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Temporal lobe dysembryoplastic neuroepithelial tumour: significance of discordant interictal spikes

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ABSTRACT – *Purpose:* Dysembryoplastic neuroepithelial tumours (DNET) are an important cause of refractory partial epilepsies. They usually occur within dysplastic cortex and tend to affect the temporal lobes. The EEG of these patients is characterised by slowing and/or epileptiform abnormalities with a multifocal distribution. We studied the EEG features of epilepsy patients with a temporal lobe DNET to assess the relationship of EEG abnormalities with the localisation of the tumour and the clinical features.

Methods: We retrospectively reviewed 16 patients with unilateral, temporal lobe DNET on MRI. The EEG abnormalities were classified as concordant to the lesion when the EEG discharges were confined to the ipsilateral temporal lobe or discordant when EEG discharges were found in other areas. Clinical and epilepsy characteristics were compared between patients with concordant and discordant EEG.

Results: Focal EEG abnormalities were found in 81% of the patients; 6/16 patients had concordant EEG abnormalities, and 7/16 patients had discordant EEG abnormalities. Epilepsy severity prior to the operation, antecedents and post-operative outcome were not different between patients with concordant or discordant EEG abnormalities.

Conclusion: Patients with temporal lobe DNET often show EEG discharges discordant to the tumour. However, they do not appear to predict the clinical and epilepsy characteristics of these patients.

KEY WORDS: DNET, epilepsy, neuroimaging, EEG, temporal lobe epilepsy

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Prof Graeme D Jackson, Brain Research Institute, Neurosciences Building, Austin Health, Heidelberg West, Victoria 3081, Australia. Tel: + (613) 9496 4076 Fax: + (613) 9496 2980 E-mail: BRI@brain.org.au Dysembryoplastic neuroepithelial tumours (DNET) are benign brain tumours with distinctive clinical and pathological features. They represent almost 10% of all tumours removed from patients with intractable partial epilepsy [1]. The term DNET was introduced by Daumas-Duport in 1988, in their review of the histology of 39 patients undergoing surgery for the problem of epilepsy [2]. All these tumours were supratentorial and intracortical, and usually located within dysplastic cortex. In another series, Daumas-Duport reported that 62% of tumours involved the temporal lobe, whereas the frontal lobe was involved in 30% of patients [3].

The neuroimaging features of DNET are described in several reports [4-6]. Low signal intensity on T1-weighted images and high signal intensity on T2-weighted images are the main signal characteristics on MR imaging [4-6]. However, pathological confirmation is still required, as the distinction between DNET, cortical dysgenesis and low grade gliomas is difficult [7, 8]. Today, DNET is listed in the World Health Organization classification of brain tumours, as a neuronal and mixed neuroglial tumour [9]. However, controversy still exists as to whether DNET should be considered as hamartomas [10], and whether they are truly separable from other brain tumours, such as gangliogliomas [10, 11].

The clinical features of DNET patients, presenting at an epilepsy surgery centre, are consistent with refractory partial epilepsy. The patients have early seizure onset, refractory complex partial seizures with or without secondary generalization, and show a normal neurological examination [2]. A DNET is usually associated with an excellent post-operative outcome in terms of seizures and absence of tumour recurrence [11, 12].

The electrophysiological features of DNET are not well described. The electroencephalographic (EEG) pattern of a brain tumour such as a glioma, typically consists of focal theta or delta waves in the region of the tumour, and if epileptic activity is present, it usually arises from areas outside the tumour proper [13]. In contrast, dysplastic cortex has intrinsic epileptogenic properties [14], and the epileptic activity arises from within the lesion. A DNET shares features of both pathologies, and the EEG features may therefore help to understand the epileptogenesis associated with this benign tumour. One study mentioned the presence of multifocal slowing or interictal abnormalities in patients with DNET [12]. It may well be that these multifocal abnormalities indicate the presence of more widespread dysplasia and may be associated with differences in clinical presentation and post-operative followup.

Here, we aim to characterize the clinical and electroencephalographic features of patients with a focal, temporal lobe DNET. In particular, we will determine the frequency of patients with EEG abnormalities not confined to the area of the tumour. Further, we will investigate whether patients with discordant EEG abnormalities differ in their clinical and epilepsy characteristics from patients with concordant EEG abnormalities.

