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Neuroradiologic Findings in AIDS: A Review of 200 Cases

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The radiologic studies of 200 consecutive AIDS patients with neurologic symptoms were evaluated to determine their diagnostic specificity and prognostic value. Of 81 patients with initially normal CT scans, four (5%) later developed progressive neurologic illness. Of 75 patients with CT evidence of diffuse cerebral atrophy, 12 (16%) later developed CT abnormalities or had postmortem CNS disease. CT scans showed mass lesions initially in 44 patients and later in an additional seven patients. Although *toxoplasma gondii* infection was the most frequent cause of these lesions, the CT characteristics of cerebral toxoplasmosis are too nonspecific to warrant diagnosis without biopsy. Preliminary evidence suggests that MRI may be more sensitive than CT in detecting intracranial disease in patients with AIDS.

As AIDS has become more widespread, it has become apparent that the neurologic manifestations of this disease are common: 39% of patients with AIDS have neurologic symptoms and 10% have these symptoms as their initial complaint [1–3]. Some of the neuroradiologic findings in AIDS patients have been described in earlier reports [4–7]. With dramatically increased numbers of such patients has come greater experience in neuroradiologic evaluation of AIDS, particularly with respect to the neuropathologic correlates of the radiologic findings. In this report, we describe the neuroradiologic findings in 200 AIDS patients with neurologic symptoms who were evaluated at the San Francisco General Hospital or the University of California Medical Center, San Francisco, from 1983 to 1985. The neuroradiologic studies were evaluated to determine their diagnostic specificity and prognostic value in this patient population.

Materials and Methods

The neuroradiologic studies of 200 consecutive patients with AIDS and neurologic symptoms were reviewed. Histopathologic examination of tissue obtained by biopsy or at autopsy was performed in 40 patients; the remaining 160 patients were followed for up to 2 years. The patients were all homosexual men ranging in age from 23 to 60 years, and the majority (56%) were in the fourth decade of life. The diagnosis of AIDS was made according to the criteria established by the Centers for Disease Control [8].

The CT scans were obtained with a GE 8800 or GE 9800 CT/T scanner using standard techniques; slice thickness was 10 mm. Intravenous contrast material (average dose, 42 g/l) was administered up to 30 min before scanning in all patients; double-dose contrast enhancement was not used. MRI was performed using a spin-echo technique on a Diasonics imager with a 0.35-T superconducting magnet. The T1-weighted scans were obtained with TR = 500 msec and TE = 28 msec; for the T2-weighted images, TR = 2000 msec and TE = 56 msec. A total of 240 CT scans and six MRI scans were obtained.

Results

The neuroradiologic findings defined three groups of patients (Table 1). The first

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TABLE 1: **Initial CT Findings vs Outcome in 200 Patients with AIDS**

Initial CT Findings	No. of Patients	New CT Lesions	CNS Abnormality at Autopsy	Risk of Progression*
Normal	81	2	2	4/81 (5%)
Atrophy	75	5	7	12/75 (16%)
Focal lesion	44	N/A	29	N/A

* Defined as the percentage of patients who later developed focal lesions on CT scans or who had significant neuropathologic findings at autopsy.

TABLE 2: **Histopathologic Diagnoses and CT Findings in 45 Patients with AIDS**

Diagnosis	No. of Patients	CT Findings		
		Normal	Atrophy Only	Focal Lesions
Toxoplasma gondii	22[a]			22
T. gondii + primary CNS lymphoma	5			5
Primary CNS lymphoma	3	1[b]	1	1
Kaposi's sarcoma	2	1[b]		1
Leukoencephalopathy	2			2
Herpes simplex II	2		1	1
Herpes simplex I & cytomegalovirus	1		1	
Cryptococcus neoformans	2		2	
Coccidioides immitis	1		1	
Candida albicans	1			1
Sterile abscess	1			1
Nondiagnostic biopsy (gliosis, inflammation)	3			3
Total	45	2	6	37[c]

[a] Includes five patients with compelling clinical evidence of cerebral toxoplasmosis but without histopathologic confirmation.
[b] CT scans performed several months before autopsy.
[c] Fourteen additional patients had focal lesions on CT, but no biopsy or autopsy was performed.

group consisted of 81 patients (40.5%) whose initial CT scans were normal. In two of these patients, CT scans obtained 6 and 32 days later, respectively, showed multiple bilateral lesions representing cerebral toxoplasmosis. In two additional patients, postmortem examination revealed CNS disease: one was found to have diffuse lymphoma 3 months after a normal CT scan had been obtained; the second, who died several months after his single CT scan showed no abnormalities, had metastatic Kaposi's sarcoma. Thus, 77 of these 81 patients had no progression of their neurologic symptoms and no CT abnormalities during follow-up.

