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## **Radiographic Findings in 32 Cases of Primary CNS Lymphoma**

Clifford R. Jack, Jr., David F. Reese and Bernd W. Scheithauer

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# Radiographic Findings in 32 Cases of Primary CNS Lymphoma

Clifford R. Jack, Jr.<sup>1</sup>  
David F. Reese<sup>1</sup>  
Bernd W. Scheithauer<sup>2</sup>

Computed tomographic (CT) or angiographic (or both) findings were analyzed in 32 cases of pathologically proved primary non-Hodgkin lymphoma of the central nervous system. CT scans were available in 28 of the 32 cases. Thirty lesions were found in the 28 cases. In comparison with previous literature, the frequency of involvement of deep central structures (30%), multiple lesions (11%), and subependymal lesions (4%) was lower and that of lesions in the periphery of the supratentorial compartment was higher (46%). In agreement with previous literature, most of the lesions were of increased density (63%), enhanced (100%), and enhanced homogeneously (71%). Twenty-nine of the 32 patients underwent cerebral angiography. In 12 patients, a homogeneous vascular stain was found that appeared in the late arterial or early venous phase and had a meningiomalike pattern. This staining pattern has not been emphasized sufficiently in previous literature. It was believed that such an angiographic pattern in a dense, homogeneously enhancing parenchymal lesion is suggestive of a primary lymphoma of the central nervous system. Magnetic resonance imaging was performed in one patient with two lesions, and both lesions demonstrated prolonged T2 relaxation times.

Primary lymphoma of the central nervous system (CNS) is a rare tumor, representing 0.2%–2% of all primary CNS malignancies [1, 2]. Various pathologic terms have been applied to this entity, including histiocytic sarcoma, reticulum cell sarcoma, microglioma, perivascular sarcoma, and perithelial sarcoma [1, 3]; such terms have been abandoned for more modern functional classifications of lymphoid neoplasia. Ninety-three percent of all CNS lymphomas are primary [4]. We analyzed the computed tomographic (CT) and angiographic findings in 32 cases of pathologically proved primary CNS lymphoma. The findings on magnetic resonance (MR) imaging, which was performed in one case, are also presented.

## Materials and Methods

The clinical records and radiographic findings of 32 patients with pathologically proved primary CNS lymphoma were studied retrospectively. Examinations were performed between 1972 and 1984. Microscopic slides were reviewed by one of us (B. W. S.), and the tumors were verified to represent non-Hodgkin lymphoma. Of the 32 patients, 28 had preoperative CT scans, with or without (or both) contrast medium (25 of the 28 also underwent cerebral angiography). Seventeen of the CT scans were obtained with early-generation scanners and 11 with late-generation scanners. The CT scans were evaluated for lesion location, density, enhancement, homogeneity of enhancement, mass effect, edema, and definition of lesion margin. For each lesion, these parameters were graded and assigned to one of three groups—none, minimum to moderate, and marked—by two of us (D. F. R. and C. R. J.). The first choice recorded at the time of initial scan interpretation was noted for each case.

Preoperative cerebral angiograms were obtained in 29 of the 32 cases (in five of these 32 cases, preoperative CT scans were not available). Each angiogram was evaluated and graded for mass effect. Medullary veins, arterial encasement, arteriovenous shunting, tumor stain, and tumor neovascularity were graded as either positive or negative. One patient underwent MR scanning on a 0.15-T scanner (Picker).

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<sup>1</sup> Department of Diagnostic Radiology, Mayo Clinic and Mayo Foundation, Rochester, MN 55905. Address reprint requests to D. F. Reese.

<sup>2</sup> Section of Surgical Pathology, Mayo Clinic and Mayo Foundation, Rochester, MN 55905.

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## Results

The ages of the 32 patients (21 males and 11 females) were 9–79 years (average, 58.8). The group showed the usual proportions of histopathologic subtypes reported in the recent literature. The first radiographic examination was done between 1972 and 1976 in nine of these patients, between 1976 and 1980 in 12 patients, and between 1980 and 1984 in 11 patients, demonstrating a fairly constant incidence over the three time periods. Three patients could be classified as being immunosuppressed: one had undergone a renal transplant, one had rheumatoid arthritis with steroid treatment, and one had multiple myeloma. The interval from pathologic diagnosis to death was documented in 16 cases. The average was 21.8 months (range, 4 days to 57 months). Seven patients were still alive at the time of this study. Follow-up was not available on the other nine patients.

