Primary Central Nervous System Lymphoma: CT and Pathologic Correlation

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Primary Central Nervous System Lymphoma: CT and Pathologic Correlation

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CT findings of 15 patients with histologically proven primary central nervous system (CNS) lymphoma were reviewed with pathologic correlation in order to evaluate variable CT patterns. There were a total of 32 lesions. Of the 15 patients studied, seven had acquired immunodeficiency syndrome (AIDS), all diagnosed within the past 3 years. The CT observations of eight non-AIDS patients were consistent with findings reported previously. Most of the lymphomatous lesions were either hyper- or isodense, round or oval masses with homogeneous contrast enhancement and variable surrounding edema. Pathologic examination showed tightly packed preserved lymphoma cells without necrosis. in AIDS patients, rim or ring enhancement of lymphoma, indistinguishable from brain abscess, was frequently seen. Histologic examination consistently showed extensive tumor necrosis with preservation of viable tumor cells at the periphery. A third and infrequent CT pattern was multiple infiltrative nonnodular solid enhancement with extensive edema. Pathologic correlation showed infiltrating viable tumor cells without necrosis. The rim- or ring-enhancing brain lesion seen in AIDS patients can either be an abscess or a primary lymphoma; proper tissue collection is essential for correct diagnosis and appropriate treatment.

Primary CNS lymphoma is still a relatively rare primary brain tumor, even with the recent increase in AIDS patients. The classic CT observations of primary CNS lymphoma have been described as solid, well-circumscribed hyperdense mass(es) with homogeneous contrast enhancement and predilection for the basal ganglia, corpus callosum, periventricular white matter, and cerebellar vermis. Other CT observations, however, such as rim- or ringlike and gyrallike patterns, have not been previously emphasized, and to our knowledge there has been no report describing the pathologic correlation. In this paper we will describe the spectrum of CT findings on primary CNS lymphoma in 15 patients and correlate these findings with tissue specimens obtained before initiation of treatment.

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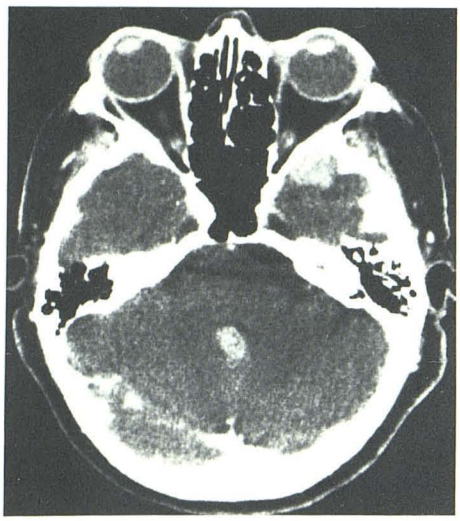
Materials and Methods

From June 1977 to June 1985, 15 patients with biopsy-proven primary CNS lymphoma were seen at The University of Texas M. D. Anderson Hospital and Tumor Institute in Houston. Ten of the patients were men and five were women. They ranged in age from 12 to 65 years (mean age, 38.4 years).

All CT scans were done before needle or open biopsy and were obtained before and after intravenous administration of 300 ml of 30% contrast medium (42 g iodine). The scans were performed on different scanners, including GE-8800 (Milwaukee, WI), GE-9800, EMI-1010 (Hayes, Middlesex, England), Siemens Somatom 2, and Siemens DR-3 (Iselin, NJ). Thirty-two lesions in our 15 patients were evaluated with CT. All biopsy or resected specimens (n = 15) were reviewed by one of the authors (JMB) and the results were correlated with the CT findings.



