

# MRI features of primary central nervous system lymphomas at presentation

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**Article abstract**—Pretreatment MRI examinations of 40 immunologically competent patients with primary CNS lymphoma (PCNSL) were evaluated (24 men, 16 women, median age 63 years). Seventy lesions were found (mean size: 19.9 mm). The number of lesions ranged from one (n = 25) to six (n = 1). The most frequent locations were the cerebral hemispheres (n = 22), the corpus callosum (n = 11), and the basal ganglia (n = 11). Cerebellar manifestations were found in 10 patients. Ocular (n = 2) and medullary cord (n = 1) manifestations were rare. Contrast enhancement was encountered in all lesions. Although 39 patients had lesions adjacent to the CSF space, leptomeningeal spread was only present in five patients. Necrosis was seen in two lesions only. Edema was extensive in 24 patients, moderate in 11 patients, and absent in five patients. Contrast-enhancing lesions in contact with the subarachnoid space and without necrosis are characteristic of PCNSL.

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Primary CNS lymphoma (PCNSL) was initially described by Bailey as perivascular sarcoma.<sup>1</sup> PCNSL are B-cell lymphomas in the vast majority of cases. The incidence is 0.43:1,000,000 per year<sup>2</sup> but seems to be increasing.<sup>3</sup> PCNSL constitute between 1 and 6% of malignant tumors of the CNS.<sup>4,5</sup> In recent years, the increasing use of chemotherapy and chemoradiotherapy has significantly increased survival of the patients, compared with the results obtained with radiotherapy alone.<sup>6–10</sup> Because symptomatic patients with PCNSL often present with lesions of considerable size, steroids are frequently administered before a histologic diagnosis has been made, rendering the diagnostic yield of resection or stereotactic biopsy rather low. Recognizing PCNSL by imaging criteria is therefore essential to avoid steroid medication and to facilitate attempts to biopsy rather than resect, which does not improve prognosis. However, few reports have focused on the specific MRI characteristics of PCNSL.<sup>11</sup> Thus, the purpose of this study was to evaluate retrospectively pretreatment MRI in 40 immunocompetent patients in order to delineate the characteristic presenting imaging features of PCNSL.

**Methods.** The archives of two University hospitals (1989 to 2000) were examined for MRI examinations of immunocompetent patients with histologically proven PCNSL. Only examinations performed before the administration of

steroids and before treatment were included. Forty patients (24 men, 16 women, age range 27 to 81 years, mean age 61.3 years) fulfilled the inclusion criteria. All MRI files were evaluated by two neuroradiologists (U.B. and W.K. in Tübingen or T.K. and W.K. in Aachen.). MRI of more than 50 additional patients with PCNSL were not included because the initial MRI was obtained after steroid treatment had been instituted. Imaging was performed on various MR scanners with field strengths from 0.5 to 1.5 T.

All patients were imaged with T2-weighted sequences. Except for one patient, who refused contrast administration, all examinations contained contrast-enhanced T1-weighted scans (0.1 mmol gadolinium–DTPA per kg bodyweight). The MRI were evaluated for lesion location, number, size, contrast enhancement, necrosis, T2 signal intensity, proximity to the subarachnoid space, and edema. Edema was rated as extensive if it exceeded the contrast-enhancing lesion in size, and as moderate if this was not the case. The size of the lesions was measured on contrast-enhanced T1-weighted images. Necrosis was defined as an area within a contrast-enhancing lesion that lacked enhancement, but produced a hyperintense signal on T2-weighted images.

