Clinical and electroencephalographic data indicative of brain tumours in a seizure population

VELUPILLAY VIGNAENDRA
M.B., B.S., F.R.A.C.P.

C. L. LIM

K. K. NG
M.B., B.S., F.R.C.R.

T. G. LOH
M.B., B.S., M.R.C.P.(Lond.)

Departments of Medicine and Radiology, University Hospital, Kuala Lumpur, Malaysia

Summary

One hundred and two patients suffering from seizures, with focal EEG signs (101 cases) and focal seizure but generalized EEG abnormalities (one case) were divided into tumour (twenty-one cases) and non-tumour (eighty-one cases) groups on the basis of contrast radiological studies. Retrospective analysis of various clinical data and EEG abnormalities, determined before the contrast radiological examinations, showed that the following were statistically significantly different between the two groups in favour of a tumoral aetiology for the seizures: age at onset of fits (>20 years), presence of focal neurological signs and increased intracranial pressure, presence of focal unilateral delta waves without accompanying epileptic discharges, beta asymmetry between the cerebral hemispheres and hyperventilation-induced electrical seizures. A brain scan was a very useful screening test for the detection of a tumoral aetiology for seizures.

Introduction

An epileptic seizure is a common presenting symptom occurring in up to 48% of brain tumours (Rasmussen and Blundell, 1961). Although the nature of the focal seizure might indicate with some accuracy the site of the cerebral lesion (Le Blanc and Rasmussen, 1974) brain tumour is only one among the many possible causes (Robb and McNaughton, 1974). It is well recognized that slow-growing gliomas, especially, can present as seizure problems for years without accompanying evidence of raised intracranial pressure or focal neurological signs (Rasmussen and Blundell, 1961; Gonzalez and Elvidge, 1962; Le Blanc and Rasmussen, 1974). There are several detailed reports on epilepsy in brain tumours (Lurid, 1952; Rasmussen and Blundell, 1961; Gonzalez and Elvidge, 1962; Arseni and

Petrovici, 1971; Le Blanc and Rasmussen, 1974; Ketz, 1974). Nevertheless, the reverse problem of brain tumours in an epileptic population is less well studied (Rasmussen and Blundell, 1961; Le Blanc and Rasmussen, 1974). Similarly, although there are reviews on the EEG in epilepsy (Hess, 1974; Gastaut and Tassinari, 1975) and the EEG in brain tumours (Van Der Drift, 1957; Magnus, Storm Van Leeuwen and Cobb, 1961; Krenkel, 1974; Hess, 1975), opinions differ on the possibility of distinguishing the aetiology of the seizure on the basis of EEG changes (Krenkel, 1974).

This study analyses the clinical data and EEG abnormalities in a seizure population who had undergone definitive contrast radiological studies to enable them to be grouped into tumour and non-tumour categories; and determines those clinical and EEG changes that are significantly different between the two groups.

Materials and methods

There were 102 patients who presented as seizures. Of these, 101 demonstrated focal EEG abnormalities (slow wave focus, epileptic focus or both) and one who had generalized EEG abnormalities was included in this study as her seizures consisted of temporal lobe focal attacks. All were subjected to appropriate contrast radiological studies (pneumoencephalograms, carotid angiograms or both) in an effort to rule out the presence of a brain tumour (neoplasm or arteriovenous malformation). Two groups of patients were thus defined, namely, group 1 with neoplasms (seventeen cases) and arteriovenous malformation (four cases) and group 2 who had no evidence of neoplasms, arteriovenous malformations (AVM) or other space-occupying lesions. Excluded from this study were patients with brain abscess and seizures as these cases were referred with a tentative diagnosis of brain abscess since they occurred in a clinical setting in which a brain abscess was the likely diagnosis (suppurative otitis media and

Correspondence: Dr V. Vignaendra, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

mastoiditis or cyanotic congenital heart disease, especially Fallot's tetralogy).

The results of clinical evaluation and EEG done just before definitive radiological studies for each patient were those used for this study.