Of the 32 patients, 28 had preoperative CT scans. These 28 patients had 30 lesions. Twenty-five patients had a single nodular lesion, two had two lesions, and one had diffuse subependymal spread involving the third and lateral ventricles. The 30 lesions were grouped into one of five categories according to location: (1) deep central (including basal ganglia, thalamus, third ventricle, and corpus callosum); (2) white matter; (3) cortical; (4) corticomedullary junction; and (5) posterior fossa. Although large lesions often involved more than one of the above zones, each lesion was assigned to only one of the above locations on the basis of the best estimate (by D. F. R. and C. R. J.) of the epicenter of the lesion. In three patients, the lesions could not be localized precisely by CT. In two of the three patients, the lesions were of the same density as the surrounding edema, and in the third patient, the CT scan revealed only intraparenchymal hemorrhage. These three cases are listed as "cannot verify" in the lesion location column of table 1, because the tumor could not be demarcated from adjacent edema or hemorrhage. However, all three lesions were in the frontal lobes. Three patients did not have contrast-enhanced CT scans and one had only a contrast-enhanced study. Tumor size could not be evaluated in the three patients with no margin definition or in the one patient with diffuse subependymal spread.

Twenty-nine of the 32 patients underwent preoperative cerebral angiography; there were 31 lesions in this group. In each of the two patients with two lesions, the angiogram failed to demonstrate any abnormality at the site of one of the two tumor nodules. Aside from mass effect (25 of 31 lesions), the only abnormality present in a significant number of cases was tumor stain. This was seen in 12 (39%) of 31 lesions. In each case, the tumor stain appeared during the late arterial or capillary phase and had a diffuse homogeneous appearance. This stain is similar to that commonly seen with meningiomas (fig. 1). Of the 31 lesions, five displayed prominent medullary veins; two, arterial encasement; none, dural arterial supply or arteriovenous shunting; and three, tumor neovascularity.

MR imaging was performed in one patient. Axial sections were obtained using a spin-echo pulse sequence (30 msec echo time, 4000 repetition time). This patient had lesions adjacent to both the third and fourth ventricles. Both lesions demonstrated a prolonged T2 relaxation time, which was

TABLE 1: Summary of CT Findings in 28 Cases of Primary Lymphoma of the Central Nervous System

Finding	No. of Lesions (n = 30)
Lesion location:	
Deep	9
White matter	9
Corticomedullary	2
Cortical	2
Posterior fossa	4
Cannot verify	3
Precontrast density:	
Markedly increased	5
Moderately increased	14
Isodense	7
Decreased	2
Cannot verify	2
Edema:	
Marked	10
Moderate	16
None	4
Degree of enhancement:	
Marked	13
Moderate	10
Cannot evaluate	7
Homogeneity of enhancement:	
Marked	11
Moderate	6
Mottled	3
Ringlike	4
Cannot evaluate	6
Definition of tumor nodule margin:	
Marked	10
Moderate	13
Poor	4
Cannot evaluate	3

Note.—Average tumor size was 3.9 cm (range, 1–8 cm). The main diagnostic choices were "tumor," eight cases; glioma, six; meningioma and lymphoma, three each; abscess and infarct, two each; colloid cyst, germinoma, hemorrhage, and metastases, one each.