Patients and methods

We retrospectively reviewed the medical files of patients with temporal lobe DNET that were seen at the Comprehensive Epilepsy Program, Austin Health, Melbourne, Australia, between 1990 and 2003. The study group consisted of 16 patients (mean age 32 ± 10 years; ten women and six men). Twelve of theses patients had undergone surgery and in all cases the diagnosis of DNET was histologically confirmed. Of the four patients who were not operated upon, two were not offered surgery as the DNET was located in an area supporting language function, and post-operative language deficits could not be excluded; one patient refused to have surgery and the remaining patient is awaiting surgery.

All patients had a clinical MRI examination, based on a protocol routinely used for patients with partial epilepsy, including T2-weighted images, and a coronal 3D sequence with contiguous slices, with and without administration of gadolinium. The MRI was performed at the Austin Hospital, using a 1.5-Tesla Siemens SP Magnetom system. All patients had an MR diagnosis of a focal, temporal lobe DNET without any other associated abnormalities [15]. The temporal lobe DNET involved the amygdala in three patients (18%), and the hippocampus in two patients (12%).

Clinical evaluation

All available clinical records were analyzed to determine the clinical presentation and epilepsy characteristics. The following characteristics were noted: age at epilepsy onset, age at operation, frequency of complex partial seizures (CPS) and secondary generalization, presence of antecedents, abnormal neurological examination, family history of epilepsy and side of the lesion. Seizure types were identified according to the classification of epileptic seizures and syndromes by the International League Against Epilepsy [16]. Patients were classified as having 'weekly CPS' if they had an average two or more CPS per week in the last two years before surgery or investigation. Patients were classified as having 'secondary generalization' if they had two or more unprovoked, generalized tonic-clonic seizures (GTCS) in the last two years before surgery or investigations. The following events were considered as significant antecedents: severe birth complications, complex febrile convulsions, history of status epilepticus, bacterial meningitis or any encephalitis, and head trauma with loss of consciousness. Simple febrile convulsions were noted as non-significant antecedents. Surgery outcome was classified according to Engel [17].

SD

 (± 11)

81

43

25

6

12

6

12

12

6

76

18

tion, were reviewed in each subject. The interictal EEG DNET patients (n = 16)investigations included routine awake and sleep EEGs. Furthermore, video EEG monitoring including ictal EEG, Mean was available for review in three patients. Both, interictal Onset of seizures (yr) 17 slowing (theta or delta) and epileptiform discharges (spikes Number Percentage % and sharp slow-waves) were classified. Intermittent slow-Weekly seizures # 13 ing was defined as polymorphic slow waves with a fre-Secondary generalized seizures # 7 guency between 0.5 and 3.5 Hz (delta) or between 3.5 Antecedents and 7 Hz (theta); spikes were defined as a transient, dis-- significant 4 tinguished from the background activity, with a duration Birth complications 0 between 20 and 70 ms., and sharp slow-waves were de-Complex febrile convulsions 1 fined as a transient, with a duration between 70 and History of status epilepticus 0 200 ms. The international 10/20 system was used to deter-Head trauma with loss of 2 mine the localisation of any of these three EEG abnormaliconsciousness ties. The EEG evaluation was undertaken by two epilep-Childhood infections 1 tologists (AL, PF), blinded to the localization of the tumour. not significant 2 Subsequently, the EEG abnormalities were compared with simple febrile convulsions 2 the radiological information of DNET localization. All EEG Abnormal neurological examination 0 abnormalities (slowing, spikes and sharp slow-waves) Family history of epilepsy 1 were classified as concordant or discordant to the tumour. Side of lesion 'Concordant' was defined as EEG abnormality ipsilateral – left 13 temporal to the DNET (right temporal DNET: T2, T4, T6, right 3 F8; left temporal DNET: T1, T3, T5, F7), and 'discordant' tion or investigation. investigation.

Table 1. Demographic and clinical data for 16 temporal lobe DNET patients.

number of patients having > 1 CPS/week * before the opera-

‡ number of patients having > 1 GTCS * before the operation or

* In the last two years.

The DNET was localized in the left temporal lobe in 12 (75%) of the 16 patients, and in the right temporal lobe in the remaining four patients.