The EEGs were recorded with 16-channel Beckman machines using nineteen scalp electrodes placed according to the international 10–20 system, at a paper speed of 30 mm/sec and time constant of 0.3 second. All EEGs were reviewed retrospectively and the following data were sought: generalized slowing of EEG rhythms, maximum site and severity of focal slow waves and of the epileptic focus, generalized epileptic discharges, beta asymmetry between the two hemispheres and the presence and the site of onset of electrical seizures occurring spontaneously or on hyperventilation. An epileptic discharge was defined as a spike, spike and wave, polyspike and wave, sharp wave or sharp and wave paroxysm.

The relevant clinical data sought in each patient for this study included sex, the age of onset, duration in months and the types of seizure (focal or generalized), presence or absence of headaches and febrile fits in the past, focal neurological signs and evidence of increased intracranial pressure. Patients who had both focal and generalized seizures were grouped under focal fits. Raised intracranial pressure was present if the patient had any of the following: significant headaches and vomiting, papilloedema or evidence on X-ray skull films.

¹¹³In-DTPA brain scans were done in eighty-six patients.

Codes were assigned for the clinical and EEG data and these were transferred to IBM punch cards and the data sorted with the aid of an IBM 82 card sorter. The clinical and EEG variables given under results were tested for significant differences between the two groups using the χ^2 test of statistical significance.

Results

In group 1 (twenty-one patients) there were nine astrocytomas, five meningiomas, one oligodendroglioma, one glioblastoma multiforme and four AVMs; one patient with an avascular tumour was not operated upon. There were twelve males and nine females. Their age at onset of seizure ranged from 19 to 76 years (mean, 36.52 years; s.d., 12.7 years). Before presentation, fits occurred during periods ranging from 3 months to 20 years, with an average of 4 years. Twenty patients had brain scans and these were positive in thirteen (65%); they included five astrocytomas, four meningiomas and four AVMs.

Group 2 included eighty-one patients of whom thirty-one were male and fifty female. Their age at

onset of episodes of fits ranged from 1 to 57 years (mean, 22.74 years; s.d., 13.18 years). The duration of periods during which their fits occurred ranged from 1 month to 30 years with an average of 5.9 years. Sixty-six patients had brain scans of whom only one was positive; this was a patient with an occlusive stroke demonstrated on a carotid angiogram.

The following clinical variables were tested for significant differences between the two groups of patients: age at onset of seizures, duration of episodes in months, type of clinical seizure, febrile fits, headaches, focal neurological signs and evidence of increased intracranial pressure. As seen from Table 1 age was a significant factor that distinguished the two groups, as the incidence of tumours in those in whom fits occurred below the age of 20 years was very low. In addition, the presence of focal neurological signs and raised intracranial pressure were significantly in favour of the tumour group ($P < 0.01$).

The EEGs were initially categorized into twenty mutually exclusive focal EEG patterns. As there were too few cases belonging to certain patterns these were eventually condensed into the groups as shown in Table 2. Unilateral focal delta waves without accompanying epileptic discharges in the tumour group was the only focal EEG variable that was significantly different from the non-tumour group ($P < 0.01$). In addition, beta asymmetry between the two hemispheres, and hyperventilation-induced electrical seizures were significantly commoner in the tumour patients (Table 3, $P < 0.01$). In group 1 patients with beta asymmetry, ten had a unilateral delta focus only, and two had unilateral delta focus with focal epileptic discharges.

A positive brain scan was strongly indicative of a brain tumour (χ^2 , 45.32; $P < 0.01$).

Discussion

The patients in this study were all epileptics encompassing a wide range in the age of onset of their fits. All were suspected of having a focal brain lesion on the basis of (a) focal EEG abnormalities (focal slow waves or focal discharges or both, 101 patients); (b) focal seizure but generalized EEG abnormality (one case).

The incidence of epilepsy in brain tumours (excluding intra-cranial haematomas and brain abscess) increases with the chronicity of the tumour growth (about 70% in astrocytomas and meningiomas and 37% in glioblastoma multiforme—Rasmussen and Blundell, 1961); the seizures are usually focal but less commonly generalized only.