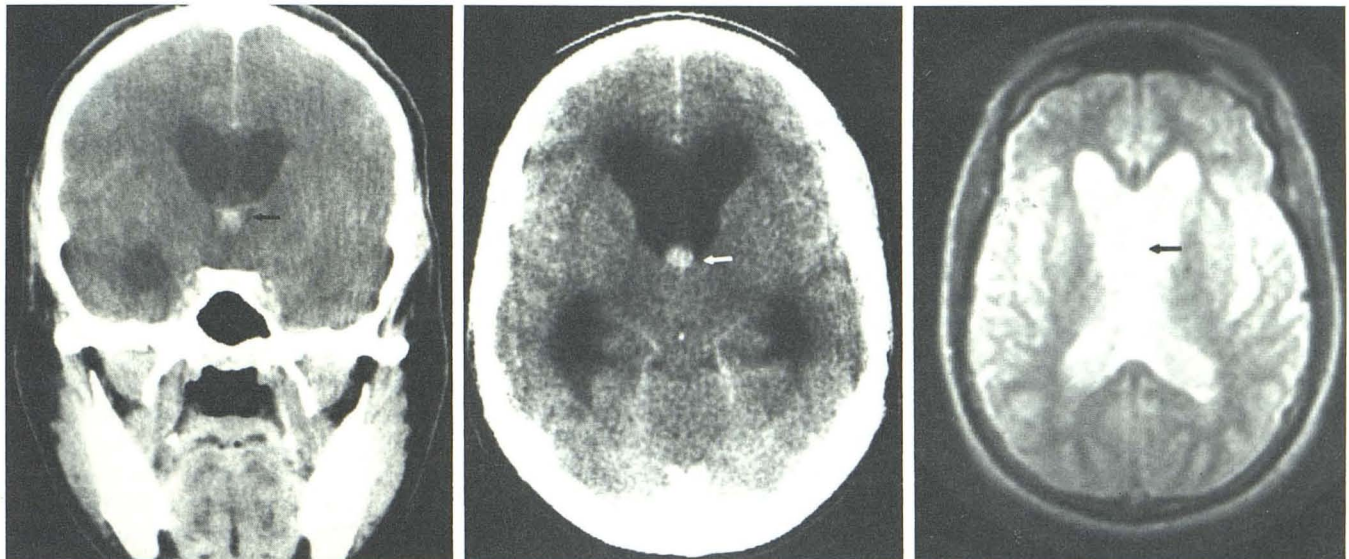
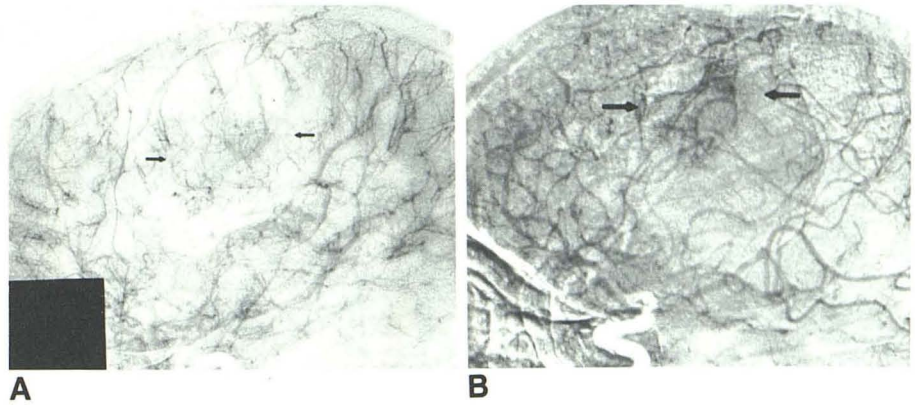
equal to that of cerebrospinal fluid (CSF). This made distinction between the lesion and ventricular fluid difficult in both instances (fig. 2).

## Discussion

Our epidemiologic data are in agreement with previous studies [1, 5]. The average age for our group was 58.8 years (range, 9–79). The average age in the Spillane et al. [1] series was  $55.6 \pm 13.6$  years (range, 25–80), while in the Enzmann et al. [5] series, the average was 44 years (range, 14–68). The nearly 2:1 male-to-female ratio in our series is also in agreement with the male predominance in the Spillane et al. [1] series. The mean survival time of 21.6 months in our series is somewhat longer than that cited in the series of Spillane et al. [1] or Mendenhall et al. [6], who cited 15.2 months with radiation therapy. Three patients (9%) in our series were immunosuppressed. The increased incidence of primary CNS lymphoma in immunosuppressed patients (especially renal transplant recipients) is well documented in the literature [2, 4–8]. Mendenhall et al. [6] stated that the incidence of primary CNS lymphoma in immunosuppressed patients is 350 times that in the general population. Patients with acquired immunodeficiency syndrome also have been shown to have a higher incidence of primary CNS lymphoma [8]. Our data do not, however, support claims that the incidence of primary



Fig. 1.—Diffuse meningeomalike vascular staining in two patients with primary CNS lymphoma. A 50-year-old (A) and 76-year-old (B) man, each with tumor in white matter of right frontoparietal lobe (arrows).

