Primary intracranial CNS lymphoma: MR manifestations.

B W Schwaighofer, J R Hesselink, G A Press, R L Wolf, M E Healy and D P Berthoty

AJNR Am J Neuroradiol 1989, 10 (4) 725-729
http://www.ajnr.org/content/10/4/725

Primary Intracranial CNS Lymphoma: MR Manifestations

Bernhard W. Schwaighofer[1]
John R. Hesselink[1]
Gary A. Press[1]
Ronald L. Wolf[1]
Mark E. Healy[2]
Dean P. Berthoty[1]

We reviewed MR scans of 10 patients with biopsy-proved primary CNS lymphoma. Twenty-five lesions were identified in 10 patients (four with AIDS and six without AIDS). In general, the typical lesion of CNS lymphoma was found to have the following MR characteristics: they were slightly hypointense on T1-weighted images and slightly hyperintense on proton density and T2-weighted images relative to gray matter; they induced mild edema and mild to moderate mass effect. In AIDS patients, 82% of the lesions were smaller than 2 cm in diameter, and were frequently located in the temporal lobes and basal ganglia; they were often multiple. In non-AIDS patients, 75% of the lesions were larger than 2 cm in diameter and were primarily found in the deep parietal lobe; most were solitary.

Primary CNS lymphoma is a relatively rare occurrence and, despite the recent increase in AIDS patients, it represents less than 1.5% of all CNS neoplasms [1–3]. Hodgkin disease rarely involves the brain; parenchymal intracranial lymphomas are almost exclusively non-Hodgkin lymphoma [1, 3]. The CT appearance of CNS parenchymal lymphoma has been well described [1, 3–8]. In general, CNS lesions are isodense or hyperdense on noncontrast CT relative to gray matter, and they enhance homogeneously after IV injection of contrast medium.

MR imaging is an effective method for demonstrating a variety of intracranial abnormalities and provides superior contrast resolution to CT. The literature includes only a few references to intracranial lymphoma visualized with MR [9–12]. The described signal intensities of these lesions range from hypo- to isointense relative to gray matter on T1-weighted images and intensity is even more variable on T2-weighted images. This article describes more fully the spectrum of MR findings in primary CNS lymphoma.

Subjects and Methods

We evaluated 10 patients with biopsy-proved primary CNS lymphoma (Table 1). The age range was 24–69 years old (mean, 49); there were two women and eight men. None of the patients had undergone either radio- or chemotherapy at the time of MR study. Of the 10 patients, four had follow-up studies after therapy was initiated (one of the four patients was studied five times). For these four patients, treatment after the initial study involved three courses of chemotherapy (methotrexate) and external-beam, whole-brain irradiation (4500–6000 rads).

Four patients presented with AIDS; the remaining six patients had no preexisting immunocompromising disease. In all patients, the CSF titers and stereotactic brain biopsy were negative for infectious diseases. Although the negative CSF and brain biopsy do not entirely exclude the coexistence of lymphoma with an opportunistic fungal, viral, or protozoan infection, there was no clinical or laboratory evidence to suggest dual pathologies. In patients with one lesion, the shortest and safest pathway for stereotactic biopsy was chosen. In the four patients with multiple lesions, only the lesion most easily reached was biopsied. Biopsy sites included the parietal, temporal, frontal, or occipital lobe; basal ganglia; thalamus;

Received September 15, 1988; revision requested November 9, 1988; revision received December 29, 1988; accepted January 5, 1989.

Dr. Schwaighofer is supported in part by fellowship J0283M (Erwin Schroedinger Stipendium), Austria.

[1] Department of Radiology and Magnetic Resonance Institute, University of California, San Diego, Medical Center, 225 Dickinson St., San Diego, CA 92103-1990. Address reprint requests to J. R. Hesselink.

[2] Mission Regional Imaging, Mission Viejo, CA 92691.

