with aspergillosis. Before (left) and after (right) contrast infusion. Low density lesion with mass effect and small area of hemorrhage in right basal ganglia region. No significant contrast enhancement demonstrated. Neuropathologic examination confirmed this lesion to be due to *Aspergillus*. It resembles a small hemorrhagic infarct.

normal. Six patients in group 2 received amphotericin for disseminated aspergillosis; this organism was identified in the lung in five patients and by brain biopsy in the other (cases 6–10, 12). The six other patients in this group did

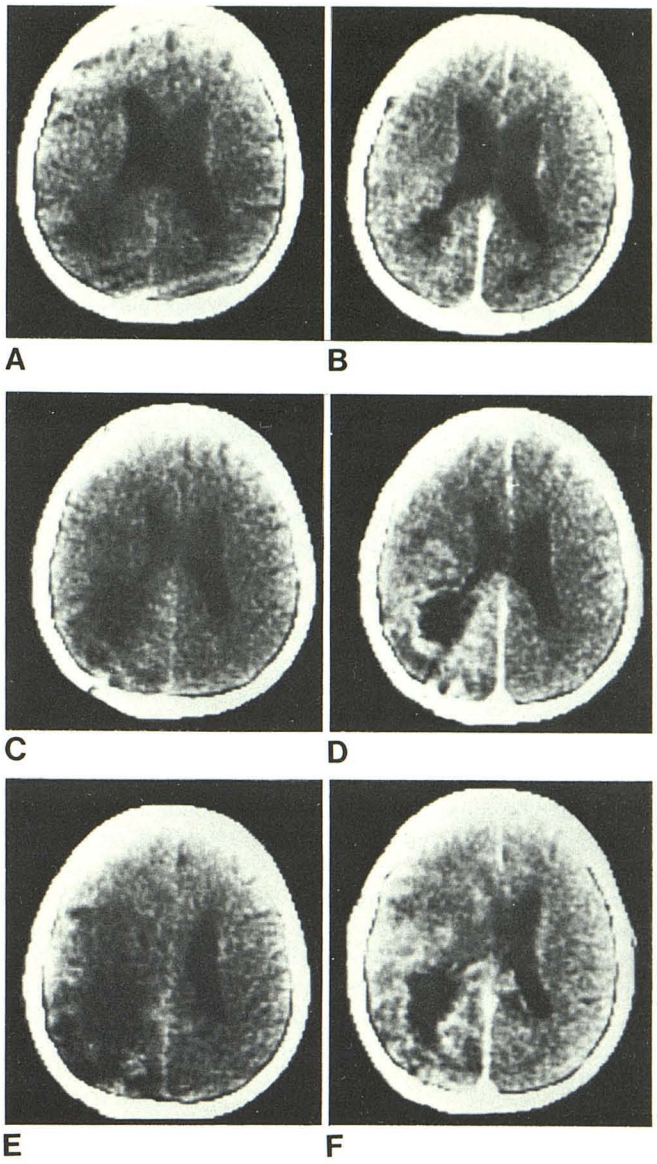

Fig. 4.—Case 8: cardiac transplant with aspergillosis. Before (left column) and after (right column) contrast infusion. Progression was rapid over 2 week period (top to bottom: initial, after 1 week, after 2 weeks). Contrast enhancement was prominent but poorly circumscribed, indicating diffuse nature of infection and patient's inability to wall off the organism.

not receive appropriate antibiotic coverage because the organism was not identified or suspected prior to death. Unlike the group with typical "ring" lesions, this group of patients, with nonspecific, poorly defined lesions, had a 100% mortality rate.

The type of organism could not be predicted from the CT scan, although hemorrhage suggested aspergillosis because of its propensity for vessel wall invasion. Aspergillosis was also characterized by an increase in size and number of lesions over 3–8 days, at times a very rapid increase. *Aspergillus* could be strongly implicated when such lesions appeared in patients known to have pulmonary aspergillosis.

The degree of enhancement did not increase as the infection spread except in one patient (fig. 4).