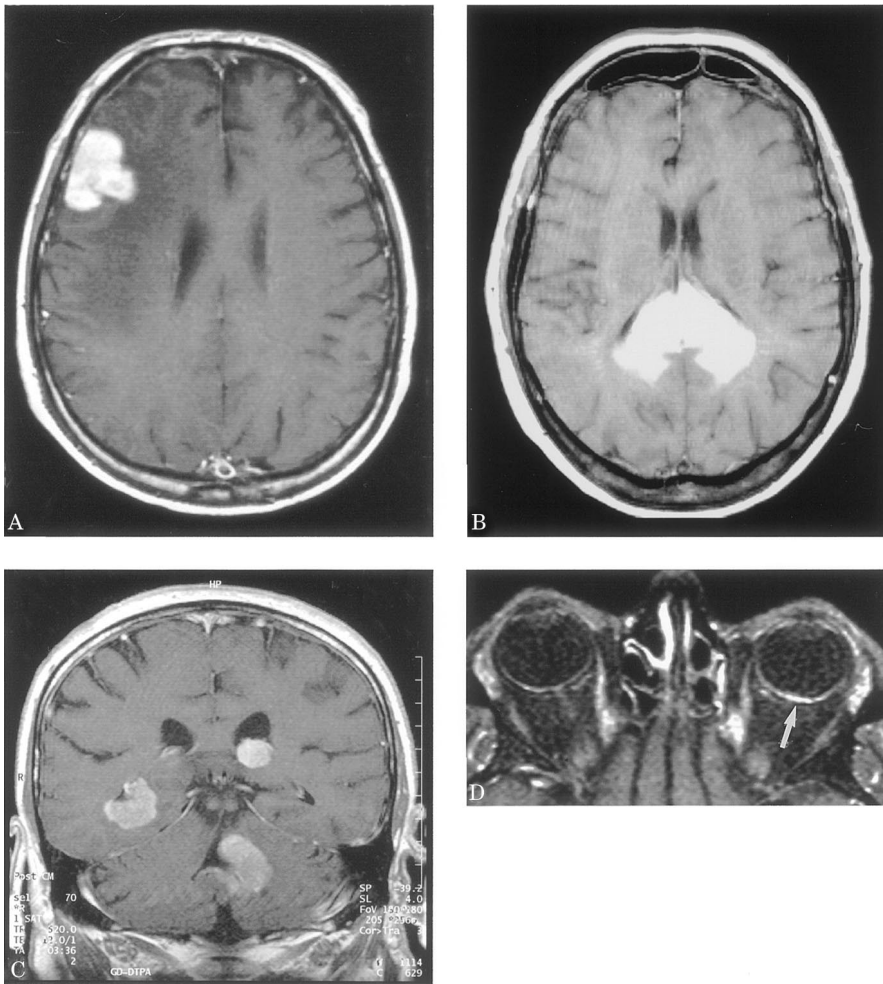
**Results.** The most frequent locations of PCNSL were the cerebral hemispheres (figure, A), followed by the corpus callosum (table). At least one hemispheric lesion was found in 22 of 40 patients. Lesions of the thalamus and basal ganglia occurred in 11 patients, often bilaterally.

Involvement of the corpus callosum was seen in 11 patients (figure, B). Cerebellar infiltration was found in 10

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*Figure. MRI features of primary cerebral lymphoma. (A) Typical hemispheric lymphoma with extensive perifocal edema. T1-weighted image after contrast administration. The lymphoma shows strong, homogenous enhancement without necrosis. It is indistinguishable from other intracerebral pathology such as metastases, glioma, or inflammation. (B) Typical lymphoma of the splenium. T1-weighted image after contrast administration. Strong homogenous enhancement of the splenic lymphoma. This is a rather characteristic finding of cerebral lymphoma. (C) T1-weighted image after contrast administration. Multiple lesions are visible in the cerebellum and the lateral ventricles. (D) T1-weighted image after contrast administration and fat suppression. Ophthalmic lymphoma of the left eye. The only imaging sign is a slight enhancement at the dorsal circumference of the left bulbus (arrow). The picture resembles uveitis. The diagnosis was confirmed by vitreal biopsy.*

patients (figure, C). Ocular involvement initially mistaken as uveitis was seen in two cases. In one patient, an increased enhancement of the dorsal bulbus was identified by MRI (figure, D)—to our knowledge, the first MRI description of an ocular lymphoma. One patient presented with a primary lymphoma of the cervical spinal cord.

The number of lesions was variable. A single lesion was

found in 25 patients (62.5%). The other patients had multiple manifestations of PCNSL already at presentation (37.5%).

The maximum number of manifestations was six. Leptomeningeal spread was found in five patients on MRI (12.5%). However, 37 patients had lesions adjacent to the subarachnoid space (97.5%). At least one periventricular lesion was detected in 24 patients. A deep manifestation without surface contact was seen only once.

Contrast enhancement was strong in 37 patients (92.5%) and moderate in two patients. Contrast injection was refused by one patient. Edema was rated in relation to the size of the contrast-enhancing lesion on T1-weighted imaging. The extent of edema was determined on T2-weighted images. Extensive edema was seen in 24 patients (60%) and moderate edema in 11 patients (27.5%). No edema was found in 5 patients (12.5%). Mass effect of PCNSL was mostly attributable to edema and not to the lesion itself. The extent of edema did not depend on the localization of the lesion. Hydrocephalus was not encountered. Necrosis was seen in two patients (5%).

The mean size of all lesions at the time of diagnosis was 19.9 mm (range 2 to 50 mm).