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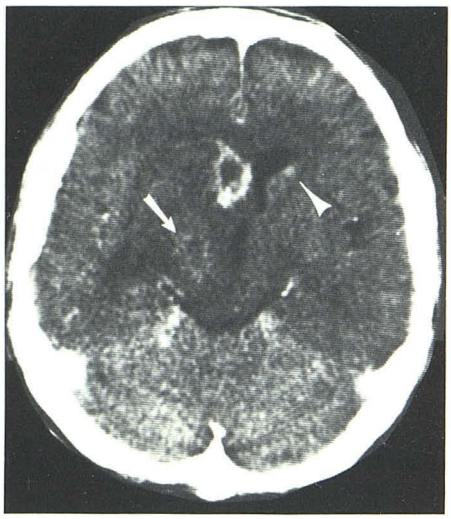

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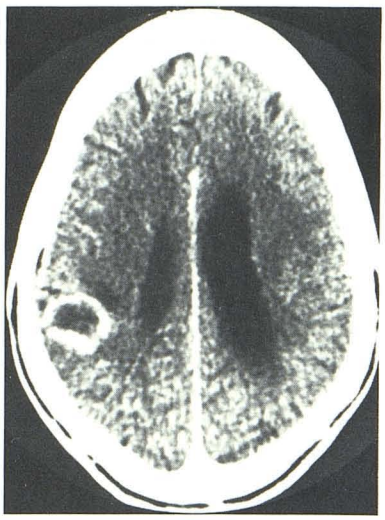

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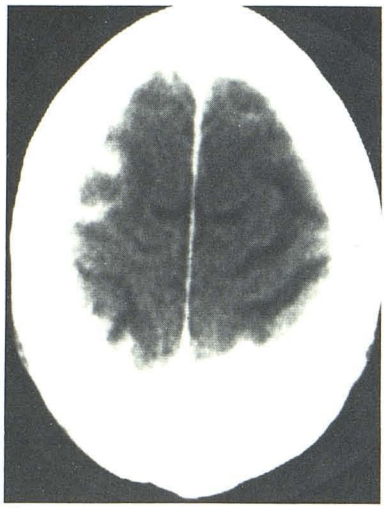

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Fig. 1.—Two solid nodular-enhancing lesions in previously healthy 66-year-old woman. Diagnosis of primary CNS lymphoma was made on surgical specimen of left temporal lesion.

Fig. 2.—Multiple-enhancing lesions in 32-year-old male AIDS patient. Irregular rim-enhancing lesion is seen in head of right caudate nucleus, in addition to poorly defined rim-enhancing lesion in right thalamus and posterior limb of internal capsule (*arrow*) and solid nodular-enhancing lesion in head of left caudate nucleus (*arrowhead*). Needle biopsy of right caudate lesion revealed lymphoma. Patient received whole brain irradiation of 5200 rad (52 Gy). Autopsy 3½ months after initial diagnosis revealed extensive necrotic lymphoma involvement in both basal ganglia and in right thalamus. There was no evidence of intracranial infection and no dissemination of lymphoma beyond CNS.

Fig. 3.—Well-defined right parietal thick ring-enhancing lesion in 24-year-old male AIDS patient proved to be lymphoma with extensive necrosis in an open biopsy specimen. Autopsy 2 months after initial diagnosis confirmed diagnosis of primary CNS lymphoma without intracranial infection.

Fig. 4.—"Gyral"-enhancing lesion in right high-convexiety parietal lobe of 35-year-old male AIDS patient. Open biopsy revealed lymphoma. Autopsy 1 month later confirmed diagnosis without evidence of CNS infection or extraneural lymphomatous involvement.

Results

CT Evaluations

Thirty-two lesions were identified on CT in 15 patients (eight non-AIDS and seven AIDS). Fifteen (47%) of the lesions were predominantly in the cortex; of these, three showed extensive infiltration into the periventricular white matter. The corticomedullary junction was primarily involved in only three (9%) of the 32 lesions. Of the remaining 17 lesions, 15 (47%) were periventricular and the other two (6%) were in the lateral basal ganglia. Vermis and basal ganglia were the favorite sites in the non-AIDS patients, and frontal lobe was the most common location in the AIDS patients. Edema surrounded 26 (81%) of the lesions; the edema/tumor ratio was greater or equal to one in 20 lesions.

