Cerebral lymphoma: clinical radiological correlation

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SUMMARY Twenty patients with primary malignant lymphoma of the brain are described. This tumour tends to involve deep, central structures with subependymal spread and there is a high incidence (30%) of multifocal disease. Many cases present a clinical picture suggesting the location and by inference the possible nature of the tumour: early mental change, somnolence and headache are prominent. In the case of a solitary lymphoma, the computed tomographic appearance is sometimes similar to that of a meningioma whereas, in multifocal disease, confusion with metastases is almost invariable. With CT, it should be possible to reduce the frequency of misdiagnosis, and thus avoid overlooking a potentially radiosensitive lesion.

Primary tumours of the brain may be classified broadly as being of either ectodermal or mesenchymal origin. It is with the diagnosis of the latter, rather than the ectodermal glioma, that this paper is concerned. Until recently, this topic would have introduced great semantic difficulties concerning the use of the terms histiocyte, reticulum cell and microglia; cellular elements of the reticuloendothelial system are present in the brain and, as in other sites, neoplastic proliferation can, and does, occur. Such tumours were previously called histiocytic sarcoma, reticulum cell sarcoma or microglioma,¹⁻⁵ but during the past decade the terms malignant lymphoma or lymphoreticular tumour have been introduced, along with the general classification into Hodgkin's or non-Hodgkin's lymphoma; we will use the terms malignant lymphoma or lymphoreticular tumour.

Whatever the preferred nomenclature, previous series have shown that these are rare tumours, comprising only 0.3-1.5% of all intracranial neoplasms.⁵⁻⁷ However, there is evidence of an increasing incidence in recent years,⁶ some tumours following immunosuppressive therapy associated with renal transplantation.⁸ Although we are not here primarily concerned with intracranial spread from systemic lymphoma, such lesions also are being detected with increasing frequency,⁹⁻¹⁴ particularly in the diffuse non-Hodgkin's variety.¹⁰ The computed tomographic (CT) appearance in such cases have been reported¹⁵ and will be discussed in relation to our own findings.

Previous accounts of primary malignant lymphoma

of the brain have stressed the almost universal failure to make the correct diagnosis before operation.^{1 16-18} It therefore seemed important to determine whether a survey of the clinical features and CT appearances might enable one to improve on this, not least because "the most remarkable clinical feature of the tumours is their response to radiotherapy".¹ Many are multiple^{5 19 20} and so readily confused with metastases; because of the results of this confusion, in particular, it seemed important to decide whether any clinical or radiographic pattern would enable the clinician to recognise the possibility of this diagnosis and so encourage biopsy even in the seemingly "hopeless" case.

Methods

Twenty patients seen at the National Hospitals for Nervous Diseases during the period 1974 to 1979 were thought, as the result of biopsy or autopsy, to have primary malignant lymphoma of the brain. The clinical presentation in all cases was neurological, but in three patients (Cases 4, 5 and 18) the presence of generalised disease subsequently became apparent. The precise terminology in pathological reports varied, and included "primary lymphoreticular tumour", "reticulum cell sarcoma" and "microglioma". The clinical records were reviewed together with the cranial CT scans and other radiological investigations. All CT examinations were performed on EMI 1010 or 5005 scanners. Enhanced scans were made in all but three of 28 examinations, by intravenous injection of 70 ml sodium iothalamate containing 420 mg I/ml immediately prior to scanning.