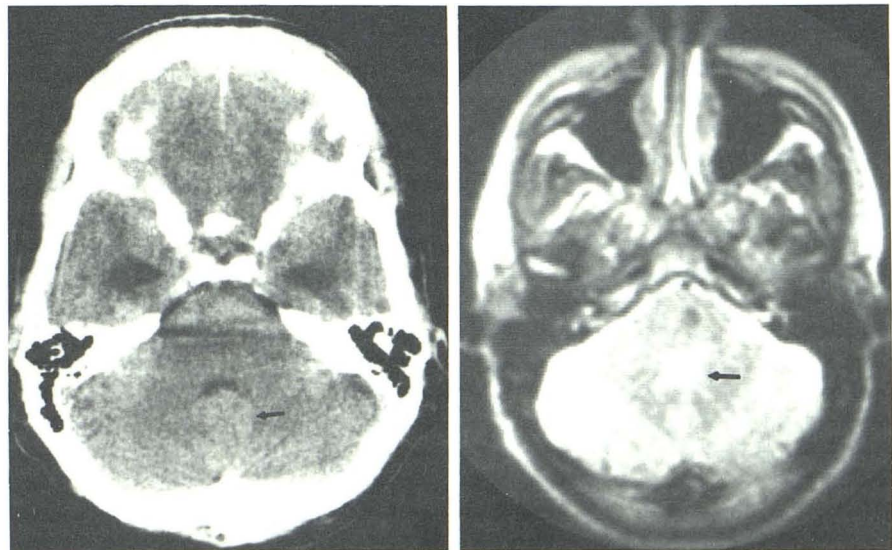


A

B

C

Fig. 2.—Lesion of third ventricle in 29-year-old man. A and B, Contrast-enhanced CT scans. Appearance similar to colloid cyst (arrows). C, Prolonged T2 relaxation time equal to that of CSF on MR imaging (arrow). Lesion cannot be demarcated from fluid in third ventricle. Second lesion in inferior vermis deformed fourth ventricle on CT (D, arrow) and CSF demonstrated T2 relaxation time equal to CSF of fourth ventricle (E, arrow). Lesion also could not be demarcated from adjacent CSF by MR.



D

E

CNS lymphoma has been increasing in recent years [1]. A possible explanation for this observation may rest with the nature of the clinical practice at our institution. The increase in transplant surgery and associated primary CNS lymphoma

at select centers in recent years may not be reflected in the neurosurgical practice at our institution. The incidence of primary CNS lymphoma, when grouped into 4-year periods dating back to 1972, has been fairly constant. No correlation





Fig. 3.—CT scan of 69-year-old man. Intensely enhancing tumor nodule in right frontal white matter has low-density center. Enhancing wall is characteristically thick, being 1.0–2.0 cm.

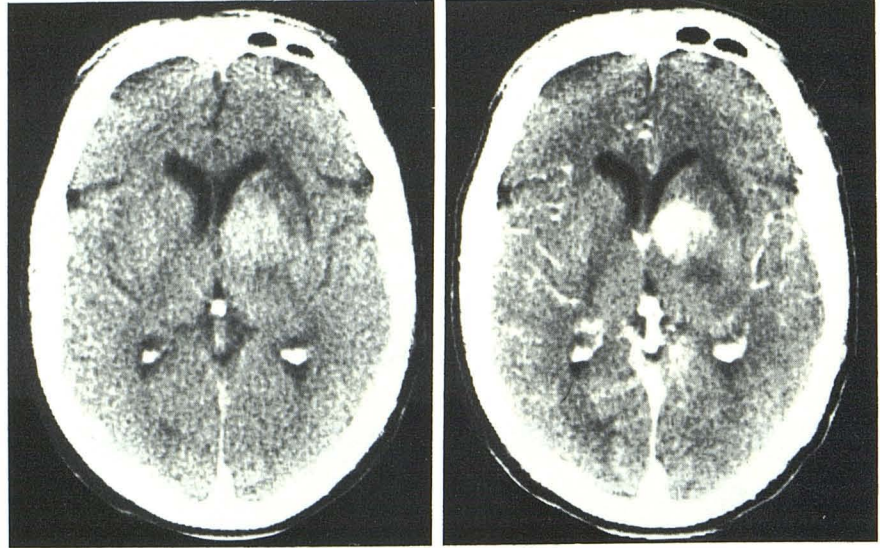


Fig. 4.—Pre- (A) and post- (B) contrast CT scans of 64-year-old man. Characteristic location and appearance of deep central lesion. Tumor nodule, in left basal ganglia, is of increased density, and enhances intensely and homogeneously.

between radiographic findings and pathologic subtype was found.