A summary of the CT observations is given in Table 1. The contrast-enhancing pattern was the only significantly different CT feature between non-AIDS and AIDS patients. In the non-AIDS patients, the solid nodular pattern (Fig. 1) was the predominant pattern and was observed in 12 (75%) of the lesions. Only two (13%) of the lesions had a rimlike pattern (Figs. 2 and 3). In the AIDS patients, the rimlike pattern was observed in seven (44%) of 16 lesions and the solid nodular pattern was seen in six (38%). The gyrallike pattern (Fig. 4) was observed infrequently (it occurred in two (13%) of 16 lesions in each group).

Pathologic Correlation

In all 15 patients the tissue diagnosis was diffuse large-cell lymphoma, which was in accordance with the working formulation for classification of non-Hodgkin's lymphoma [1]. None of the 15 lesions examined had an associated infectious process microscopically. The microbiologic cultures in seven AIDS patients were negative for bacteria, viruses, and protozoa. Of the 15 lesions biopsied or resected, the enhancing CT patterns were solid nodular in six, rim or ringlike in seven, and gyrallike in two.

TABLE 1: **CT Characteristics of Primary CNS Lymphoma**

	Non-AIDS (n = 8)	AIDS (n = 7)
Number of Lesions	16	16
Multiplicity	3	4
Location		
Frontal lobe	2	8
Parietal lobe	1	3
Temporal lobe	2	0
Occipital lobe	1	1
Basal ganglia	4	2
Thalamus	0	1
Vermis	6	1
Size (cm)		
<2	9	6
2–5	6	7
>5	1	3
Shape		
Round	8	7
Oval	5	4
Multilobular	1	3
Infiltrative	2	2
Precontrast CT Density		
Hyperdense	6	3
Isodense	10	9
Hypodense	0	3
Mixed	0	1
Degree of Contrast Enhancement		
Marked	14	13
Moderate	2	3
Contrast-Enhancing Pattern		
Solid nodular	12	6
Rim or ringlike	2	7
Gyrallike	2	2
Mixed (nodular + rim)	0	1

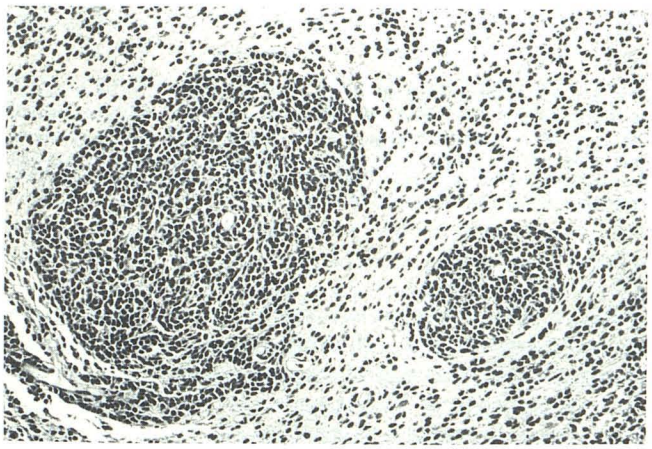

Fig. 5.—Extensive lymphomatous infiltration (same patient as in Fig. 1) with characteristic dense concentric perivascular cuffing. No necrosis is present. ×525.

The solid nodular patterns (six patients) all showed tightly packed and preserved lymphoma cells without necrosis (Fig. 5). Only one of these patients was immunosuppressed.

The rim- or ringlike patterns (seven patients) all demonstrated extensive necrosis with preservation of tumor cells at the periphery (Fig. 6). Five of these seven patients had AIDS.