Results

1 CLINICAL PRESENTATION

The age of the patients ranged from 25 to 80 years

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Table 1

Case	Age, sex	Symptoms						
		Duration	Headache	Fatigue	Cortical	Pyramidal	Fits	Ataxia
1	25 F	4 w	+	+	+	0	+	0
2	54 F	6 m	+	+	0	0	0	+
3	63 F	2 m	0	0	+	+	0	+
4	59 M	2 m	+	0	+	0	+	0
5	39 M	2 m	+	+	+	+	0	0
6	43 M	6 m	+	0	0	0	+	+
7	52 M	4 w	0	† (2 y)	+	+	+	0
8	63 M	2 m	+	0	+	0	0	0
9	64 M	3 m	0	+	+	0	0	0
10	58 F	3 m	+	† (6 m)	+	0	0	+
11	80 M	6 m	+	+	+	0	0	0
12	50 M	3 m	+	0	0	+	0	0
(18 m later)		3 w	+	0	+	0	0	+
13	33 M	2 w	+	0	0	0	0	0
14	73 F	1 m	+	0	0	0	0	0
15	62 F	9 d	0	0	+	+	0	0
16	42 F	4 w	+	0	0	0	0	0
17	52 M	3 m	0	+	+	+	+	+
18	81 M	2 m	0	+	+	0	+	0
19	70 M	4 m	0	0	0	+	0	0
20	69 M	2 w	0	0	+	0	0	+

*These patients are detailed further in table 2.

† = homonymous hemianopia.

Table 2 Patients with abnormal blood or spinal fluid cytology

Case	WBC/mm ³ peripheral blood	Comments	Bone marrow	CSF	Notes
4	17-19,000	85% neutrophil 14% lymphocyte 1% monocyte			Later developed limb root signs suggestive of spinal seeding
5	1974 16-24,000	Myelocytes and toxic granulation	Primitive cells 1% unidentifiable		ESR: 62 mm/h
	1977 25,900	93% neutrophils 7% lymphocytes			After 4500 r to tumour and 2000 r to neuraxis ESR: 12 mm/h
17				Histiocytes and occasional plasma cell	
18		Toxic granulation and shift to left	Large primitive cells probably lymphoid		Liver enzymes persistently elevated

(mean $\pm$ SD = 55.6 $\pm$ 13.6). The duration of neurological history was usually short, varying from only nine days to six months (average nine weeks) except in one patient who may, in retrospect, have been developing memory impairment for two years.

Tables 1-5 summarise the prominent symptoms

Table 3 Symptoms

Symptom	Number
Disturbance of higher function:	13
speech disturbance	5
memory impairment	4
"confusion"	2
dyscalculia	1
visual disturbance	1
Headache	12
Fatigue	9
Weakness	7
Epilepsy	6

Table 4 Physical signs

Sign	Number
Pyramidal weakness	16
Papilloedema	11
Sensory disturbance	5
Dysphasia	5
Homonymous hemianopia	4
Amnesia	4
Global dementia	2

and signs, and the results of blood and cerebrospinal fluid analyses.

Disturbance of higher function and headache were the commonest symptoms. Nine patients (45%) specifically mentioned undue fatigue, which did not appear to signify drowsiness. In one patient (Case 10) the complaint of fatigue preceded the memory disturbance and poor concentration by three months.

Table 1 continued

Signs					Investigations			
Pyramidal	Higher function	Sensory	Ataxia	Papilloedema	ESR mm/h	M bands	CSF protein mg/100 ml	Lymphocytes/mm ³
+	+	0	0	0	26	0	—	—
0	0	+	+	+	19	—	—	—
+	+	0	+	0	10	—	135	8
+	+	0	0	+	11	—	1500	256*
+	+	0	0	+	*	—	116, 180	8*
0	(+)+	0	0	+	—	—	—	—
+	+	0	0	0	20	0	44	3
+	+	0	0	0	—	—	—	—
+	+	0	0	0	4	—	—	—
+	+	+	+	0	—	—	—	—
0	+	0	0	0	26	—	—	—
+	0	0	0	+	2	—	33	9
+	0	0	+	+	6	0	—	—
0	0	0	+	+	33	0	—	—
+	(+)	+	0	0	33	0	—	—
0	+	0	0	+	34	—	—	—
+	(+)	+	0	0	29	—	44	24*
+	+	0	0	+	57	0	210	28*
+	0	+	0	0	—	—	—	—
+	0	0	+	+	2	0	—	—