The CT data in our series with regard to tumor density, enhancement, edema, and size are in agreement with most previous series [1–3, 5, 9, 10]. Nineteen of 28 lesions in our series were of increased density. Similar results are cited by Valavanis et al. [11], Spillane et al. [1], Kazner et al. [9], and Radvany and Levine [10]. All lesions that could be evaluated for contrast enhancement showed enhancement, and 17 of 24 enhanced homogeneously. All referenced series cited similar results [1–3, 5, 9, 10]. We did have a higher incidence (four of 24) of ringlike enhancement than has been described previously [5]. The enhancing wall of the tumor nodule was quite thick in all four of our cases. This is in sharp contrast to the thin wall commonly seen with abscess [12]. This may be a helpful differential point in immunosuppressed patients who have an increased incidence of both primary CNS lymphoma and abscess [5] (fig. 3).

A prominent peritumoral edema zone was common in our series (26 of 30). This was also seen in the series of Enzmann et al. [5], Tallroth et al. [3], and Tadmor et al. [2]. All four lesions that did not have an associated edema zone were small and were deep or located in the posterior fossa. The tumor nodules in our series were generally large (average size, 3.9 cm), which also agrees with previous literature [5]. Tumor nodule margins in our series were well defined in 23 of 27 lesions. Previous literature, conversely, has emphasized blurred tumor margins [9, 11]. We found that the prominent edema zone around the tumor nodule in most cases provides a well defined margin. All four tumors with poor margin demarcation were lesions with only a moderate zone of edema.

Our CT data with regard to lesion location, multiplicity, and the incidence of subependymal spread differ from previous literature [1, 2, 5, 11]. In our series, 30% of lesions were

located in deep central structures, 46% peripherally, and 13% in the posterior fossa. Although the division of supratentorial lesions into deep central and peripheral locations may be somewhat artificial, we believe that the lack of central involvement in our study was in striking contrast to the rate of involvement cited in previous large series. We sought to emphasize this finding by grouping supratentorial lesions in this manner. Tadmor et al. [2] stated that more than 50% of lesions were in the basal ganglia, whereas Spillane et al. [1] cited a 60% involvement rate of deep structures. Enzmann et al. [5] found the basal ganglia were involved in 50% of the cases of single lesions and in 100% of the cases of multiple lesions (fig. 4). Conversely, our data do not support a central location as a hallmark of primary CNS lymphoma (figs. 5 and 6).

In our series, the finding of 13% of the lesions in the posterior fossa is slightly higher than the overall average of 8% noted by Valavanis et al. [11].

Our data also differ from the existing CT literature with regard to lesion multiplicity [1, 5, 6]. Eleven percent of our patients had more than one lesion (including one with multiple subependymal nodules). Spillane et al. [1], however, cited a multiplicity rate of 30%; Enzmann et al. [5], 43%; and Mendenhall et al. [6], 50%. Our data suggest a need to deemphasize multiplicity as characteristic of primary CNS lymphoma. Spillane et al. [1] found subependymal spread in three of 20 cases, whereas this finding was only present in one of 28 in our series.

The correct diagnosis appeared as the diagnosis of choice on the CT report in only three (11%) of 28 patients in our series. The efficacy of CT in correctly predicting this diagnosis is therefore quite poor. This has also been noted in previous series [1]. Spillane et al. [1] suggested that, if the lesions are multiple on CT, the scan most often is labeled (incorrectly) metastases. In our series, of the two patients with multiple



Fig. 5.—Pre- (A) and post- (B) contrast CT scans of 70-year-old woman. Characteristic location and appearance of peripheral lesion. Tumor nodule is in left temporal white matter, is isodense, and enhances intensely and homogeneously.