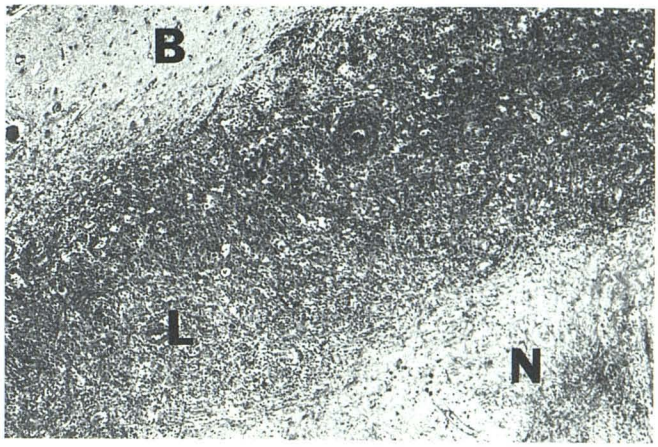

Fig. 6.—Extensive central necrosis (N) surrounded by rim of viable lymphoma (L). Normal brain tissue is identified outside lymphoma (B). ×200 (same patient as in Fig. 3).

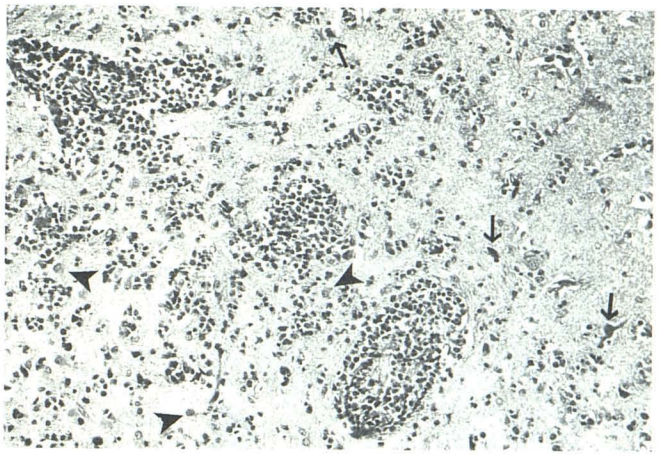

Fig. 7.—Loosely clustered perivascular cuffings of viable lymphoma cells, with minimal infiltration into intervening brain tissue where residual neurons (*arrows*) and reactive astrocytes (*arrowheads*) can be identified. No necrosis is present. ×525 (same patient as in Fig. 4).

The gyrallike patterns (two patients) were seen in the cortical region. Microscopically, the tumor cells were loosely clustered, forming perivascular cuffs with infiltration into the interlacing reactive brain tissue (Fig. 7). One lesion was observed in an AIDS patient and the other in an immune-competent 12-year-old patient.

Discussion

Primary CNS lymphoma is a relatively rare primary brain tumor and there is controversy regarding its cell of origin. "Perithelial sarcoma" [2], primary reticulum cell sarcoma of brain [3, 4], and microgliomatosis [5], with its possible perivascular or microglial origin, have been used to describe the same primary neoplastic lymphoproliferative process in the CNS. The term "primary malignant lymphomas of CNS" has generally been accepted in recent years because these lym-