Neuropathologic findings, available for all in group 2, confirmed the patients' inability to confine or wall off the infecting organism. Patients with different fungal infections showed similar neuropathologic changes which represented a hybrid of cerebral infection and infarction. Vessel wall invasion by *Aspergillus* (septated, branching hyphae) was a prominent finding resulting in vessel destruction, thrombosis, hemorrhage, and cerebral infarction. Focal areas of necrosis with surrounding acute and chronic inflammatory cells were widely dispersed. However, severe and widespread *Aspergillus* invasion was distinguished by its relative lack of inflammatory infiltrate. *Aspergillus* invasion was not limited to the brain parenchyma; meningitis with vascular invasion and ventriculitis were commonly present.

In patients with toxoplasmosis, the findings included multiple necrotic foci with *Toxoplasma* seen both intra- and extracellularly. Blood vessels themselves were necrotic resulting in small hemorrhages. The inflammatory infiltrate was primarily perivascular. The *Herpes zoster varicellosus* meningoencephalitis was characterized by mononuclear perivascular infiltrates, scattered areas of infarction, moderate neuronal loss, intranuclear eosinophilic inclusion bodies, and diffuse meningitis. In none of these patients was the formation of an abscess wall detected around areas of necrosis and inflammation. The extent of neuropathologic involvement in these poorly localized infections was greatly underestimated by the abnormalities detected on the CT scan.

Patients with CNS aspergillosis all had disseminated disease; the most likely origin was pulmonary, since the lungs were always involved. CNS candidiasis also occurred in the context of disseminated disease. *Herpes zoster* and one of the two toxoplasmosis infections were limited to the CNS; the other toxoplasmosis infection involved the CNS and the myocardium.

Discussion

Immunocompromised patients are susceptible to "opportunistic" organisms which are normally of low pathogenicity in man but are more resistent to antibiotic therapy because of their reproduction and growth pattern. The decreased host resistance in immunosuppression derives from defects in three main areas of defense: decreased phagocytosis, impaired cell mediated immune response, and altered humoral response (gamma globulin) [12]. These defects can arise from the primary disease itself and/or immunosuppressive therapy required for its treatment.

The CT scan appearance of CNS infections seems to be a function less of the specific infecting organism and more of the host's reaction to it. Therefore, the same organism can be handled differently, depending on the host's immune status. The CT scan accurately reflects this interaction of host and organism by the pattern of contrast enhancement. Despite their susceptibility to opportunistic agents, some immunocompromised patients are still able to mobilize enough of a defense to forestall rapid spread of the organism and to eventually wall off the infection (i.e., form an abscess). The CT scan appearance of this interaction is that of typical "ring" contrast enhancement. In our series of patients, this occurred with *Nocardia* and *Toxoplasma* but not with fungi. This "ring" pattern may not represent the abscess capsule itself, but indicates the infection is localized and an abscess is evolving [24]. Hence, a brain abscess caused by opportunistic organisms may have CT scan findings identical to those of the more usual bacterial agents. In our series of patients, the same organism, (*Toxoplasma gondii*) produced both the typical "ring" appearance in one patient and the more nonspecific findings in others. Lesions caused by Aspergillus fumigatus were consistently of the nonspecific type in this series of immunosuppressed patients; however, in normal hosts capsule formation, in abscess or granuloma formation, and "ring" contrast enhancement have been described [2, 16, 25, 26].

If a patient was unable to localize the infection, the lesions were of poorly circumscribed low density and usually exhibited little contrast enhancement. The role of corticosteroids in limiting enhancement is difficult to determine. Although corticosteroid treatment can reduce the degree of contrast enhancement, it is not likely to eliminate it [27]. These lesions resembled cerebral infarction but were often distinguished by the rapid increase in their size and number. The CT scan resemblance to infarction is understandable since in aspergillosis and mucormycosis, fungal invasion of vessel walls characteristically results in thrombosis and infarction [16, 17]. *Toxoplasma gondii* infects all types of cells in the brain and can cause thrombosis and cerebral infarction by disruption of endothelial cells [18, 19]. In addition, the inflammatory infiltrate in compromised hosts with fungal infections may be conspicuous by its absence, especially early in the course of the infection. When rapid spread was recognized on the CT scan, typically the extent of the disease was underestimated compared to the neuropathologic examination, especially in aspergillosis. A CT scan showing poor localization and no "ring" contrast enhancement presaged an extremely poor prognosis.