Table 5 Nine patients with fatigue

Case	Site of lesion
1	Left frontal
2	Right thalamus
5	Corpus callosum and subependymal periventricular
7	Right temporo-parietal and basal ganglia
9	Hypothalamic/suprasellar
10	Right basal ganglia
11	Left thalamus
17	Suprasellar/hypothalamic and basal ganglia
18	Multiple, frontal and parietal

Table 6 Site of lesions of CT

Site	Case numbers	Total
Frontal	1, 4, 15, 18	4
Occipital, parietal and/or temporal	6, 7, 11, 12, 13, 15, 18	7
Basal ganglia/thalamus	7, 10, 17, 2, 11, 12, 19	7
Corpus callosum/septum pellucidum	3, 5, 8, 12, 17	5
Suprasellar/hypothalamic	3, 9, 17, 19	4
Subependymal/periventricular	5, 8, 13	3
Cerebellar	14	1
(Multiple tumours)	7, 11, 12, 13, 15, 18	6)

Seven of the nine patients thus affected proved to have lesions of the basal ganglia, corpus callosum, suprasellar or hypothalamic regions. Two patients (Cases 5 and 8), one of whose tumour was periventricular, also had systemic disease. All three cases with peripheral blood or bone marrow evidence of generalised disease presented with a neurological syndrome. One was subsequently shown to have abnormal cells in the CSF, and an additional patient's spinal fluid was similarly involved but without peripheral blood involvement. Electrophoresis of plasma proteins was performed on seven occasions, but no discrete bands or abnormal protein were found. CSF protein was elevated in four out of seven examinations; excluding the two patients with abnormal cells present, an additional six specimens of CSF revealed a lymphocytosis.

2 COMPUTED TOMOGRAPHY (Tables 6 and 7)

Site: multiple tumours, of which three involved the thalamic/basal ganglia region, were found in 30% of

the cases. Altogether seven patients (36%) exhibited tumours of that region. Another four (20%) were situated in the suprasellar/hypothalamic region (fig 1). The corpus callosum was specifically affected in five cases (25%) (fig 2) and a further three showed subependymal or periventricular spread. One such patient (fig 3) had peripheral blood and bone marrow abnormalities. Thus twelve cases (60%) were shown to have tumours involving deep central structures.

Attenuation: there were 29 separately identifiable tumours in the 20 patients studied. They were well defined, usually with irregular or lobulated edges; in two cases they were smoothly rounded. Only five were isodense before contrast at the first examination. One tumour of initially mixed attenuation (Case 10) became isodense after treatment. Three tumours were of mixed hypodense and isodense attenuation, two were uniformly hypodense and one mixed hypo/hyperdense. The majority, 18 altogether, were