However, in a seizure population, the reported incidence of brain tumours seems dependent on several factors among which are the types of seizure,

TABLE 1. Clinical variables

Clinical data	Tumour patients	Non-tumour patients	χ^2 value	d.f.
Age of onset of fits				
< 20 years	1	40		
20 years and above	20	41	13.81	1
Focal neurological signs				
Present	11	10		
Absent	10	71	16.37	1
Raised intracranial pressure				
Present	2	0		
Absent	19	81	7.91	1
Duration of fits (years)				
< 5	14	55		
5-10	4	12		
> 10	3	14	0.29	2
Type of seizure				
Focal	15	56		
Generalized	6	25	0.04	1
Febrile fits				
Present	0	9		
Absent	21	72	2.25	1
Headaches				
Present	5	12		
Absent	16	69	0.97	1

TABLE 2. Focal EEG patterns

EEG patterns		Tumour patients	Non-tumour patients	χ^2 value	d.f.
Unilateral focal delta waves without accompanying epileptic discharges	Yes	12	11		
	No	9	70	18.09	1
Unilateral focal epileptic discharges only	Yes	1	14		
	No	20	67	2.09	1
Unilateral focal delta waves + focal epileptic discharges (unilateral or bilateral)	Yes	6	28		
	No	15	53	0.27	1
Bilateral independent focal delta waves + focal epileptic discharges (unilateral or bilateral)	Yes	2	21		
	No	19	60	2.58	1
Bilateral independent focal epileptic discharges only	Yes	0	3		
	No	21	78	0.81	1
Bilateral independent focal delta waves without focal epileptic discharges	Yes	0	3		
	No	21	78	0.81	1

TABLE 3. Other (non-focal) EEG patterns

EEG (non-focal) patterns		Tumour patients	Non-tumour patients	χ^2 value	d.f.
Hyperventilation-induced electrical seizures	Present	4	1		
	Absent	17	80	11.78	1
Beta asymmetry between the two hemispheres	Present	12	11		
	Absent	9	70	18.09	1

age of the patient population, particularly the age at onset of fits, and the special interests of the institution, as in studies on neuropathological specimens obtained at surgery for intractable focal seizures. Thus the incidence of tumours in an epileptic population is given as: 17% for all ages in a population of chronic temporal lobe epileptics (Green, 1967); 20% of patients operated on for chronic intractable focal epilepsy, particularly temporal lobe epilepsy, 80% of whom have astrocytomas and none of whom have evidence of increased intracranial pressure (Rasmussen, 1968); and 9.5% of temporal lobe epileptics, 70% of whom have gliomas and about 80% developed their fits after the age of 25 years (Currie *et al.*, 1971). The incidence of tumours in the present group of investigated patients was 21%.

The age of onset of seizures appeared to be a significant factor in distinguishing the two groups. Similar to the observations of Currie *et al.* (1971) the incidence of tumours in patients who had their fits dating from an age below 20 years was very low. However, the duration of fits, the presence of febrile fits in the past, headache and the type of seizure (whether focal or generalized) did not differ significantly between the two groups. Fischgold and Buisson-Ferey (1961) similarly noted that the type of seizure did not give an indication of the presence of tumour in adult epileptics. The present observations on the duration of fits in the presence of brain tumours is similar to that of Rasmussen and Blundell (1961) and of Gonzalez and Elvidge (1962) who found that astrocytomas can present as seizures for years without evidence of focal neurological signs or raised intracranial pressure. On the other hand, the presence of focal neurological signs and increased intracranial pressure were highly significant in this seizure population in favour of brain tumours.