The second group consisted of 75 patients (37.5%) whose initial CT scans showed evidence of diffuse cerebral atrophy only. Five of these patients later developed focal lesions on CT that were shown to be caused by *Toxoplasma gondii* infection. At postmortem examination, seven additional patients were found to have CNS disease, including two cases of cryptococcal meningitis, two cases of herpes simplex encephalitis, and one case each of toxoplasmosis, coccidioidomycosis, and primary CNS lymphoma. Sixty-three of the 75 patients had unchanged repeat CT scans or remained neurologically stable during follow-up.

The third group included 44 patients (22%) who had one or more focal lesions, with or without concomitant atrophy, on initial CT scans. Thus, a total of 51 patients (including seven patients from groups 1 and 2) had focal lesions that were detected on initial or subsequent CT scans. Neuropathologic diagnoses, obtained at autopsy or by biopsy, were available for 29 of these patients; compelling clinical diagnoses were made in five patients. No diagnosis was available for 17 patients who either refused biopsy or autopsy or were lost to further clinical follow-up.

The histopathologic diagnoses and CT findings in 40 patients (20%) who had a biopsy or postmortem examination are listed in Table 2; the five patients with compelling clinical evidence of cerebral toxoplasmosis, including positive serum and CSF titers and an objective clinical response to chemotherapy, but without histopathologic confirmation, are also included in this table. Infection with *T. gondii* was the most frequent histopathologic diagnosis, either alone (17 patients) or in conjunction with primary CNS lymphoma (five patients). There were no demonstrable differences in the CT scans of patients with toxoplasmosis only and those with toxoplasmosis and lymphoma. The most common CT finding associated with toxoplasmosis was a large low-density area that showed ring enhancement upon injection of contrast material (18 of 27 patients, 68%) (Fig. 1). These lesions were multiple in 11 patients and the most common site was within the basal ganglia (20 patients, 75%) (Fig. 2). The mass effect of basal lesions often resulted in compression of the third ventricle, dilatation of the lateral ventricles, and obliteration of the sylvian fissures (Fig. 3). Smaller low-density lesions that showed variable enhancement after injection of contrast material were noted in 16 of these 27 patients (Fig. 4).

In eight patients with toxoplasmosis and focal abnormalities other than ring-enhancing lesions, the CT scans showed single or multiple hypodense areas with less mass effect. These hypodense lesions were usually peripheral rather than central, and in the majority of cases there was slight enhancement adjacent to the lesion, usually around its cortical surface (Fig. 5). In two patients the CT scans showed high-density areas within low-density lesions (Fig. 6) that enhanced homogenously upon injection of contrast medium; these findings were thought to represent hemorrhage into necrotic lesions and were confirmed by histopathologic evaluation in both cases. One additional patient had CT evidence of ventricular dilatation only; postmortem examination 24 hours later revealed diffuse cerebral toxoplasmosis. Most of the patients with toxoplasmosis had CT evidence of atrophy.

Eighteen patients in whom histopathologic data are available did not have toxoplasmosis, either alone or with lymphoma (Table 2). Of three patients with primary CNS lymphoma, one had bilateral, small ring-enhancing lesions in the paraatrial regions (Fig. 7), one had evidence of atrophy, and the third had a normal CT scan 2 months before his autopsy diagnosis. One patient with metastatic Kaposi's sarcoma had a single diffusely enhancing mass lesion in the right frontal lobe; the second patient with Kaposi's sarcoma had a normal

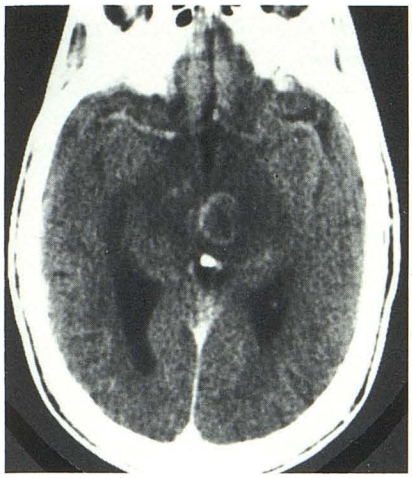


Fig. 1.—Toxoplasmosis abscess. Single ring-enhancing lesion in left thalamus with extension to upper brainstem and into right thalamus as well.