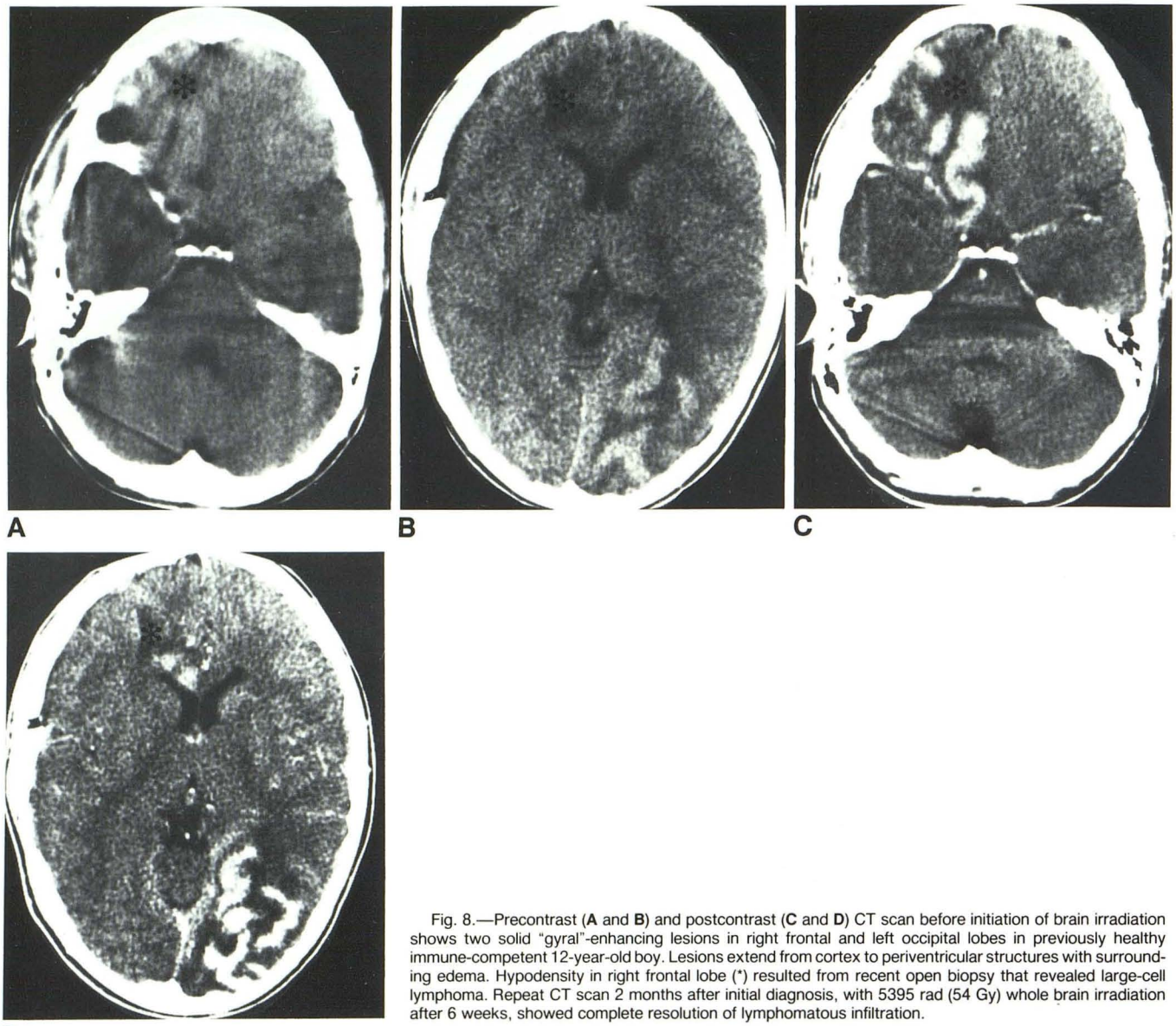

Fig. 8.—Precontrast (**A** and **B**) and postcontrast (**C** and **D**) CT scan before initiation of brain irradiation shows two solid "gyral"-enhancing lesions in right frontal and left occipital lobes in previously healthy immune-competent 12-year-old boy. Lesions extend from cortex to periventricular structures with surrounding edema. Hypodensity in right frontal lobe (*) resulted from recent open biopsy that revealed large-cell lymphoma. Repeat CT scan 2 months after initial diagnosis, with 5395 rad (54 Gy) whole brain irradiation after 6 weeks, showed complete resolution of lymphomatous infiltration.

phomas are similar to a wide range of extraneural malignant lymphomas [6–11]. It is postulated that these lymphomas might be the neoplastic counterparts of the normal process of lymphocyte transformation [12, 13]. There is evidence of an increasing incidence in recent years, particularly among allograft transplant recipients [14–16] and AIDS patients [17–19]. The AIDS epidemic, however, has contributed most significantly to this increase. Of the 15 patients in this series, five diagnoses were made between 1977 and 1982 and none was related to AIDS. Of the remaining 10 patients, all seen within the past 3 years, seven had AIDS.