Despite an extensive literature on the EEG in brain tumours (Van Der Drift, 1957; Magnus, Storm Van Leeuwen and Cobb, 1961; Krenkel, 1974; Hess, 1975) the study, in a seizure population, of those EEG changes that are closely associated with brain tumours has not received equal attention. Rasmussen and Blundell (1961) state that the EEG in epileptics with brain tumours was usually indistinguishable from that obtained in non-tumour focal epileptics and only a small proportion showed focal slow wave abnormalities suggestive of a progressive expanding lesion; typical 3-per-second spike and wave patterns were not associated with brain tumours; however, atypical spike and wave discharges, even though bilateral and synchronous, were found in association with brain tumours particularly in those sited in the frontal and temporal lobes. Fischgold and Buisson-Ferey (1961) mention that EEG contributes to the early diagnosis of

cerebral tumours in seizure patients; however, in 126 adult epileptics, 75% with tumours and 44% without tumours had a delta focus. Nevertheless, these authors do not discuss whether these delta foci occurred alone or in combination with an irritative focus. Oller-Daurella (1975) states that in an adult seizure population the finding of polymorphous focal delta waves raised the possibility of a brain tumour. The detailed EEG analysis of the present study showed that the presence of unilateral focal delta waves without accompanying epileptic discharges in the tumour group was the only focal EEG pattern that was significantly different from the non-tumour patients ($P < 0.01$). Other focal EEG abnormalities which included unilateral focal epileptic discharges, unilateral focal delta waves plus focal epileptic discharges, bilateral independent focal delta waves plus focal epileptic discharges and bilateral independent focal delta waves without epileptic discharges were not by themselves significantly different between the two groups. Nevertheless, there were patients with brain tumours who showed these EEG patterns (Table 2). Hess (1961) similarly suggests that epilepsy is more likely to be of tumoral aetiology if an EEG slow wave focus is not associated with epileptic discharges. Beta asymmetry between the two hemispheres occurred significantly more often in the present tumour group. However, in the patients with tumours and beta asymmetry there was a significant number with unilateral delta focus without interictal epileptic discharges. Surprisingly, hyperventilation-induced electrical seizures occurred significantly more often in the tumour group ($P < 0.01$), especially, in those harbouring astrocytomas (two cases) and arteriovenous malformations (two cases). This latter observation differs somewhat from those of Krenkel (1974) who noted that the activation of an epileptic focus by hyperventilation is a feature of arteriovenous malformations.

Table 4 shows further analysis of the significant clinical variables, namely, age at onset of fits and presence of focal neurological signs and increased intracranial pressure, in the group of patients with unilateral focal delta wave without epileptic discharges. Furthermore, in the group of epileptics having focal neurological signs but without unilateral focal delta waves only, in their EEG the association with brain tumours was significant at the 0.05 level (nine tumour cases, three non-tumour cases; χ^2 , 5.72). It appears that the significant difference between groups 1 and 2 (with unilateral focal delta waves only) is influenced by the presence of focal neurological signs ($P = 0.05$) but not by the age of onset of fits or the presence of raised intracranial pressure.

Indications of brain tumours in a seizure population

TABLE 4. Clinical variables in twenty-three patients with unilateral focal delta waves without epileptic discharges

Clinical data		Tumour (12 patients)	Non-tumour (11 patients)	Total	χ^2 value	d.f.
Age at onset of fits	<20 years	1	4	5	2.65	1
	20 years and above	11	7	18		
Focal neurological signs	Present	9	3	12	5.24	1
	Absent	3	8	11		
Increased intracranial pressure	Present	2	0	2	2.02	1
	Absent	10	11	21		

Brain scans proved a useful test for identifying tumours in the seizure patients ($P<0.01$). Besides meningiomas, brain scans were positive in all those with arteriovenous malformation. McRae (1974) similarly mentions the value of brain scans in identifying meningiomas and arteriovenous malformations. Fischgold and Buisson-Ferey (1961) also found positive brain scans a useful indicator of brain tumours in epileptics.

References

ARSENI, C. & PETROVICI, I.N. (1971) Epilepsy in temporal lobe tumours. *European Neurology*, **5**, 201.

CURRIE, S., HEATHFIELD, K.W.G., HENSON, R.A. & SCOTT, D.F. (1971) Clinical course and prognosis of temporal lobe epilepsy. A survey of 666 patients. *Brain*, **94**, 173.

FISCHGOLD, H. & BUISSON-FEREY, J. (1961) Ambulatory methods of examination of patients with epilepsia tarda. In: *Electroencephalography and Cerebral Tumours* (Ed. by O. Magnus, W. Storm Van Leeuwen and W. A. Cobb). *Electroencephalography and Clinical Neurophysiology*, Supplement 19, pp. 197–203.