Table 7 CT findings

Case no and interval between repeated CT studies	Location of lesion	Attenuation of lesion	Surrounding oedema	Ventricles			Enhancing characteristics
				Compression	Displacement	Dilatation	
1	Left frontal	Isodense with hypodense centre	++	+	+	0	Enhancement with hypodense centre
2	Right thalamus	Hypodense with isodense ring	++	+	+	+	Irregular ring
3	Suprasellar, genu of corpus callosum	Hyperdense	+	+	0	+	Very dense homogenous
4	Right frontal	Hyperdense	++	+	+	0	Slight, irregular
5	Splenium, septum pellucidum	Hyperdense	++	+	0	+	Contrast not given
3 y 9 m	Supratentorial, subependymal posterior fossa	Hyperdense	++	+	0	+	Uniform
			++	+	+	+	Uniform
6	Left occipital and temporo-parietal, corpus callosum	Mainly hypodense with isodense periphery	+	+	+	0	Irregular ring
7	(i) Right temporo-parietal (ii) Basal ganglia/internal capsule	Hyperdense Hypodense	++ +	0 +	0 +	0 +	Slight
8	Splenium—around trigones and periventricular to anterior horns	Mixed: mainly hyperdense	+++	+	0	+	Marked, homogenous
9	Hypothalamic, suprasellar inferior, frontal, L > R	Homogeneously hyperdense	+++	+	0	+	
10	Right basal ganglia, internal capsule	Mixed: mainly hyperdense	+++	+	+	+	Homogenous, except for centre
16 d	Same, smaller	Mixed: mainly hyperdense	++	+	0	+	As above, less marked
1 m	Smaller again	Isodense	++	0	0	No change	As above, less marked
11	(i) Thalamus, temporal (ii) ?right temporal	Hyperdense Hyperdense	++ ++	+	+	+	Contrast not given
12	(i) Splenium thalamus, posterior parietal and occipital. Possibly multifocal (ii) Right lentiform nucleus	Hyperdense Hypodense	++ 0	+	+	+	Marked
13	Multifocal left and right parietal, left posterior temporal	Hyperdense	+++	+	+	0	Homogenous enhancement of all lesions
4 w	Right craniotomy just visible. Left lesion smaller	Hyperdense	++	+	0	0	Homogenous enhancement of all lesions
2 w	Left lesion bigger	Hyperdense	+++	+	+	0	Homogenous enhancement of all lesions
4 w	Left lesion larger, new lesions around right horn and left frontal horns	Hyperdense	+++	++	++	0	Homogenous enhancement of all lesions
4 w	Craniotomy left parietal						
2 w	Only right temporal and left parieto-temporal remain, small						
14	Right cerebellar hemisphere	Hyperdense	++	+	+	+	No contrast given
15	Multifocal right fronto-parietal	Isodense	+++	+	+	0	Marked, homogenous
16	Right medial temporal	No scan					
17	Suprasellar, hypothalamus, basal ganglia and septum pellucidum	Hyperdense	+++	+	+	0	Irregular, very dense in parts
18	(i) Right frontal (ii) Left parietal	Isodense	0	0	0	0	Dense, homogenous
1 m	Multiple, bilateral nodules	Isodense	0	0	0	0	Dense, homogenous
19	Right thalamus, hypothalamus	Mixed hypo and hyperdense	+	0	0	0	Partial
1 m	Lesions larger	More hyperdense in previous hypodense centres	++	+	0	0	Partial
20	Slight atrophy only						
7 m	Left anterior temporal posterior frontal	Hyperdense	+++	+	+	0	Dense homogenous

Fig 1 (Patient 3). (a) before (b) after intravenous contrast medium. Enhancing tumour in the corpus callosum, septum pellucidum and basal ganglia.

Fig 2 (Patient 8). (a, b) sections through ventricles after intravenous contrast medium. Massive enhancing tumour extending from corpus callosum to surround trigones. Marked perilesional oedema.

hyperdense before contrast enhancement. One large, dense and uniformly enhancing lesion had developed a low attenuation centre when the CT examination was repeated after two weeks because of marked deterioration in the patient's condition (fig 4). Enhancement characteristics: the largest group, 12 tumours, showed dense homogenous enhancement. Two lesions showed ring enhancement (fig 5) and another two, peripheral enhancement with hypodense centres. Irregular or partial enhancement was seen in the remainder. Lesions which were initially hyperdense tended to enhance most strongly. The presence and degree of oedema, the characteristics of the ventricular system and the presence or absence of hydrocephalus are recorded in table 7.

3 ISOTOPE SCANS

Only three radionuclide scans were performed. Two showed non-specific deep uptake or isotope, while the third—a temporal tumour—was normal.

Fig 3 (Patient 5). (a-d) Post-contrast sections following resection of lesion at right trigone (note clips in d) and radiotherapy to the region. An enhancing tumour low in the posterior fossa (a) causes hydrocephalus. The lateral and third ventricles are outlined by enhancing tumour, except in the area previously irradiated. The spared right temporal horn is dilated to a greater degree than its fellow.

4 ANGIOGRAPHY

Ten patients underwent cerebral angiography. A mass was shown in every case, with increased capillary circulation in three, which was derived from dural vessels in one (fig 6). Increased medullary veins were seen in one other case. In Case 3 the anterior cerebral arteries passing through the tumour were smoothly narrowed (fig 7). Bilateral subdural haematomas in Case 11 were probably incidental.