The classic CT appearance of primary CNS lymphoma has been well described [20–25]. In general, these lymphomas present as relatively large, sharply demarcated, hyper- or isodense, round or oval mass lesions located in the basal ganglia, corpus callosum, periventricular white matter, and cerebellar vermis. Moderate-to-marked homogeneous contrast enhancement is usually observed without central hypodensity. Multiple lesions are frequently present.

CT observations of 16 lesions in our eight non-AIDS patients agree with previous reports [20–25]. The tumor masses are pathologically composed of densely packed neoplastic cells of lymphoreticular origin with a characteristic pattern of dense perivascular concentric cuffing. Hypercellularity, not hypervascularity, without necrosis may be responsible for the hyper- or isodensity of the tumor mass on the noncontrast CT and for the homogeneous enhancement on the postcontrast CT. The pathologic examination of our tissue specimens with the solid nodular CT pattern supports this postulation.

The CT and pathologic findings in the AIDS patients, however, are frequently different from the classic pattern. Nearly half the lesions have an abscesslike appearance, with rim or

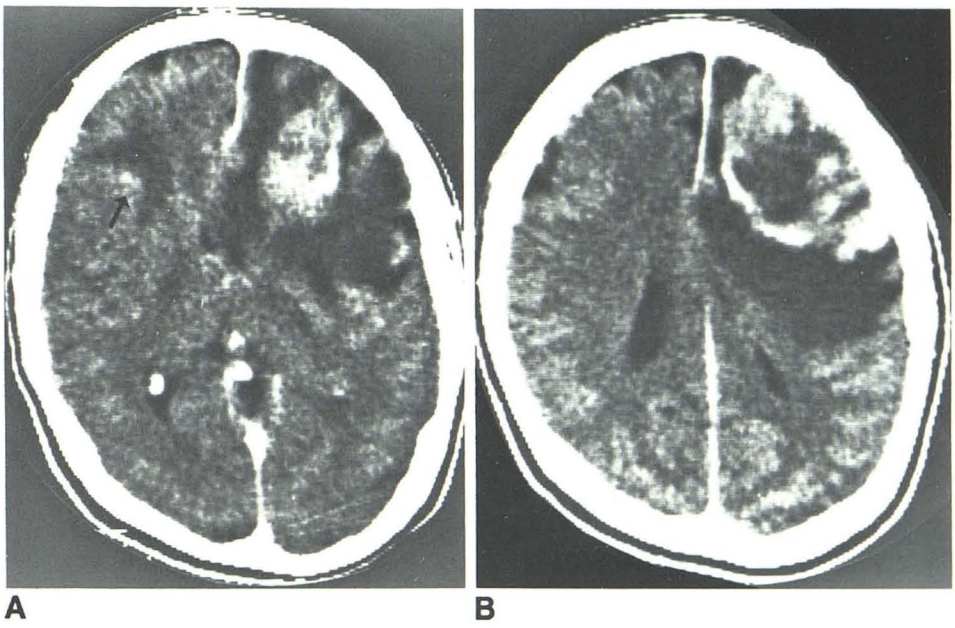

Fig. 9.—**A** and **B**, Left frontal irregular rim-enhancing lesion with partial solid nodular mass in 35-year-old male AIDS patient. This pathologically proven necrotic lymphomatous lesion cannot be differentiated from glioblastoma multiforme. A small additional solid-enhancing lesion is seen in right frontal corticomedullary junction (*arrow* in **A**).

ring enhancement and central hypodensity. This observation is less common in non-AIDS patients. Pathologic examination consistently showed extensive necrosis of the tumor mass with preservation of viable tumor cells at the periphery. Central necrosis had also been reported as a common finding of CNS or extraneural lymphomas in the organ transplant recipients who, like AIDS patients, are immunocompromised [26, 27]. We have no explanation for this central necrosis. Extensive immunomorphologic examinations of these cases should provide further understanding.