AJNR **10:725–729, July/August 1989**
0195–6108/89/1004–0725

TABLE 1: Patient History and Biopsy Location

Case No.	Age	Gender	Presenting Symptoms	AIDS	Lesions		Lesion Biopsied
					No.	Location	
1	29	M	Dysmetria, lower extremity weakness	Yes	1	Frontal	Frontal
			1 month later		1	Frontal (decreased size)	
2	48	M	Hemiparesis	No	2	Parietal	Parietal
			4 months later		3	Parietal/occipital (increased size)	
3	74	M	Fluent aphasia	No	1	Temporal	Temporal
4	24	F	Visual loss	No	1	Thalamus	Thalamus
5	60	M	Disoriented, decreased equilibrium	No	1	Basal ganglia	Basal ganglia
6	51	M	Cranial nerve (V–X) palsies, cerebellar ataxia	Yes	2	Cerebellum/brainstem	Cerebellum
			3 months later		2	Cerebellum/brainstem (increased size)	
7	58	F	Hemiparesis	No	1	Parietal	Parietal
8	69	M	C3-sensory deficit	No	1	Parietal	Parietal
9	24	M	Nerve palsies	Yes	1	Brainstem	Brainstem
			10 days later		1	Brainstem	
			1 month later		1	Brainstem (decreased size)	
			2 months later		0	0	
			3 months later		0	0	
10	44	M	Hemiparesis/seizures/headaches	Yes	13	Temporal/frontal/thalamus/basal ganglia/cerebellum	Temporal

brainstem; or cerebellum. One biopsy site was chosen for each patient.

MR was performed with a 1.5-T superconducting magnet.* In all cases, spin-echo pulse sequences were used: T2-weighted images were obtained with 2000–3000/70–80/1–2 (TR/TE/excitations) and proton density weighted images were obtained with 2000–3000/20–30/1–2. Axial images were obtained from the foramen magnum to the vertex. Supplemental sagittal views were used for midline lesions. A slice thickness of 5 mm, with a 2.5-mm interval between successive slices, was used in all patients. Axial T1-weighted images (600–800/20) were then obtained in all patients. The slice thickness was 5 mm with a 2.5-mm interval between successive slices in the majority of patients. A 256 × 256 matrix and 20-cm field of view corresponding to a 0.75 × 0.75-mm pixel size was used in all examinations.

The location, size, and number of lesions were noted. The signal intensity of each lesion was described as hyperintense, isointense, or hypointense relative to gray matter. We also performed a comparative analysis to judge the ability of each of the three different sequences (T2-weighted, proton density, and T1-weighted) to detect the lesion, to characterize it, and to define its relationship to other brain structures. Mass effect was graded on all sequences as mild, moderate, or marked. We classified edema in this manner as well: mild edema = less than a 1-cm rim, moderate edema = a 1–2-cm rim, and marked edema = greater than a 2-cm rim. The internal texture of each lesion was labeled as homogeneous or heterogeneous.

* General Electric, Milwaukee, WI.

Results

A summary of the MR observations is given in Table 2. Twenty-five lesions were identified in 10 patients (six without AIDS and four with AIDS). Seven patients had only one lesion. One patient had two lesions, one had three, and one had 13 lesions. The majority of the lesions (19, or 76%) were periventricular or in the basal ganglia. Two lesions (8%) were located in the brainstem, and two were in the cerebellum. One (4%) of the remaining lesions was in the cortex, and the other was located at the corticomedullary junction. The temporal lobes and basal ganglia were the most common sites in the AIDS patients, and the parietal lobe was the most common location in the non-AIDS patients. In AIDS patients, the masses were smaller than 2 cm in 82%, while in non-AIDS patients lesion size was greater than 2 cm in 75% (Figs. 1 and 2).