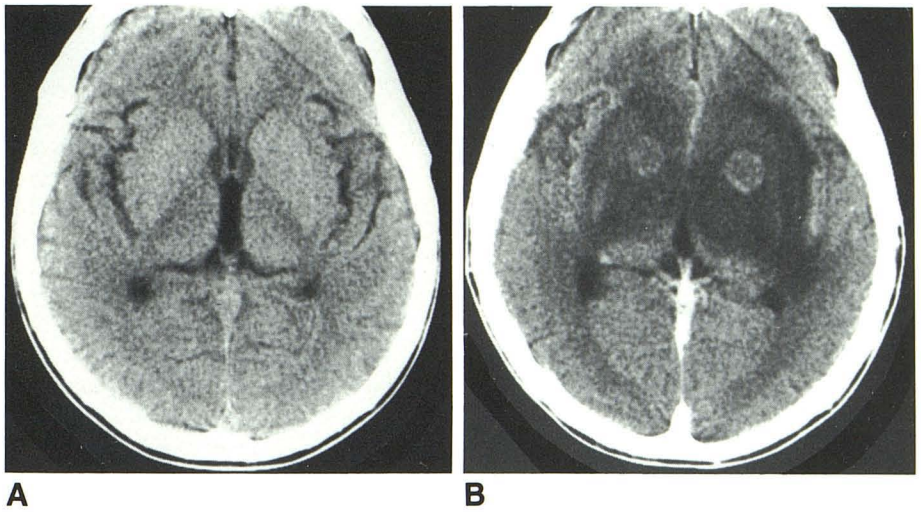


Fig. 2.—Bilateral toxoplasmosis abscesses. **A**, Normal scan. **B**, Bilateral ring-enhancing lesions with surrounding edema 30 days later. Note compression of third ventricle.