Discussion

Primary lymphoreticular tumours of the brain are rare, but increasing in frequency.^{6 20} Nevertheless, in none of our patients was the correct diagnosis suspected on clinical grounds, nor, at the outset, did the CT opinion improve on this.

It is now well known to oncologists, pathologists and radiotherapists that intracranial, and indeed all nervous system involvement from systemic lymphoma also is becoming commoner.⁹⁻¹⁴ Secondary neurological complications may arise in as many as

Fig 4 (Patient 13). (a) Initial CT; rounded left posterior temporal tumour with surrounding oedema. The choroid plexus is displaced anteriorly (b, c) after intravenous contrast medium: bilateral tumours are seen. (d, e) pre- and post-contrast scans after a sudden deterioration in the patient's clinical state following biopsy of the lesion shown in (c): the larger tumour is now of mixed attenuation and shows less contrast enhancement. Probable central necrosis is also suggested by follow-up examinations after a further two weeks (f, g) and six weeks (h, i). The tumour is, however, enlarging rapidly.

Fig 5 Right thalamic lesion showing marked ring enhancement. (a) before (b) after intravenous contrast medium.

25-30% of patients,⁹ the highest incidence being in diffuse, poorly differentiated disease of non-Hodgkin's type.^{10 11 14} Although meningeal, peri-

vascular, spinal epidural and peripheral nerve spread occurs in the majority, up to 7% can be expected to develop parenchymal lesions of the brain.⁹ With that exception, the picture closely resembles the pattern first seen in leukaemias as new treatments altered the natural history.¹⁰ Secondary nervous system lesions in lymphoma are most likely in patients with long-standing illness and bone marrow involvement.^{9 12 13} But occasionally, neurological manifestations may be predominant at the outset^{9 13} even though the tumour is shown subsequently to be part of generalised disease: our cases 4, 5 and 18 are examples. From the point of view of the neurological presentation, they can be considered alongside the remainder of this group in whom, apparently, the intracranial lesions were primary or isolated. Although the presence of generalised disease was not actively excluded by bone marrow examinations or lymphography in every patient, this does not invalidate the main purpose of

Fig 6 (Patient 16). Dural supply to temporal tumour. Right carotid angiogram (a) arterial phase prominent, tortuous. Meningeal vessels (arrows) arise from the intracavernous internal carotid artery (open arrows) giving rise to a well-defined tumour blush (b).

the study, since no patient was suffering from secondary involvement in the context of previously known disease.

Several workers have written of the clinical presentation of primary brain lymphoma as being dependent entirely on the site and size of the tumour and the way in which it spreads,^{4 19} without remarking upon any pattern of distribution. Sites of predilection reported have included the frontal and temporal lobes or cerebellum,^{1 21} but Abbott and Kernohan in 1943²² already noted a tendency for the tumours to occur deep in the brain. From pathological studies, Jellinger *et al*⁵ again observed some predilection for frontal and temporal lobes, with conspicuous involvement of the basal ganglia (18%)

Fig 7 (Patient 2, cf fig 1). There is marked narrowing of the ascending portion of the anterior cerebral artery (especially marked between the arrows) as it passes through the tumour.

and corpus callosum (8.6%). In their series of 68 cases, 22% were found to have multiple tumours, the proportion ranging from 10% to 43% in other series.^{18 19} Thalamic or basal ganglia involvement is also reported.^{8 23} Most significantly perhaps, Zimmerman noted⁶ a "peculiar predilection" for the septum pellucidum, with the basal ganglia, cerebral lobes, brain stem and cerebellum being the other sites in his 208 autopsies. Half of these cases were primary in the brain. He did not record that the anatomical predisposition differed between the two groups, but also noted the tendency for spread "on and beneath" the ependymal lining. Pathologically, Adams²⁰ confirmed the favoured sites of corpus callosum, fornices and periventricular zones (as well as frontal and temporal lobes and the tendency to multiplicity) but thought that he had "not succeeded in defining a diencephalic-hypothalamic syndrome as would be suggested by the frequent involvement of the wall of the third ventricle".