On T2- and proton density weighted images, four of the tumors were hyperintense, 17 were slightly hyperintense, and four were isointense. On T1-weighted images, two lesions were hypointense, 21 were slightly hypointense, and two were isointense. Nine (36%) lesions were homogeneous and

TABLE 2: MR Characteristics of Primary CNS Lymphoma

	Patients Without AIDS ($n = 6$)	Patients with AIDS ($n = 4$)
Number of lesions	8	17
Multiplicity	1	3
Location		
Frontal lobe		2
Parietal lobe	4	
Temporal lobe	1	3
Occipital lobe	1	
Basal ganglia	1	6
Insula		1
Thalamus	1	1
Brainstem		2
Cerebellum		2
Size (cm)		
<2	2	14
2–5	5	3
>5	1	
Signal intensity		
T2-weighted and proton density		
Hyperintense	2	2
Slightly hyperintense	4	12
Isointense	2	3
T1-weighted		
Hypointense	1	1
Slightly hypointense	6	15
Isointense	1	1
Homogeneous		
Yes	3	6
No	5	11
Edema		
Mild (<1 cm)	5	14
Moderate (1–2 cm)	2	3
Marked (>2 cm)	1	
Mass effect		
Mild		3
Moderate	6	13
Marked	2	2

16 (64%) were heterogeneous, suggesting areas of necrosis. The isointense masses were detected by the surrounding edema, which appeared as regions of prolonged T2 relaxation time. Marked edema surrounded one of the tumors, moderate edema surrounded five, and 19 had a small rim of edema. In six of these last 19 lesions, it was difficult to distinguish tumor from edema owing to their similar signal intensity. Four lesions caused noticeable mass effect, 18 had minor mass effect, and three had no mass effect. Sixteen of the 25 lesions (64%) showed heterogeneous texture on MR that we interpreted as regions of central necrosis.

Three of the four patients reexamined after treatment had AIDS. Two patients with one lesion each on initial MR study demonstrated a decrease in tumor size on the follow-up studies at 1 month (one patient's lesion disappeared entirely after two months). The other AIDS patient with multiple lesions on initial MR study showed an increase in tumor size, but follow-up study was delayed until 3 months after therapy. The one non-AIDS patient reevaluated 4 months after treatment had an increase in tumor size and an additional lesion.

In all 10 patients the tissue diagnosis was diffuse large-cell lymphoma, a type of non-Hodgkin lymphoma. None of the lesions examined had an associated infectious process histologically.

Discussion

Primary CNS lymphoma is a relatively rare disorder. Controversy has surrounded the origin of primary brain lymphoma, which has also been described as reticulum cell sarcoma, microglioma, periepithelial sarcoma, adventitial sarcoma, plasmacytic myeloma, round cell sarcoma, and reticulohistiocytic granulomatous encephalitis [13–16]. Despite this confusion of terminology, primary CNS lymphoma is now thought to be the counterpart of malignant lymphoma at other sites. There is evidence of increasing incidence in recent years, particularly among immunocompromised patients such as allograft recipients and AIDS patients [5].

In our series the typical MR appearance of primary CNS lymphoma was slightly hypointense on T1-weighted images and slightly hyperintense on proton density and T2-weighted images relative to gray matter. In general, lesions were sharply demarcated, round, oval, or, rarely, gyrallike masses surrounded by a small rim of edema. For the size of the mass we saw characteristically little mass effect on the adjacent structures. Lesions had homogeneous or heterogeneous signal characteristics. Tumor-edema differentiation was more difficult in heterogeneous lesions. Sometimes, T1-weighted sequences were helpful in making this distinction.

In our series, primary CNS lymphoma lesions were multiple or solitary, and were found predominantly in the basal ganglia, periventricular region, and thalamus. Cerebellar and brainstem involvement can also occur (Fig. 3). Differences between AIDS and non-AIDS patients were noted in location and size of lesions: in non-AIDS patients, predominantly large, solitary lesions (75% were greater than 2 cm in diameter) were found, mostly located in the deep white matter of the parietal lobes; in AIDS patients, multiple small lesions (82% were less than 2 cm in diameter) were found, most often in the basal ganglia and temporal lobes. No differences between these groups were seen in the amount of mass effect, edema, and tumor-edema separation.