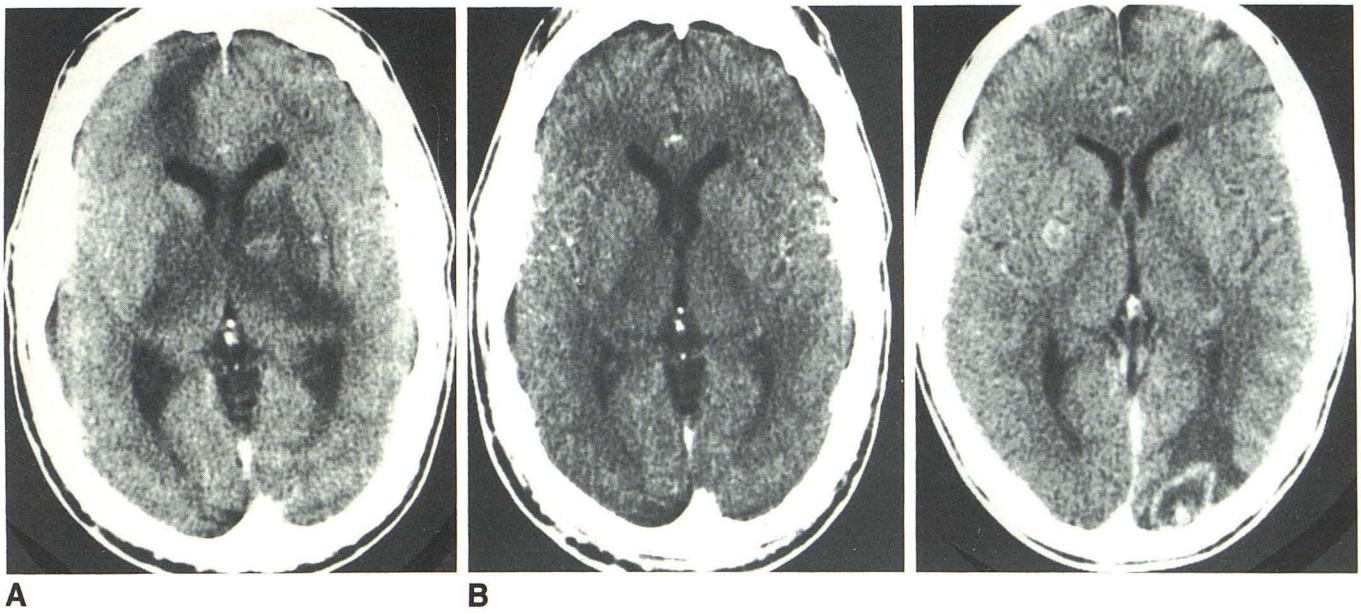


Fig. 3.—Multifocal toxoplasma abscesses. **A**, Right frontal nonenhancing and left basal ganglia ring-enhancing lesions with secondary compression of third ventricle and slight hydrocephalus. **B**, Near-complete resolution of all abnormalities after 20 days of therapy.

Fig. 4—Multifocal toxoplasma abscesses. Multiple deep and peripheral ring-enhancing lesions with and without edema.

CT scan several months before his autopsy diagnosis. Leukoencephalopathies were diagnosed in two patients. In one, CT scans showed widening of the frontal horns and bilateral low density of the adjacent white matter; these changes were more vividly displayed on MRI scans (Fig. 8). Neuropathologic evaluation at autopsy revealed a bifrontal leukoencephalitis characterized by demyelination and multinucleated giant cells. The second patient, in whom progressive multifocal leukoencephalopathy was diagnosed both by biopsy and at autopsy, had bilateral low-density areas near the external capsules without mass effect. One patient with herpes simplex type II encephalitis had bilateral low-density mass lesions with enhancement adjacent to the sylvian fissures; in the other patient with herpes simplex II and in the patient with mixed herpes simplex I and cytomegalovirus encephalitis, CT scans showed atrophy. Cerebral atrophy only was noted on the CT scans of the two patients with cryptococcal meningitis and the patient with coccidioidomycosis. The patient with *Candida albicans* infection had CT scans showing persistent, multiple, bilateral ring-enhancing lesions. The CT findings in