FEG features

Focal EEG abnormalities were found in 13 (81%) of the 16 patients (table 2). None of these patients had continuous polymorphic or rhythmic slowing. Six patients had EEG abnormalities concordant with the localization of the tumour (MR and EEG of one of these patients is shown in figure 1); one of these six patients had slowing only, and five had both slowing and discharges. Seven patients (54%) had discordant EEG abnormalities. Five of these seven patients had EEG abnormalities in the area of the tumour and in other areas (MR and EEG of one of these patients is shown in figure 2). The abnormalities localised to the tumour consisted of discharges only (three patients), and both slowing and discharges (two patients); the abnormalities distant from the DNET consisted of discharges only (two patients) and both slowing and discharges (four patients). Finally, two patients with discordant EEG abnormalities had abnormalities distant to the DNET only. Both of these patients had discharges.

was defined as EEG abnormality extratemporal (parietal, occipital, or Fp1 or Fp2-electrodes) or contralateral temporal to the DNET. Therefore, a patient with right temporal DNET and slowing, spikes or sharp slow-waves seen only over T2, T4, T6 or F8 would be classified as having concordant EEG abnormalities, whereas if some abnormalities were found to be over T1, T3, T5, F7, Fp1, Fp2, O1, O2, P3 or P4, then this patient would be classified as having discordant EEG abnormalities.

Three or more interictal EEGs acquired prior to the opera-

Assessment of electro-clinical features in relation to the EEG findings

The clinical features were compared between patients with concordant and discordant EEG findings using Student's t-test. Level of significance was set at 5%.

Results

Clinical features

EEG evaluation

All 16 patients had recurrent seizures, refractory to medications, all patients had CPS (table 1). The mean age at seizure onset was 16 years (SD \pm 11), with a range between two and 34 years. The duration of epilepsy before surgery was 13 years (SD \pm 9). Significant antecedents were found in four (25%) of the 16 patients; two had a head trauma with loss of consciousness, one had a prolonged febrile convulsion, and one had a meningoencephalitis during early childhood. The tumour was completely removed in all patients.





Figure 1. Figure shows an EEG sequence (1A) and a representative MR image (1B) of a patient with EEG abnormalities concordant with the localisation of the tumour. The EEG shown was acquired using the international 10-20 system of electrodes placement. It is a bipolar montage. The EEG shows right temporal sharp slow-waves. The figure 1B shows a T2-weighted coronal slice at the level of temporal lobes, acquired at a 3T GE scanner. The DNET is characterized by high signal intensity, and is localised in the right inferior and middle temporal gyri (arrow).

	EEG abnormalities			
Number of patients without EEG abnormality	3 (19%)			
Presence of any EEG abnormality	13 (81%)			
	Concordant	Disc	ordant	
Number of patients	6 (46%)	7 (54%)		
		Only discordant	Discordant + concordant	
– Slowing	1	0	0	
– Slowing + spik	e 5	0	2	
– Spike	0	2	3	

Table 2. Interictal EEG features in 16 patientswith DNET.

Ictal EEG was captured in three patients during inpatient video EEG monitoring. Overall, a total of ten seizures were recorded. Ictal EEG discharges were concordant to the DNET in all three cases. These three cases also had concordant interictal EEG abnormalities.

Electro-clinical association

Patients with concordant and discordant EEG abnormalities were not different in their clinical characteristics (*table 3*). Twelve patients underwent surgery, four with concordant EEG, five with discordant EEG and three without EEG abnormalities. One patient with congruent EEG was lost in the follow-up period; so post-operative outcome could only be compared between three concordant and five discordant subjects. There was no general difference between these patients.

The MR images showed radiological white matter involvement in one of the six patients with concordant EEG abnormalities, and in six of the seven patients with discordant EEG abnormalities.