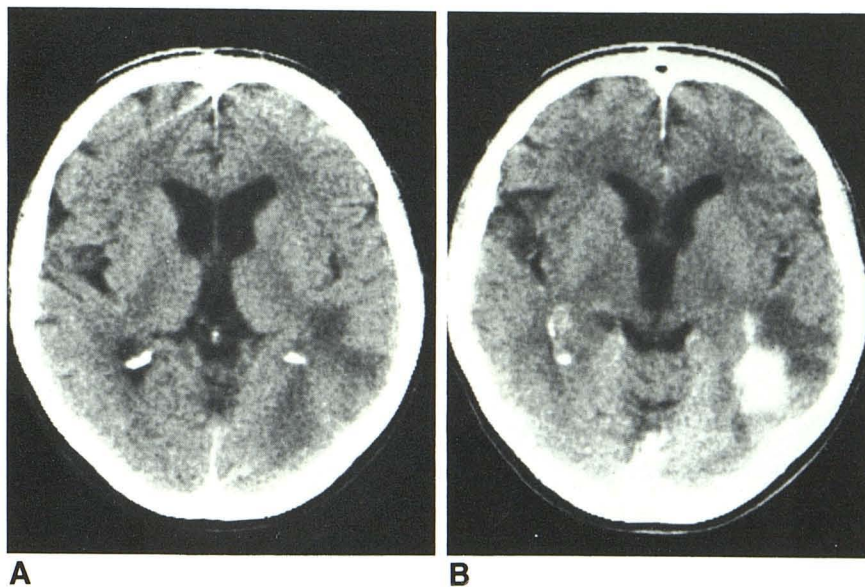
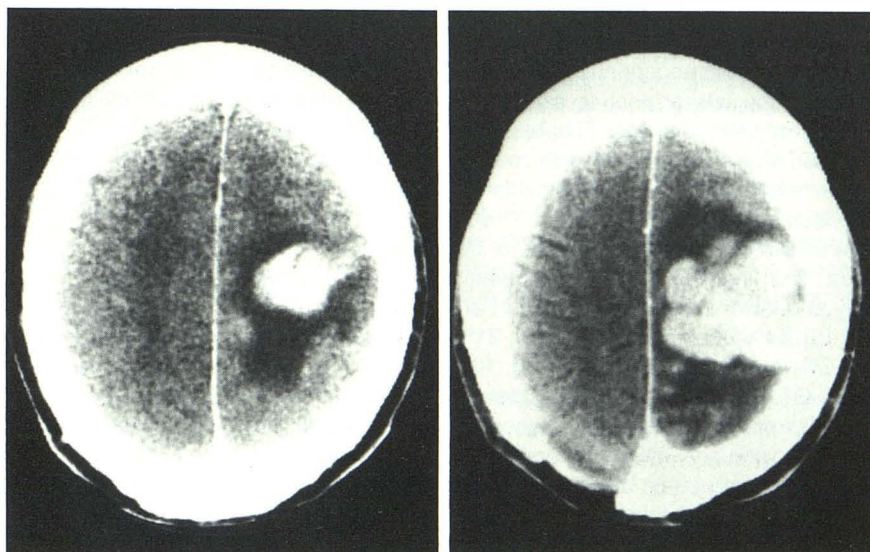


Fig. 6.—Contrast-enhanced CT scans. Intensely and homogeneously enhancing peripheral lesions.



lesions, one was diagnosed as having metastases and the other as having lymphoma. The patient with diffuse subependymal spread of tumor was misdiagnosed as having a germinoma. Spillane et al. [1] also suggested that the most common misdiagnosis for a solitary lesion is meningioma, whereas in our series these lesions were most often labeled tumor. Enzmann et al. [5] stated that primary CNS lymphoma in immunosuppressed patients is most often misdiagnosed by CT as abscess. In our series, two of the three immunosuppressed patients were diagnosed as having glioma and one as having meningioma. The two patients in our series with noncortical lesions who were misdiagnosed as having meningioma were studied on early-generation CT scanners. Presumably, the lesions were believed to be intraventricular meningiomas at the time of preoperative CT interpretation. Based on the operative report, the two lesions were subsequently assigned to the deep and white matter locations when reviewed for this study. The third tumor misdiagnosed as a meningioma was cortical in location and presumably was

believed to be extraaxial at the time of preoperative interpretation.

Twenty-five (81%) of our 31 cases displayed a mass effect angiographically. This compares with 100% (14 of 14) in the Kishikawa et al. [13] series. Prominent medullary veins were found in five of 31 lesions in our series, in one of 10 in the series of Spillane et al. [1], and in five of 14 in the series of Kishikawa et al. Arterial encasement was described as a hallmark of primary CNS lymphoma by Leeds et al. [14] and has been mentioned in other series: Spillane et al. [1], one of 10; Enzmann et al. [5], one of seven; and Kishikawa et al. [13], four of 14. This finding was rare in our series, being present in only two of 31 lesions. Dural arterial supply was described in one of 10 cases by Spillane et al. [1]; none of our cases demonstrated this finding. Arteriovenous shunting was not seen in any of our cases. Tumor neovascularity was seen in three of 31 cases in our series and in two of 14 cases in the Kishikawa et al. [13] series. The only characteristic angiographic finding of primary CNS lymphoma in our series