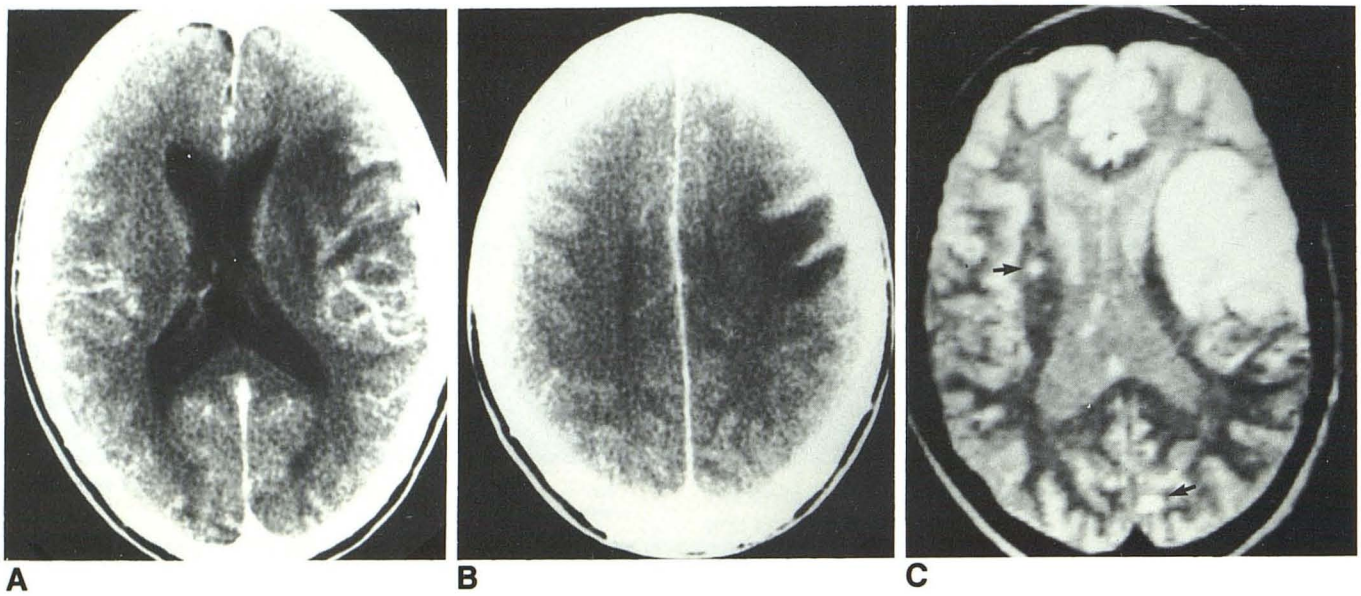


Fig. 5.—Atypical toxoplasmosis. **A** and **B**, CT scans showing left parietal edema with gyral enhancement and compression of left lateral ventricle. **C**, MRI scan obtained with spin-echo sequence (TR = 2000 msec, TE = 56 msec) on same day shows additional lesions in right corona radiata and in left occipital lobe (*arrows*).

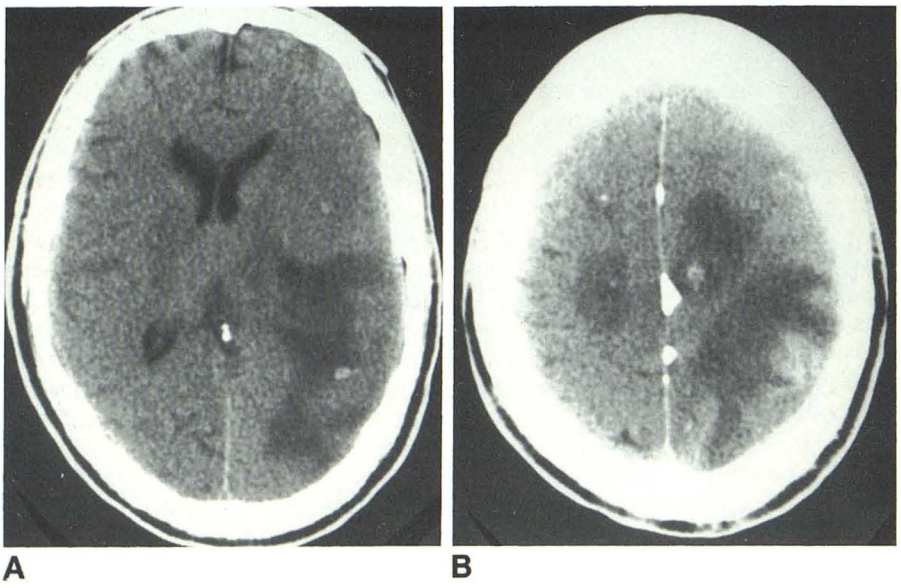


Fig. 6.—Hemorrhagic toxoplasmosis. **A** and **B**, Noncontrast scans showing bilateral low-density lesions containing focal areas of hemorrhage, which were confirmed at autopsy. Note mild left-to-right shift caused by mass effect of large left posteroparietal lesion.

the patient whose brain abscess was culture-negative consisted of bilateral ring-enhancing lesions in the vicinity of the basal ganglia and a solid lesion in the left parietal lobe; this scan was indistinguishable from those of patients with cerebral toxoplasmosis.

Histopathologic diagnoses were not available in 22 patients with focal lesions on CT. Five patients had compelling clinical evidence of cerebral toxoplasmosis. The remaining 17 patients had CT evidence of atrophy and small, usually nonenhancing, hypodense lesions distributed throughout the brain. None of these patients came to biopsy or postmortem examination; only one underwent serial CT scanning, which showed no significant change in the cerebral lesions over 3 months.

Discussion

The increasing number of AIDS patients and the high incidence of neurologic manifestations in this syndrome have led to a rapid increase in the frequency of neuroradiologic evaluation in patients with AIDS. Because these patients may have neurologic abnormalities seldom found in immunocompetent patients, and because the neuroradiologic findings are often confusing and nonspecific, it is particularly important to