The mean age in our patients, the male predominance and the duration of history before diagnosis were very similar to those in previous reports.^{1 5 6 20 24 25} As before,⁴ headache was prominent, and in nine cases out of twelve, was accompanied by papilloedema. We would not therefore agree with Hubert⁴ that signs of raised intracranial pressure were rare, so that it is not possible to be certain of the mechanisms underlying the interesting complaint of fatigue. It is, however, well known that mental changes which may include apathy, drowsiness and defects of memory are both prominent and frequent in tumours of the corpus callosum.²⁶ In a

similar manner, somnolence is not uncommon when a tumour invades the thalamic or subthalamic regions,²⁷ presumably due to involvement of the reticular projections destined for the diencephalon. Medial thalamic tumours tend to cause mental deterioration early, whereas more lateral lesions produce hemisensory changes or hemiparesis. In the latter case, the sensory or motor symptoms may appear early, with little disturbance of intracranial pressure. Hemianopic field defects may also be present. In tumours of the thalamic region or corpus callosum, headache is typically an early and prominent symptom; combined with mental symptoms, unaccompanied by other deficit, this suggests a mid-line tumour. Similarly, in tumours of the septum pellucidum,²⁸ memory disturbance without any serious clouding of consciousness tends to develop at an early stage, just as occurs in lesions of the splenium. True disconnection syndromes would enable diagnosis of callosal tumour, and autonomic disturbance suggest a hypothalamic lesion.

Computed tomography showed tumours of such deep, midline structures in 12 cases. Although there was not a perfect correlation, tables 3-5 indicate that the clinical presentation was suggestive in the majority of cases. Thus, headache was early and prominent; basal ganglia, thalamic, callosal, and septal tumours did cause obvious mental change including memory disturbance progressing to dementia; subependymal or periventricular lesions also caused an amnesic state and so did two cases of suprasellar/hypothalamic region tumours. Seven of these twelve cases complained of fatigue, while only two of the remaining eight patients did so. Three of the nine cases with fatigue also exhibited papilloedema; none of the seven other patients with swollen discs complained of fatigue. It would appear that mere raised intracranial pressure alone was not the sole mechanism, although there is no certain way to dissociate raised pressure from the production of such a symptom even in the absence of papilloedema.

Previous reports of CT findings in primary lymphoma of the brain^{16-18, 24} point to both the frequency of multifocal tumours (30-43%) and the incidence of deep, central, lesions. Kazner *et al*,¹⁶ and Tallroth²⁵ found three basal ganglia and one suprasellar tumour in ten patients; Tadmor *et al*,¹⁷ one lesion spreading through the corpus callosum and one basal ganglia tumour; and in fourteen cases, Enzmann *et al*¹⁸ found involvement of the basal ganglia or corpus callosum in all six patients with multiple lesions and also in three of eight patients with solitary tumours. A subacutely developing "psycho-organic syndrome" with "somnolence" was the usual clinical presentation in these patients, but the authors did not emphasise the correlation with

radiological localisation. Similar localisation was also a feature of secondary tumours.¹⁵ The tendency to subependymal spread has been confirmed in several reported cases.^{24, 29}

The conspicuous tendency for the majority of tumours to be of higher attenuation than brain^{16, 17, 24} has been confirmed, although lesions isodense before contrast enhancement were the majority finding in two series.^{18, 25} Some tumours including a few of our own, have been of low attenuation, and others mixed.^{17, 18} Most tumours show striking enhancement. The characteristic perivascular distribution of the cellular infiltrate and presumably close relationship of tumour cells to blood vessels rarely permits the cells to outgrow their blood supply, but the occurrence (especially in Case 10) of lesions with non-enhancing centres may imply that this is not invariably the case. Nevertheless, dense homogenous enhancement is the rule. This may lead to the misdiagnosis of meningioma^{16, 30} as occurred in three of our cases; glioma and metastases were other incorrect suggestions. Kazner *et al*¹⁶ considered the CT appearances to be particularly similar to those of melanoma metastases, medulloblastoma, or, in the case of single suprasellar lesions, pituitary adenoma.