Although CNS lymphoma has a typical MR appearance, difficulties may arise in differential diagnosis, especially if the lesion is more than slightly hyperintense on T2-weighted images and/or it appears in a cortical or subcortical location. The differential diagnosis of primary CNS lymphoma includes metastasis, infection, primary glial tumor, and, less frequently, meningioma. In differentiating lymphoma from these other possibilities, T2-weighted sequences seem to be most valuable. In our experience, metastatic lesions are more likely to be surrounded by extensive edema and mass effect, whereas lymphoma usually presents with mild edema and mild to moderate mass effect. It is, however, very difficult to differentiate infectious and inflammatory processes from CNS lymphoma, since both may have central necrosis manifest by heterogeneous texture in the lesion [17]. Moreover, opportunistic infections in immunocompromised patients will present with less edema due to a diminished inflammatory response [18]. Thus, differentiation between lymphoma and an infectious process becomes more difficult, and biopsy may

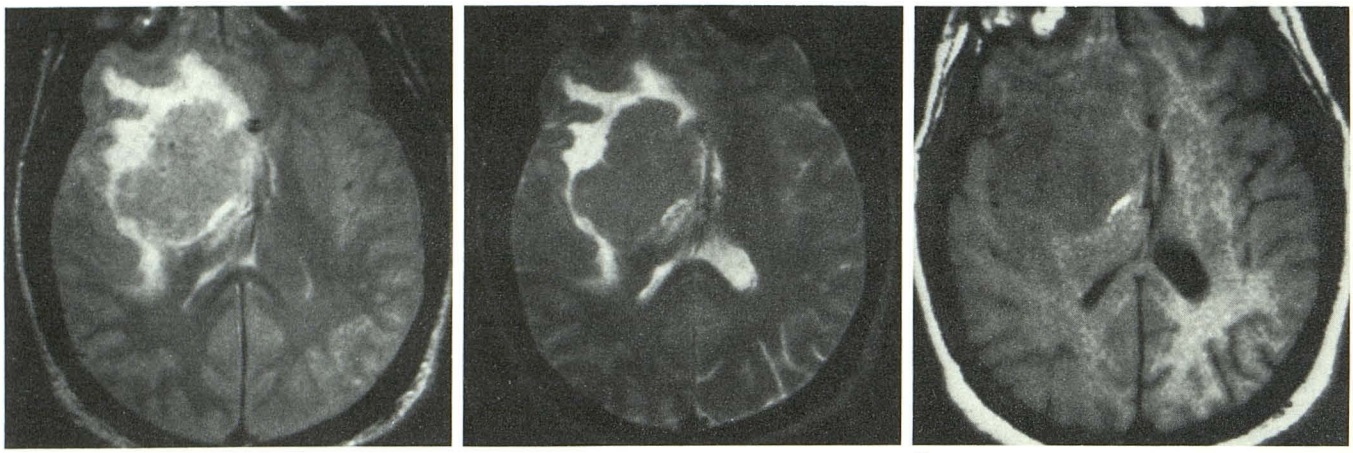

Fig. 1.—*A–C*, Case 5. 60-year-old man with lymphoma in right deep white matter and basal ganglia. Proton density and T2-weighted images, 3000/30, 80 (*A* and *B*), 600/20 (*C*), show a large, slightly hyperintense lesion relative to gray matter with mild edema and mild mass effect for the lesion size. On the T1-weighted image, tumor and edema are slightly hypointense relative to gray matter.