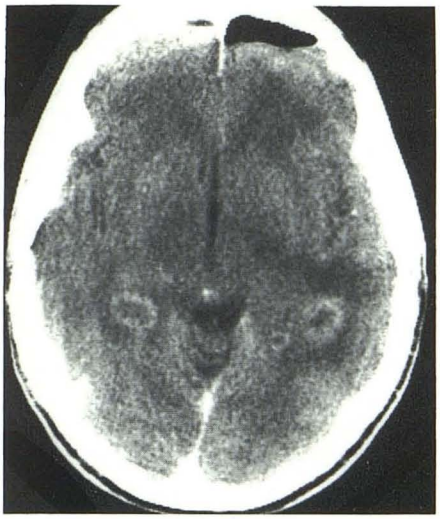
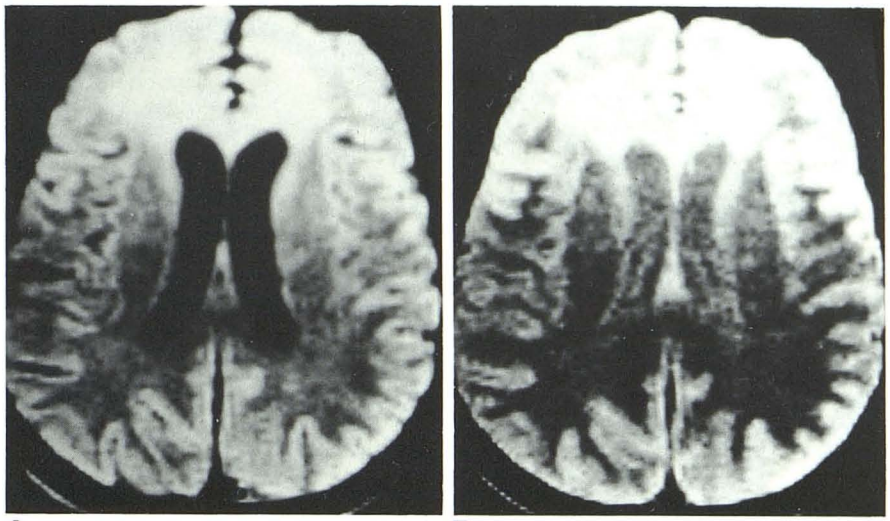


Fig. 7.—Lymphoma mimicking toxoplasmosis. Enhanced scans show bilateral ring-enhancing lesions with surrounding edema that is indistinguishable from toxoplasma abscesses.



A B

Fig. 8.—Bifrontal leukoencephalitis. MRI shows widening of frontal horns and bilateral increases in signal intensity of adjacent white matter. **A**, T1-weighted scan; TR = 500 msec, TE = 28 msec. **B**, T2-weighted scan; TR = 2000 msec, TE = 56 msec.

correlate such findings with the natural history and histopathology of AIDS-related neurologic illnesses.

Of the 200 patients in this study, those who had initially normal CT scans constituted the largest group. Two of these 81 patients developed CT changes consistent with a diagnosis of toxoplasmosis; at autopsy, one additional patient was found to have primary CNS lymphoma and another had metastatic Kaposi's sarcoma. Thus, only four of 81 patients (5%) with initially normal CT scans later developed CT or histopathologic evidence of neurologic disease.

Patients with initial CT evidence of atrophy only (group 2) appeared to be at higher risk. Most of these patients were young, and there is little doubt that their atrophy was related to AIDS and not to normal aging. In all but three cases, the ventricular dilatation was proportional to the widening of the sulci and fissures. Recent studies have demonstrated a high incidence of primary CNS infection with human T-lymphotropic virus type III (HTLV-III), the virus thought to be causally related to AIDS [10]. As it has been suggested that such infection frequently may be the cause of encephalopathy in AIDS patients [11], it is possible that the cerebral atrophy seen in AIDS patients in whom additional cerebral abnormalities have not been identified may reflect infection with HTLV-III. Five of the 75 patients in this group subsequently developed cerebral toxoplasmosis that was evident on CT scans; seven other patients developed lesions that were found at autopsy, including cryptococcal meningitis in two, herpes simplex encephalitis in two, and toxoplasmosis, coccidioidomycosis, and primary CNS lymphoma in one each. Thus, of 75 patients in whom the initial CT scans showed evidence of atrophy only, 12 (16%) developed further neurologic abnormalities that were detected by repeat CT scanning or postmortem examination.

Once the presence of focal abnormalities on the CT scan was established, evaluation of further scans was complicated by variations in treatment administered by different physicians, by patient compliance, and by the duration of follow-up. Therefore, the presence of new lesions on subsequent CT scans probably does not reflect the sensitivity or the prognostic value of such studies in our patients.