An unusual gyrallike, solid-enhancing pattern, which to our knowledge has not been previously described, occurred in three patients. One child with normal immune status had extensive gyrallike lesions interlacing with edematous but tumor-free brain tissue in two different locations (Fig. 8). The lesions extended from the cortex into the periventricular white matter. The tissue specimen revealed viable tumor cells clustered together without necrosis. The lesions responded to cranial irradiation and disappeared completely (by CT) immediately following the completion of treatment. The second patient, who had AIDS, had more subtle gyrallike enhancement in the parietal cortex (Fig. 4). The biopsy specimen showed loose clusters of viable cells without necrosis. The patient died of cytomegaloviral pulmonary infection and sepsis 3 weeks later. Autopsy results showed extensive necrosis of lymphoma, probably resulting from radiation therapy. There was a small number of viable neoplastic cells within the meninges and around the large vessels bordering the necrosis. No evidence of infection was found in the brain. The biopsy specimens in these two patients were unfortunately too small and fragmented for a more detailed CT-pathologic correlation. The third patient, also an AIDS patient, had associated solid-nodular and ring-enhancing lesions. Biopsy of the gyrallike lesion was not done.

Differential diagnosis of primary CNS lymphoma includes meningioma, metastasis, brain abscess, enhancing infarction, and primary glial tumor. Solitary hyperdense-enhancing lymphoma, when situated near the surfaces of the brain, should be differentiated from meningioma; angiography may be necessary to confirm or exclude the latter. Metastatic lesions, either solitary or multiple, are more difficult to differentiate. Classic CT findings of hyper- or isodensity, homogeneous enhancement, and periventricular location might be helpful to make primary CNS lymphoma the more likely diagnosis. Nevertheless, tissue proof is mandatory, particularly when no primary malignancy is known. The solid-enhancing pattern and the favored locations can distinguish lymphoma from brain abscess without difficulty, although the early cerebritis stage of an abscess might be confusing.

It is impossible to differentiate ring- or rim-enhancing CNS lymphoma from brain abscess, particularly when the patient is immunosuppressed. Opportunistic CNS infections in immunocompromised patients are common [19, 28, 29]. Toxoplasmosis is the most frequent CNS parenchymal infection in AIDS patients [28, 29]. Common findings of extensive necrosis in malignant lymphoma and toxoplasmosis in immunocompromised patients often cause a diagnostic dilemma and delay the proper management. Cases of lymphoma misdiagnosed as toxoplasmosis at biopsy have been reported in AIDS patients [19, 28]. An example of how this might occur was seen in a patient with AIDS in our series. On two occasions, needle biopsy of a ring-enhancing lesion revealed only necrotic tissue without viable cells. The third tissue collection, open biopsy, finally revealed a small portion of viable lymphoma cells at the periphery of extensive necrotic tissue. A large necrotic-enhancing lymphomatous mass may occasionally mimic a malignant glial tumor (Fig. 9). The rare gyrallike lymphomatous involvement can sometimes be confused with an enhancing-resolving infarction.

In conclusion, adequate tissue specimens are essential for

correct diagnosis and initiation of appropriate treatment of primary CNS lymphoma, since lymphomas may mimic brain abscesses on CT, particularly in immunosuppressed patients. Multiple samples or a carefully directed biopsy with immediate frozen section confirmation of the adequacy of viable tissue is mandatory.

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