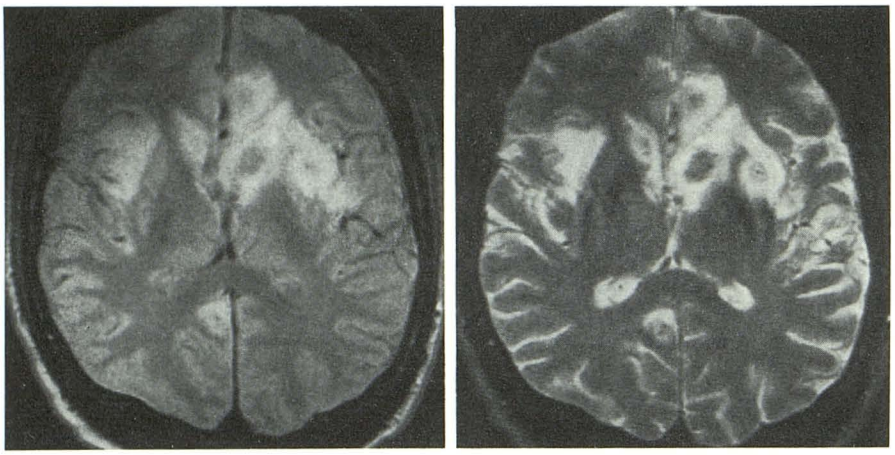

Fig. 2.—*A* and *B*, Case 10. 44-year-old man with AIDS presenting with multiple lesions. Proton density and T2-weighted images (3000/30, 80) show small, slightly hyperintense lesions relative to gray matter with mild edema and mass effect.

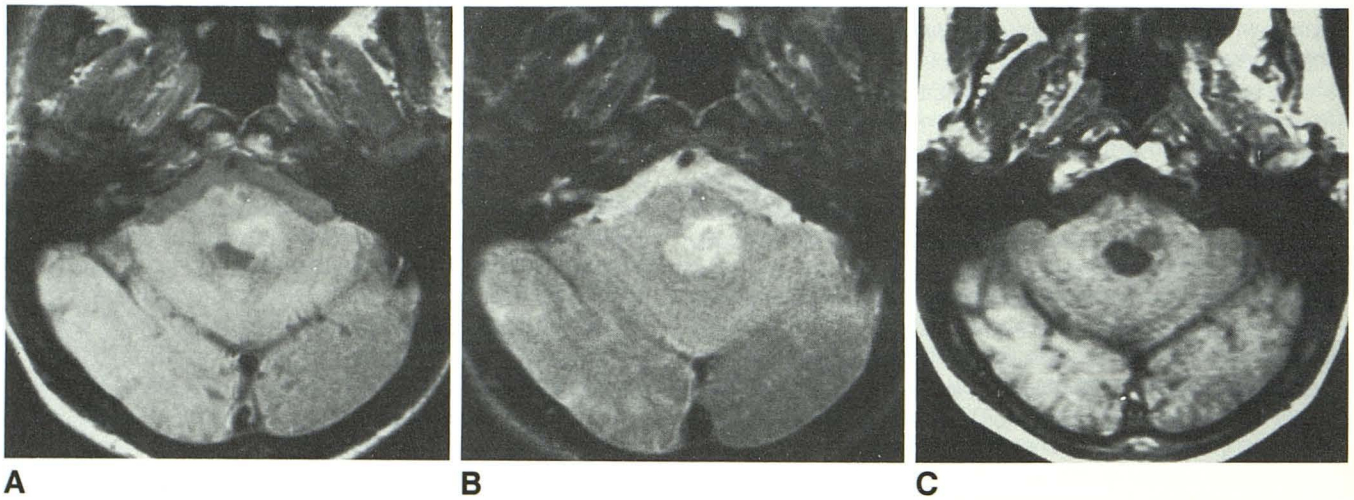

Fig. 3.—*A–C*, Case 6. 51-year-old man with AIDS presenting with a brainstem lesion. Proton density and T2-weighted images 3000/30, 80 (*A* and *B*), 600/20 (*C*), show a small, slightly hyperintense lesion relative to gray matter in left pons with moderate edema and mild mass effect. On the T1-weighted image, tumor appears hypointense relative to gray matter.

be required in such instances. Primary glial tumors generally show more mass effect than lymphoma [10, 12]. Lymphoma, when situated near the surface of the brain, may be difficult to distinguish from meningioma because of their similar MR appearance [10, 12]. However, we encountered no difficulty in differentiating lymphoma from meningioma in our cases, since none of the tumors appeared in a location consistent with meningioma.

In the four patients reexamined after therapy, both patients with multiple lesions on the initial MR study showed an increase in tumor size. These studies were performed 3 and 4 months after therapy and the findings may reflect regrowth of tumor after an initial response. However, both patients who presented with a single lesion showed a decrease in tumor size 1 month after the initial study. In the patients showing a decrease in tumor size, MR was well able to follow the diminishing size of the tumor and edema. The signal intensity of the lesions did not change after radiotherapy. No significant difference in the response of therapy between AIDS and non-AIDS patients was noted, although the number of patients studied was small.