The signal intensity of the lesions on T2-weighted images was variable. The lesions were uniformly hyperintense in 6 patients and hypointense in 13 patients, compared with normal white matter. The PCNSL manifestations were heterogeneous in signal intensity in 21 patients. No interrelations among location, edema, contrast

**Table** Location, size, and number of primary CNS lymphoma primary manifestations

Location	Lesions, n (%)	Mean (range) size, mm
Hemispheric	22 (31.4)	5 (5–40)
Centrum semiovale (deep)	1 (1.4)	5 (5)
Corpus callosum	11 (15.7)	29.7 (2–50)
Basal ganglia and thalamus	11 (15.7)	15.4 (3–40)
Infundibulum	2 (2.9)	7.5 (5–10)
Ventricle	6 (8.6)	19.1 (6–30)
Brainstem	4 (5.7)	6 (4–10)
Cerebellar	10 (14.3)	20 (5–40)
Spinal cord	1 (1.4)	20 (20)
Eye	2 (2.9)	9 (8–10)
Total	70 (100.0)	19.9

enhancement, or number of lesions were established. Thin section orbital examinations were performed in patients with clinically suspected ocular lymphoma (n = 2) (figure, D).

**Discussion.** The imaging modalities employed for the initial diagnostic workup of PCNSL include contrast-enhanced cranial CT (CCT) and MRI. Imaging signs of PCNSL in CT have been reported.<sup>12</sup> The appearance and diagnostic criteria of PCNSL on MRI have not been documented in larger series of patients before any treatment, including steroids. The largest report on MRI findings in PCNSL included 20 patients, 13 of whom received an IV contrast agent.<sup>11</sup>

Although MRI has been proven to have a better contrast resolution, CT is more readily available and cheaper. Despite the higher costs, most patients with PCNSL are examined by MRI. Reasons to use MRI in these patients include that the diagnosis remained unclear after CT or that MRI was regarded useful for planning a biopsy. Furthermore, MRI is the preferred imaging technique for staging purposes, especially if a spinal manifestation has to be excluded. The sensitivity of MRI for the detection of leptomeningeal disease in lymphoma is lower than in solid tumors and estimated to be around 20%. Therefore, the exclusion of leptomeningeal seeding from PCNSL is not possible with imaging methods alone. CSF analysis after lumbar puncture remains indispensable.

A bulky infiltration of the corpus callosum that is not accompanied by necrosis is suggestive of PCNSL. Gross callosal infiltration without necrosis is rarely encountered in other forms of pathology. However, this imaging feature was present only in a minority of patients in our series. Basal ganglia involvement by PCNSL is a frequent finding. It has been reported as the cause of a movement disorder<sup>13</sup> but is often asymptomatic.

The high incidence of cerebellar involvement in our patients was somewhat surprising because supratentorial rather than infratentorial lesions are commonly considered typical of PCNSL. The percentage found in this study is higher than in other series.<sup>11</sup> Cerebellar involvement is not associated with a higher percentage of hydrocephalus, as might be suspected.

Ocular lymphoma may pose a significant diagnostic problem for the clinician as well as for the radiologist. The clinical presentation is mostly steroid-resistant uveitis, and a conclusive diagnosis is commonly impossible without vitreal biopsy. However, ocular lymphomas are real PCNSL and will cause brain infiltration if not properly treated. The largest study on this topic showed cerebral involvement in 23 of 24 patients.<sup>14</sup> In our hospital files, all patients with biopsy-proven ocular lymphoma developed intracerebral lesions or contralateral ocular involvement. However, ocular involvement is difficult to detect with cross-sectional imaging methods. To our knowledge, our figure (D panel) is the first to

show the imaging findings of ocular lymphoma. The imaging presentation of very subtle contrast enhancement may easily be overlooked. In this case, imaging followed clinical suspicion and we would not regard MRI or CT as the appropriate screening modality for ocular lymphoma. Therefore, we do not routinely perform thin section orbital MRI examinations of patients with PCNSL who do not have clinical symptoms suggestive of ocular involvement.

The incidence of medullary cord lymphoma has been estimated at about 1% of PCNSL.<sup>5</sup> Very few cases have been reported in the literature. However, spinal cord lymphoma may occur and must therefore be included in the differential diagnosis of spinal cord neoplasms. Neither characteristic nor specific imaging findings of this disease have been established.

All patients but one had at least one manifestation of the PCNSL that was in contact with the CSF space. This number exceeds prior reports.<sup>11</sup> Therefore, deep location in the brain without CSF contact does not support the diagnosis of PCNSL. Nearly all cases of PCNSL displayed a moderate to strong contrast enhancement. Conversely, necroses are rarely found in patients with PCNSL.