REFERENCES

1. Berg B, Franklin G, Cuneo R. Nonsurgical cure of brain abscess: early diagnosis and follow-up with computerized tomography. *Ann Neurol* **1978**;3:474–478
2. Claveria IE, duBoulay GH, Moseley IF. Intracranial infections: investigation by computerized tomography. *Neuroradiology* **1976**;12:59–71
3. Joubert MJ, Stephanov S. Computerized tomography and surgical treatment in intracranial suppuration. *J Neurosurg* **1977**;47:73–78
4 Kaufman DM, Leeds NE. Computed tomography (CT) in the diagnosis of intracranial abscesses. *Neurology* **1977**;27: 1069–1073
5. New PFJ, Davis KR, Ballantine HT. Computed tomography in cerebral abscess. *Radiology* **1976**;121:641–646
6. Nielsen H, Gyldensted C. Computed tomography in the diagnosis of cerebral abscess. *Neuroradiology* **1977**;12:207–217
7. Rosenblum ML, Hoff JT, Norman D. Decreased mortality from

brain abscesses since the advent of computerized tomography. *J Neurosurg* **1978**;49:658–668
8. Rosenblum M, Hoff J, Norman D. Nonoperative treatment of brain abscess in selected high-risk patients. *J Neurosurg* **1980**;52:217–225
9. Stevens EA, Norman D, Kramer RA. Computed tomographic brain scanning in intraparenchymal pyogenic abscesses. *AJR* **1978**;130:111–114
10. Stephanov S. Experience with multioculated brain abscesses. *J Neurosurg* **1978**;49:199–203
11. Garfield J. Management of supratentorial intracranial abscess: a review of 200 cases. *Br Med J* **1969**;2:7–11
12. Liske E, Weikers NJ. Changing aspects of brain abscesses. Review of cases in Wisconsin 1940 through 1962. *Neurology* **1964**;14:294–300
13. Armstrong D, Young LS, Meyer RD. Infectious complications of neoplastic disease. *Med Clin North Am* **1971**;55:729–745
14. Hotson JR, Pedley TA. The neurological complications of cardiac transplantations. *Brain* **1976**;99:673–694
15. Kingsley DPE, Kendall BE. Cranial computed tomography in leukemia. *Neuroradiology* **1978**;16:543–546
16. Mukoyama M, Gimple K, Poser CM. Aspergillosis of the central nervous system. *Neurology* **1969**;19:967–974
17. Young RC, Bennett JE, Vogel CL. Aspergillosis. The spectrum of the disease in 98 patients. *Medicine* **1970**;49:147–173
18. Carey RM, Kimball AC, Armstrong D. Toxoplasmosis. Clinical experiences in a cancer hospital. *Am J Med* **1978**;54:30–38
19. Frenkel JK, Nelson BM, Arias-Stella J. Immunosuppression and toxoplasmic encephalitis. *Hum Pathol* **1975**;6:97–111
20. Ruskin J, Remington JS. Toxoplasmosis in the compromised host. *Ann Intern Med* **1976**;84:193–199
21. Parker JC, McCloskey JJ, Knauer KA. Pathobiologic features of human candidiasis. A common deep mycosis of the brain, heart and kidney in the altered host. *Am J Clin Pathol* **1976**;63:991–1000
22. Palmer DL, Harvey RL, Wheeler JK: Diagnostic and therapeutic considerations in *Nocardia asteroides* infection. *Medicine* **1974**;53:391–401
23. Baumgartner WR, Reitz BA, Oyer PE, Stinson EB, Shumway NE. Cardiac homotransplantation. *Curr Probl Surg.* In press
24. Enzmann DR, Britt RH, Yeager AS. Experimental brain abscess evolution: computed tomographic and neuropathologic correlation. *Radiology* **1979**;133:113–122
25. Venugopal PV, Venugopal TV, Thiruneelakantan K. Cerebral aspergillosis: report of two cases. *Sabouraudia* **1977**;15:225–230
26. Danziger A, Price H. Computed axial tomography in intracranial aspergillosis. A report of 2 cases. *S Afr Med J* **1978**;54:706–708
27. 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