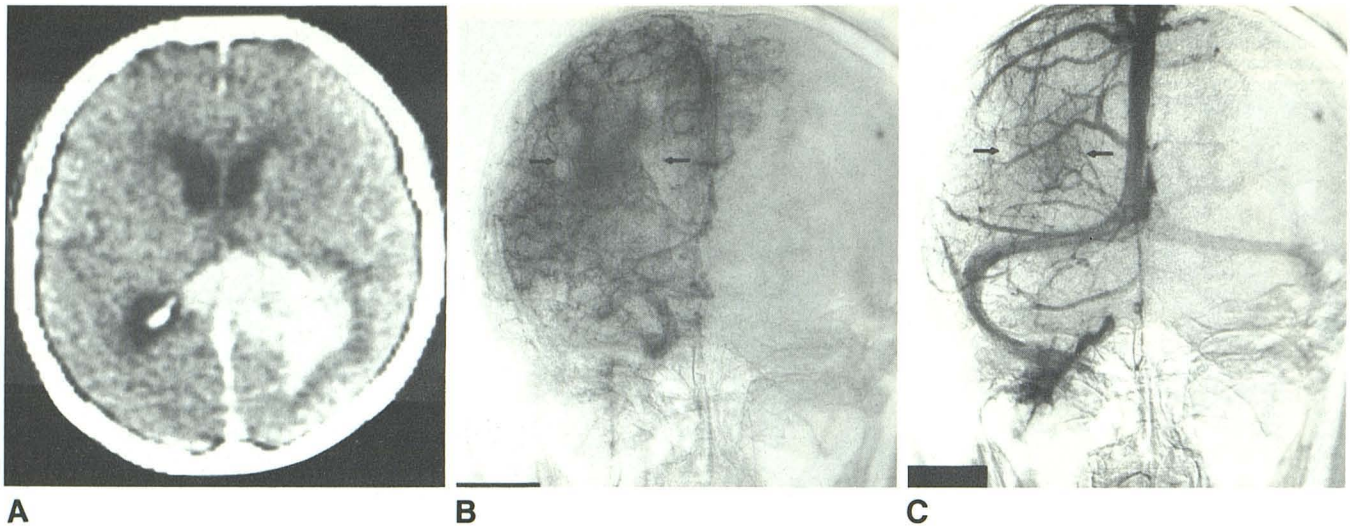


Fig. 7.—CT and angiographic findings characteristic of primary lymphoma of central nervous system in 72-year-old woman. A, CT scan. Large, enhancing right temporal lesion involves splenium of corpus callosum. Angiographically,

lesion demonstrates diffuse homogeneous cloudlike stain (B, arrows) that persists into venous phase (C, arrows).

was a diffuse, homogeneous, cloudlike tumor stain that appeared in the late arterial or capillary phase and persisted through the venous phase. This blush had the same appearance commonly associated with meningiomas, except that the vascular supply was intraaxial in all cases (fig. 1). This was demonstrated in 12 (39%) of 31 cases in our series and required film-subtraction technique for demonstration in most cases. This finding has been described previously, but generally at a lower incidence: Spillane et al. [1], 30%; Enzmann et al. [5], 14%; Kishikawa et al. [13], 21%; Schaumburg et al. [15], 7%; and Gunderson et al. [16], 100%.

Our CT and angiographic studies indicate that neither method alone will consistently demonstrate findings that are specific for primary CNS lymphoma. However, our data suggest that a combination of CT and angiographic findings may be characteristic of this entity. Angiographically, the lesion should demonstrate the diffuse vascular staining pattern described above. The lesion on CT should be unifocal, large, well defined, dense, homogeneously enhancing, and surrounded by a prominent zone of edema (fig. 7).

Both Tallroth et al. [3] and Radvany and Levine [10] stated that a combination of CT and angiographic findings is characteristic of primary CNS lymphoma, whereas Spillane et al. [1] and Enzmann et al. [5] cited characteristic CT findings and found that angiography was not useful.

The one MR examination of a primary CNS lymphoma in our series did not demonstrate any specific findings. Prolongation of T2 relaxation time in and around most CNS tumors and other lesions has been well documented in the literature [17, 18].

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