GASTAUT, H. & TASSINARI, C.A. (Ed.) (1975) Epilepsies. In: *Handbook of Electroencephalography and Clinical Neurophysiology*, Vol. 13, Part A. Elsevier Scientific Publishing Company, Amsterdam.

GONZALEZ, D. & ELVIDGE, A.R. (1962) On the occurrence of epilepsy caused by astrocytoma of the cerebral hemispheres. *Journal of Neurosurgery*, **19**, 470.

GREEN, J.R. (1967) Temporal lobectomy, with special reference to selection of epileptic patients. *Journal of Neurosurgery*, **26**, 584.

HESS, R. (1961) Significance of EEG—signs for location of cerebral tumours. In: *Electroencephalography and Cerebral Tumours* (Ed. by O. Magnus, W. Storm Van Leeuwen and W. A. Cobb). *Electroencephalography and Clinical Neurophysiology*, Supplement 19, pp. 75–110.

HESS, R. (1974) Electroencephalography. In: *Handbook of Clinical Neurology*, Vol. 15 (Ed. by P. J. Vinken and G. W. Bruyn), pp. 498–532. North-Holland Publishing Company, Amsterdam.

HESS, R. (Ed.) (1975) Brain tumours and other space occupying processes. In: *Handbook of Electroencephalography and Clinical Neurophysiology*, Vol. 14, Part C. Elsevier Scientific Publishing Company, Amsterdam.

KETZ, E. (1974) Brain tumours and epilepsy. In: *Handbook of Clinical Neurology*, Vol. 16 (Ed. by P. J. Vinken and G. W. Bruyn), pp. 254–269. North-Holland Publishing Company, Amsterdam.

KRENKEL, W. (1974) The electroencephalogram in tumors of the brain. In: *Handbook of Clinical Neurology*, Vol. 16 (Ed. by P. J. Vinken and G. W. Bruyn), pp. 418–454. North-Holland Publishing Company, Amsterdam.

LE BLANC, F.E. & RASMUSSEN, T. (1974) Cerebral seizures and brain tumours. In: *Handbook of Clinical Neurology*, Vol. 15 (Ed. by P. J. Vinken and G. W. Bruyn), pp. 295–301. North-Holland Publishing Company, Amsterdam.

LUND, M. (1952) Epilepsy in association with intracranial tumor. *Acta psychiatrica et neurologica scandinavica*, Suppl. 81, 11.

MAGNUS, O., STORM VAN LEEUWEN, W. & COBB, W.A. (1961) Electroencephalography and cerebral tumors. *Electroencephalography and Clinical Neurophysiology*, Suppl. 19.

MCRAE, D.L. (1974) Radiology in epilepsy. In: *Handbook of Clinical Neurology*, Vol. 15 (Ed. by P. J. Vinken and G. W. Bruyn), pp. 533–558. North-Holland Publishing Company, Amsterdam.

OLLER-DAURELLA, L. (1975) The EEG and the evolution of epilepsy. In: *Handbook of Electroencephalography and Clinical Neurophysiology*, Vol. 13, Part A (Ed. by H. Gastaut and C. A. Tassinari), pp. 74–93. Elsevier Scientific Publishing Company, Amsterdam.

RASMUSSEN, T. (1968) The role of surgery in the treatment of focal epilepsy. *Clinical Neurosurgery*, **16**, 288.

RASMUSSEN, T. & BLUNDELL, J. (1961) Epilepsy and brain tumour. *Clinical Neurosurgery*, **7**, 138.

ROBB, P. & MCNAUGHTON, F. (1974) Etiology of epilepsy. In: *Handbook of Clinical Neurology*, Vol. 15 (Ed. by P. J. Vinken and G. W. Bruyn), pp. 271–273. North-Holland Publishing Company, Amsterdam.

VAN DER DRIFT, J.H.A. (1957) *The Significance of Electroencephalography for the Diagnosis and Localization of Cerebral Tumors*, pp. 1–132. H. E. Stenfort Kroese, N. V., Leiden.