Previous studies by ourselves and others [1, 3, 6] have indicated the high incidence of cerebral toxoplasmosis in patients with AIDS. In the present study, toxoplasmosis was the most common histopathologic diagnosis. Most patients with *T. gondii* infection appear to have characteristic CT findings, especially low-density mass lesions in the basal ganglia that enhance upon injection of contrast medium; these lesions are often multiple and bilateral and may develop rapidly. In two patients, follow-up CT scans demonstrated characteristic lesions 6 and 32 days, respectively, after normal CT scans had been obtained (Fig. 2).

The response of cerebral toxoplasmosis to pyrimethamine and sulfadiazine varied in degree and in latency. CT scans showed resolution of lesions as early as 20 days and as late as 6 months after the initiation of treatment (Fig. 3). Despite therapy, complete resolution was not the rule. Patients whose lesions did disappear with therapy usually had persistent CT evidence of atrophy. Double-dose contrast enhancement was not used in this study, however; it is possible that nonenhancing lesions or "completely resolved" lesions might have shown enhancement with such a technique [6]. Our experience also indicates that despite resolution of lesions on CT scans, cerebral toxoplasmosis will recur when treatment is discontinued. We have therefore recommended that once a diagnosis of toxoplasmosis has been established, lifelong antibiotic therapy should be administered [1].

Although it is tempting to suggest that AIDS patients with CT evidence of mass lesions be treated empirically for toxo-

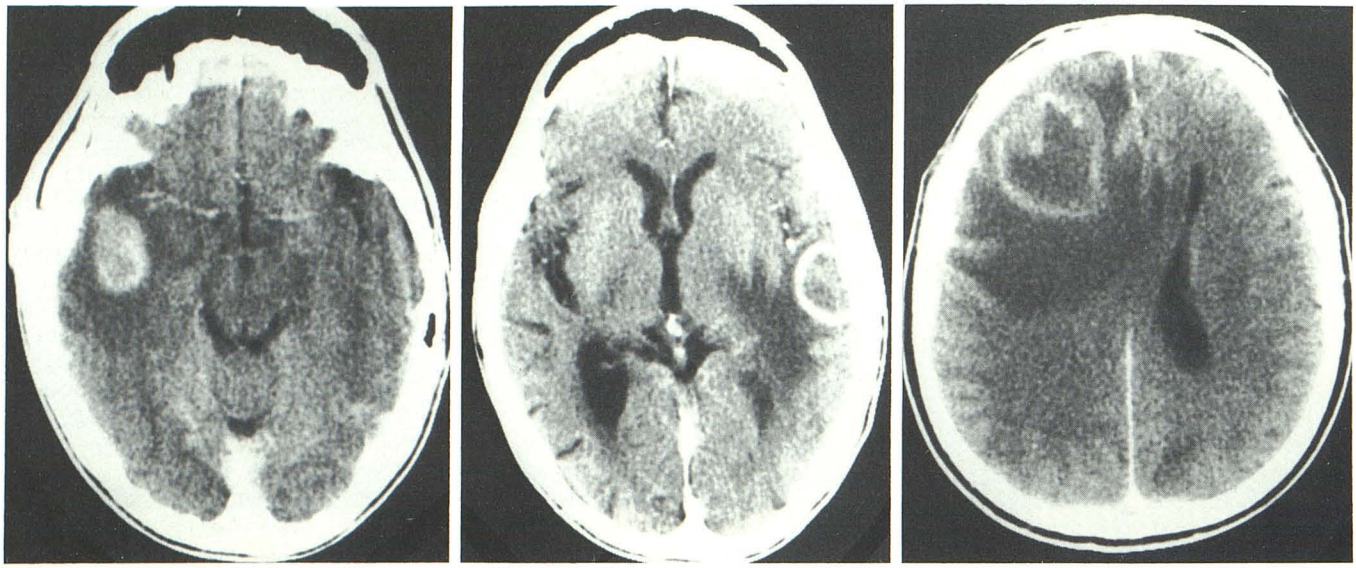


Fig. 9.—Atypical toxoplasmosis. **A**, Homogeneously enhancing right temporal lobe lesion with surrounding edema. **B**, Scan obtained 2 months later, during treatment for toxoplasmosis, shows a new left temporoparietal ring-enhancing lesion with surrounding edema. Original lesion in right temporal lobe has resolved.