Most lesions were of a considerable size at presentation (mean diameter nearly 20 mm). Therefore, it may be speculated that cerebral infiltration by a lymphoma causes few clinical symptoms unless the tumors are located in sensitive areas such as the infundibular stalk (mean size 7.5 mm). Callosal infiltration without necrosis is the single most specific imaging finding of PCNSL but is only found in a minority of patients.

Differential diagnosis of PCNSL on MRI includes mainly malignant gliomas, metastases, and inflammatory disorders, specifically demyelinating disease. The recognition of characteristic features of PCNSL such as superficial location, contrast enhancement, and absence of necrosis may facilitate a stereotactic procedure before the administration of steroids.

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## NeuroImages

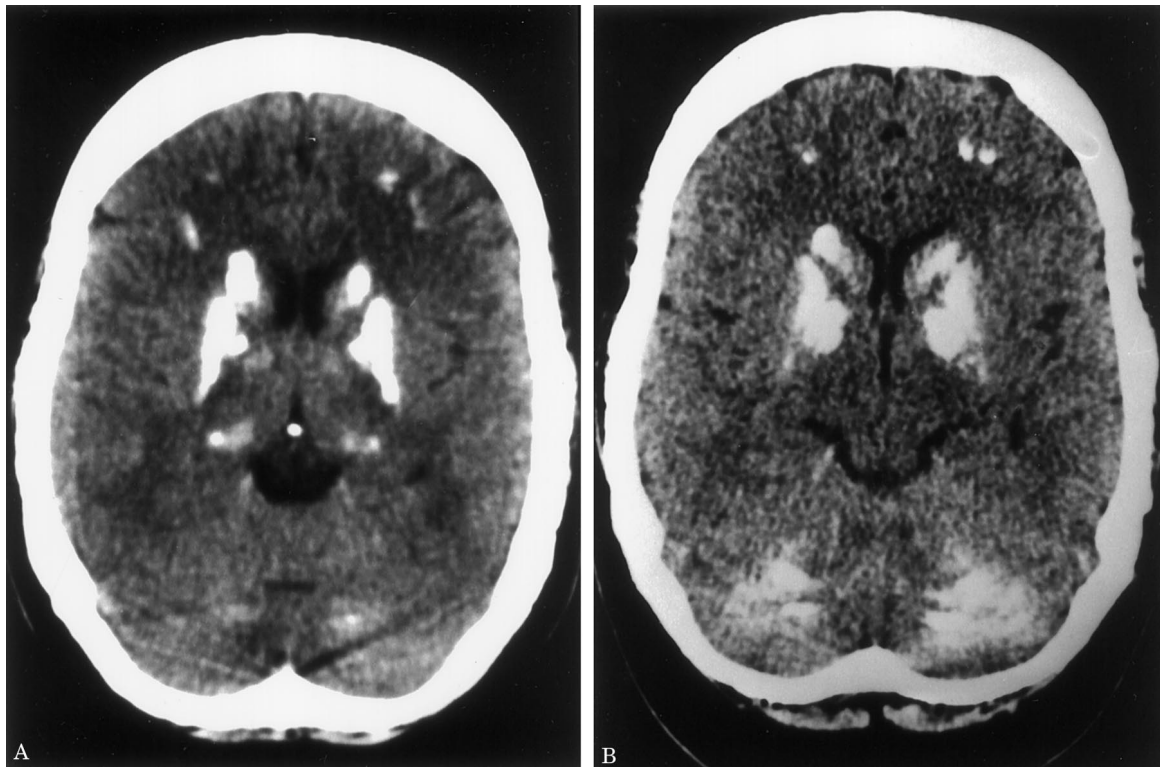


Figure. (A and B) Noncontrast head CT scans show bilaterally symmetric calcifications involving the frontal lobes, basal ganglia, thalami, and cerebellum.

### Symmetric intracerebral calcifications

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A 38-year-old woman with a history of Albright's osteodysplasia, tetany, hypocalcemic coma, and pseudohypoparathyroidism type 1A presented for treatment of epilepsy. In pseudohypoparathyroidism, there is end-organ resistance to the action of parathyroid hormone (PTH) associated with hypocalcemia, hyperphosphatemia, elevated PTH, and mineral deposition in bone and other ectopic sites. Approximately 50% of these patients develop basal ganglia calcifications. Intracerebral bilateral symmetric calcifications can be seen in this and other disorders of calcium

metabolism, and in other unrelated disorders.<sup>1</sup> Commonly affected areas are the globus pallidus, caudate nucleus, putamen, thalamus, dentate nucleus, and cerebral gray matter (figure).<sup>2</sup> The extent of calcifications has not been shown to correlate with the duration of metabolic disease or serum calcium, but in idiopathic cases seems to be related to age.<sup>1,2</sup>

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