Other neuroradiologic diagnostic procedures have been used for the detection of intracranial lymphoma, including angiography, radionuclide scanning, plain films, and CT. The advantages of MR are its noninvasive nature, high contrast resolution, and multiplanar imaging capability. The latter provides better topographical information and more precise localization for biopsy.

In conclusion, our data indicate that the typical lesion of CNS lymphoma has the following MR characteristics: intracranial lesion, iso- or slightly hyperintense relative to gray matter on proton density or T2-weighted images, minimal mass effect, and mild (less than 1 cm) edema. Nevertheless, in many cases, biopsy for histologic examination may be required for correct diagnosis and appropriate treatment. In patients with multiple lesions, coexistence of infection still cannot be excluded with a single biopsy.

REFERENCES

1. Jack CR, O'Neill PB, Banks PM, Reese DF. Central nervous system lymphoma: histologic types and CT appearance. *Radiology* **1988**;167: 211–215
2. So YT, Beckstead JH, Davis RL. Primary central nervous system lymphoma in acquired immune deficiency syndrome: a clinical and pathological study. *Ann Neurol* **1986**;20:566–572
3. Whelan MA, Kricheff II. Intracranial lymphoma. *Semin Roentgenol* **1984**; 19:91–99
4. Enzmann DR, Kirkorian J, Yorke C, Hayward R. Computed tomography in leptomeningeal spread or tumor. *J Comput Assist Tomogr* **1987**;2: 448–455
5. Lee YY, Bruner JM, Van Tassel P, Libshitz HI. Primary central nervous system lymphoma: CT and pathologic correlation. *AJNR* **1986**;7:599–604
6. Palacios E, Gorelick PB, Gonzalez CF, Fine M. Malignant lymphoma of the nervous system. *J Comput Assist Tomogr* **1982**;6:689–701
7. Whelan MA, Kricheff II. Intracranial lymphoma. *Semin Roentgenol* **1984**;19:91–98
8. Yang PJ, Burt TB, Stricoff DD, Seeger JF. Intracranial non-Hodgkin lymphoma occurring after treatment of Hodgkin disease. *Radiology* **1986**;161:541–543
9. Brant-Zawadzki M, Berry I, Osaki L, Brasch R, Murovic J, Norman D. Gd-DTPA in clinical MR of the brain: 1. intraaxial lesions. *AJNR* **1986**;7:781–788, *AJR* **1986**;147:1223–1230
10. Karnaze MG, Sartor K, Winthrop JD, Gado MH, Hodges FJ III. Suprasellar lesions: evaluation with MR imaging. *Radiology* **1986**;161:77–82
11. McKinstry CS. Intracranial malignant lymphoma. *J Neurosurg* **1987**; 67:476–477
12. Uhlenbrock VD, Beyer HK, Grote W. Kernspintomographie bei Hirntumoren. *Fortschr Roentgenstr* **1985**;143:501–507
13. Yuile CL. Case of primary reticulum cell sarcoma of the brain. *Arch Pathol* **1938**;26:1039–1044
14. Kiey TD, Adams RD. Reticulum cell sarcoma of the brain. *Arch Neurol Psychiatr* **1943**;50:552–564
15. Russell DS, Marshall AHE, Smith FB. Microgliomatosis. *Brain* **1948**;71: 1–15
16. Bailey P. Intracranial sarcomatous tumors of leptomeningeal origin. *Arch Surg* **1929**;18:1359–1402
17. Sze G. Infection and inflammatory diseases. In: Stark DD, Bradley WB Jr, eds. *Magnetic resonance imaging.* St. Louis: Mosby, **1988**:316–353
18. Levy RM, Bredesen DE, Rosenblum ML. Neurological manifestations of the acquired immunodeficiency syndrome (AIDS): experience at UCSF and a review of the literature. *J Neurosurg* **1985**;62:475–495