Fig. 10.—Mixed toxoplasmosis and lymphoma. Large peripheral ring-enhancing right frontal lesion with surrounding edema and subfalcine herniation. This scan is indistinguishable from scans of patients with toxoplasmosis alone.

plasmosis, our experience indicates that this would be unwise. One patient, for example, whose CT scans showed lesions thought to be typical of cerebral toxoplasmosis was found to have primary CNS lymphoma. Another patient, while receiving empiric treatment for toxoplasmosis, developed new lesions after the initial focal abnormalities had resolved almost completely. This clinical picture suggests the emergence of another disease (Fig. 9). Five of six patients with multiple intracranial abnormalities had toxoplasmosis in addition to a second process; these processes were identified within the same lesion by needle biopsy in three patients and were in different sites in each of the other three. Therapy for toxoplasmosis alone would leave the second disease untreated. Therefore, biopsy appears to be necessary in all AIDS patients with CT evidence of mass lesions. If a patient has evidence of progression on subsequent CT scans, additional biopsies may be necessary to rule out the presence of multiple simultaneous intracranial diseases [12].

Lymphoma was the second most common pathologic finding in this series. Of the three patients with primary CNS lymphoma, one had a normal scan, one had atrophy only, and the third had bilateral ring-enhancing lesions that mimicked toxoplasmosis (Fig. 7). There were no differentiating features on CT to distinguish patients with toxoplasmosis from those with toxoplasmosis and lymphoma (Fig. 10). In contrast, progressive multifocal leukoencephalopathy can usually be distinguished from toxoplasmosis on CT scans by the absence of mass effect and enhancement and by the limitation of lesions to the white matter. These features were seen on the CT scans of the patient with progressive multifocal leukoencephalopathy and on the scans of the patient with bifrontal leukoencephalitis.

In several patients whose CT scans were normal, autopsy revealed CNS disease. There are several possible explanations for this apparent insensitivity of CT scanning. The first is a lengthy interval between CT scanning and postmortem diagnosis, which occurred in three of our cases. One patient with cryptococcal meningitis, whose initial CT scan showed only atrophy, developed a cryptococcoma that was discovered at autopsy 3 months later; two patients with normal CT scans were each found several months later to have a mass lesion (metastatic Kaposi's sarcoma and primary CNS lymphoma) that may well have been detected by follow-up CT scans. A second possible explanation is that toxoplasmosis, particularly in profoundly immunocompromised patients, frequently causes diffuse encephalitis without a secondary reaction. Thus, the brain is overwhelmed with *T. gondii*, but there is no abscess or focal lesion. In one patient, the presence of diffuse toxoplasma encephalitis without focal abscess formation was confirmed by autopsy 1 day after a normal CT scan had been obtained. A third possibility, which probably reflects an inherent limitation of this imaging technique, is that CT is insensitive despite the presence of local reaction. We have documented this with combined MRI and autopsy studies. Lesions missed by CT scans have ranged in size from a few millimeters to 2 cm or larger.

There is some indication that MRI may be more sensitive than CT in detecting intracranial abnormalities in patients with AIDS [1, 9]. All six MRI scans obtained in this series showed abnormalities that were not demonstrated by CT. In one patient with a normal CT scan, MRI showed multiple focal lesions; biopsy of these lesions led to the diagnosis of toxoplasmosis. Three of the patients who had MRI scans had CT evidence of atrophy only: in one, MRI demonstrated high

signal intensity throughout the white matter of both cerebral hemispheres, which was found at autopsy to represent leukoencephalopathy, and in the other two demonstrated focal lesions that have yet to be identified. One patient with toxoplasmosis had atypical findings on the CT scan; MRI revealed several lesions that were not evident on the CT scans (Fig. 5). Thus, it appears that MRI may be a valuable supplement to CT, especially when the CT scan shows evidence of atrophy only.

This study indicates that many AIDS patients with neurologic symptoms have normal CT scans and little risk of neurologic progression. In patients with CT evidence of diffuse cerebral atrophy, which in itself is nondiagnostic, there is a significant risk of neurologic and radiologic progression. Although *T. gondii* infection is the most frequent finding in patients with CT evidence of mass lesions, many diseases can mimic the CT appearance of toxoplasmosis, and AIDS patients often have multiple simultaneous intracranial abnormalities. Thus, it is unwise to assume that these lesions are caused by *T. gondii*, and biopsy is therefore recommended.

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