Discussion

Dysembryoplastic neuroepithelial tumours (DNET) are an important cause of partial epilepsy, refractory to medical treatment [2]. The young age at seizure onset, the presence of bone deformity close to the tumour, and the presence of foci of cortical dysplasia suggested a developmental origin [2, 9]. The DNET usually tend to involve temporal lobes. The clinical findings in our study are similar to previous reports regarding surgically-treated

	Patients with concordant EEG (six patients)	Patients with discordant EEG (seven patients)
Sex (male/female)	1:5	4:3
Onset of seizures (yr)	21 (± 10)	12 (± 9)
Weekly seizures #	5.7 (± 8)	4.5 (± 8)
Antecedents		
Head trauma with loss of consciousness	1 (17%)	1 (12%)
Family history of epilepsy	1 (17%)	0
Side of lesion		
– left	6 (100%)	5 (72%)
– right	0	2 (28%)
Outcome		
Engel 1	2 (34%)	3 (43%)
Engel 2-3	0	0
Engel 4	1 (16%)	2 (28%)
Lost to follow-up	1	
Patients not undergoing surgery	2	2

Table 3. Clinical features in DNET patients with concordant and discordant EEG findings.

See table 1.

DNET patients [2]. EEG findings were reported in one previous study, and were characterized by "slowing or interictal abnormalities with a multifocal distribution, which may affect areas congruent within the tumour, but also contralateral and distant areas" [12].

In our study, we aimed to assess the frequency of discordant EEG abnormalities, and their association with clinical features.

We found that interictal EEG abnormalities are very common in patients with a temporal lobe DNET. Furthermore, these abnormalities were found, in 44% of the patients, in a location discordant to the tumour. As with other brain lesions, we found that slowing (theta or delta) on EEG is often localized to the area of the tumour, while epileptiform discharges were either localized to the lesion or widespread and distant to the tumour. Interestingly, in the three patients with ictal studies the localisation of the ictal EEG abnormalities was similar to the interictal EEG abnormalities. However, the small number does not permit us to draw any general conclusions.

The presence of epileptiform discharges remote to the lesion may suggest the presence of a structural abnormality distant to tumour, such as a second focus of dysplastic tissue. Alternatively, it may reflect a functional abnormality distant to the tumour.





Figure 2. Figure shows an EEG sequence (2A) and a representative MR image (2B) of a patient with EEG abnormalities discordant with the localisation of the tumour. The EEG montage was done as indicated in figure 1. The EEG (figure 2A) shows bifrontal, sharply contoured theta. The MRI image in figure 2B shows a, T2-weighted coronal slice at the level of temporal lobes. The DNET is characterized by high signal intensity on the left antero-mesial temporal lobe (arrow). This patient showed involvement of the amygdala, hippocampus and anterior-inferior part of the insular cortex.

A DNET is often surrounded by dysplastic tissue, and histologically the dysplasia often goes beyond the boundaries of lesion seen on MR [11]. None of our patients had an obvious second abnormality; however, subtle foci of dysplastic tissue outside the DNET may be responsible for the independent interictal discharges. Gloor et al. thought that localized slow intermittent activities could represent abnormalities in the underlying white matter [13]. It is possible that in our population the presence of discharges distant to the DNET is related to such a mechanism. The presence of white matter involvement in the majority of patients with discordant EEG seems to support this hypothesis. Alternatively, the discordant EEG abnormalities may represent functional changes only. Recurrent seizures may induce a functional change in distant areas, as suggested in the animal literature [18, 20].

As a second aim, we investigated the relevance of discordant EEG abnormalities for clinical features. In patients with other epileptogenic pathologies, it has been reported that the presence of EEG abnormalities distant to the lesion [13, 18-20] may predict a more severe epilepsy or poor post-operative outcome. In temporal epilepsy, such as that associated with hippocampal sclerosis (HS) or tumours [21-23], almost 40-50% of patients have interictal epileptiform abnormalities not localized to the lesion [23, 24]. This frequency is in the same range as found for our temporal lobe DNET patients. In HS, bitemporal interictal epileptiform discharges are a predictor for worse outcome [23], and patients with unilateral interictal discharges have a higher likelihood of remaining seizure-free postoperatively. We did not observe this relationship, although our sample was too small to allow definite conclusions. In our sample, we could not detect a general difference in the clinical features between patients with concordant or discordant EEG abnormalities. In particular, the duration of the epilepsy before surgery did not predict post-operative seizure outcome. Overall, the complete excision of the structural lesion appears to be associated with seizurefreedom and good outcome in the vast majority of patients.

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Labate *et al.*

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