Of meningiomas, those arising in the parasellar, middle fossa, tentorial or sphenoid regions are most likely to be confused with lymphoma. They are both characteristically high density, homogeneously enhancing masses; sometimes there is little surrounding oedema, but nearly two-thirds of our cases exhibited more significant oedema. The high incidence of bone sclerosis renders sphenoid ridge meningiomas less frequently misdiagnosed.³⁰ On the other hand, posterior fossa lymphoma is quite likely to be mistaken for a meningioma.¹⁶ Overall, the particular localisation of most lymphomas and the subacute illness that usually results should combine to make the clinician wary. Those lymphomas that are not characteristically central, or are of mixed density without homogenous enhancement (table 7) simulate the appearance of gliomas. Only biopsy is likely to distinguish them.

More importantly, multifocal tumours, found in 30% of our patients, are invariably misdiagnosed as metastases. The latter, with more than 50% of increased attenuation and two-thirds showing homogenous enhancement³⁰ do share with lymphomas many CT characteristics. The radio-sensitivity of lymphomas, both primary and secondary^{1, 7, 20, 31} is crucial; failure to raise the possibility of lymphoma means, in some cases, not to proceed to biopsy. Early radiotherapy can induce considerably prolonged survival time.^{7, 20, 31} Regression of tumour was documented in cases 10 and 13 of this series (fig 8). Littman and Wang recorded⁷ one

Fig 8 Serial CT studies showing excellent response to radiotherapy (all post-contrast). (a) pre-treatment. (b) after 16 days. (c) after 6 weeks. (d) after 5 months. (Patient 10).

patient alive and working ten years after treatment. A further eight of nineteen patients survived from between three and six years. Although the general impression may be that cerebral lymphoma is a radiosensitive tumour, with some cases of long-term survival, the overall figures indicate a worse prognosis than for extraneural lymphoma.⁷ The five year survival rate is probably comparable to the figures reported for glioblastoma multiforme.⁷

Are there other diagnostic tests? The most helpful adjunct to CT is examination of the CSF.^{13 14 31} Cytocentrifugation is important and there is elevation of protein content and pleocytosis in many cases. Spinal fluid was abnormal in six of seven cases in our series. Our examples (Cases 4, 5, and 18) of generalised disease presenting with a primarily neurological syndrome suggest that more general staging of the process is indicated when CT appearances, CSF and biopsy, when possible, show lymphoma of the brain. None of our seven cases suitably investigated showed abnormal immunoglobulins, as reported by Gunderson and colleagues.³² But these workers were probably correct in suggesting that the association indicated a link between primary lymphoma of brain and generalised, non-Hodgkin's disease. The tumours are morphologically identical³³ although the origin of the isolated intracranial tumour remains uncertain.⁹

Angiography gave no specific clues to the diagnosis; narrowing of arteries, as seen in one case, has been reported previously in this condition³⁴ but is, of course, non-specific.

In conclusion, we suggest that many patients with either isolated lymphoma of the brain or primary intracranial manifestation of systemic disease present a recognisable clinical picture:

(1) tumour tends to involve deep, central, structures such as the corpus callosum, basal ganglia, septum pellucidum and suprasellar region. There is par-

ticular tendency to subependymal spread.

(2) there is a high incidence (30%) of multifocal disease.

(3) the symptoms and signs are in keeping with the typical distribution of lesions, in that early mental change and somnolence are characteristic. Headache is prominent.

(4) the usual CT appearance is, in the case of the solitary tumour, very similar to that of meningioma. The subacute history and particular sites of lymphoma should distinguish between them in the typical example. In multifocal disease, confusion with metastases is almost invariable.

(5) spinal fluid examination, where possible, can provide important information and in certain cases bone marrow samples may show generalised disease. But with the particular aid of the CT scan, it should be possible to reduce greatly on the frequency of misdiagnosis, and thus avoid missing a potentially radio-sensitive lesion. When the diagnosis remains in doubt, biopsy should be performed.

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