

# Atypical Lennox–Gastaut syndrome successfully treated with removal of a parietal dysembryoplastic tumour

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Focal brain lesions may be associated with the atypical form of Lennox–Gastaut syndrome (LGS). We describe a drug resistant LGS patient with daily seizures and a left parietal dysembryoplastic neuroepithelial tumour. Pre-surgical evaluation showed, in addition to diffuse paroxysmal EEG discharges associated with atonic and tonic axial seizures, lateralizing EEG and clinical signs pointing to left hemisphere origin of the seizures. The patient was treated with lesionectomy and after 12 months of follow-up is still seizure free. This case suggests that in patients with LGS and focal lesions the possibility of correct identification of the epileptogenic zone using anatomico-electro-clinical correlations may be the key element for ‘curative’ surgery.

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## INTRODUCTION

Lennox–Gastaut syndrome (LGS) is a ‘catastrophic’ epileptogenic encephalopathy, identified by three sets of signs: (1) generalized seizures, typically axial tonic, atonic (-astatic) and atypical absences; (2) interictal electroencephalogram (EEG) characterized by abnormal, slow background rhythm, diffuse 2–5 Hz spike-and-wave complexes, and paroxysmal fast discharges during sleep; (3) diffuse cognitive dysfunction often associated with personality disorders<sup>1,2</sup>. This syndrome usually develops in early childhood, although onset in early adult life has been described<sup>3</sup>. In one-third of cases the aetiology is unknown (cryptogenic LGS). In the remainder, LGS is related to different genetic and acquired factors, i.e. brain malformations, perinatal hypoxic–ischaemic insults, infections and tuberous sclerosis<sup>2,4</sup>.

Several LGS cases show focal anatomical, clinical or EEG features that constitute an atypical form of the disease. In particular, atypical LGS may be associated with focal brain lesions in the frontal lobes<sup>5,6</sup> although extrafrontal lesions have also been reported<sup>7</sup>.

Epilepsy surgery of LGS generally includes corpus

callosotomy, in an attempt to avoid simultaneous involvement of both hemispheres. This procedure, giving rise to cognitive disturbances, has only been shown to reduce the number of epileptic drop attacks<sup>8,9</sup>. The presence of focal lesions raises the possibility of defining an epileptogenic zone in order to perform ‘curative’ surgery.

We report a case of atypical LGS, studied with video-EEG monitoring, successfully treated with resection of left parietal dysembryoplastic neuroepithelial tumour (DNET). Diagnostic procedures and therapeutic surgical options are discussed.

## CASE REPORT

A right-handed, 19 year-old male, with no family history of epilepsy, born from an uncomplicated pregnancy and delivery and with normal developmental milestones, experienced his first attack at the age of 11 years. Further episodes followed, characterized by: (1) generalized tonic seizures with abrupt loss of consciousness, flexion of the neck associated with bilateral elevation and abduction of the arms and involvement of distal limb muscles (most often

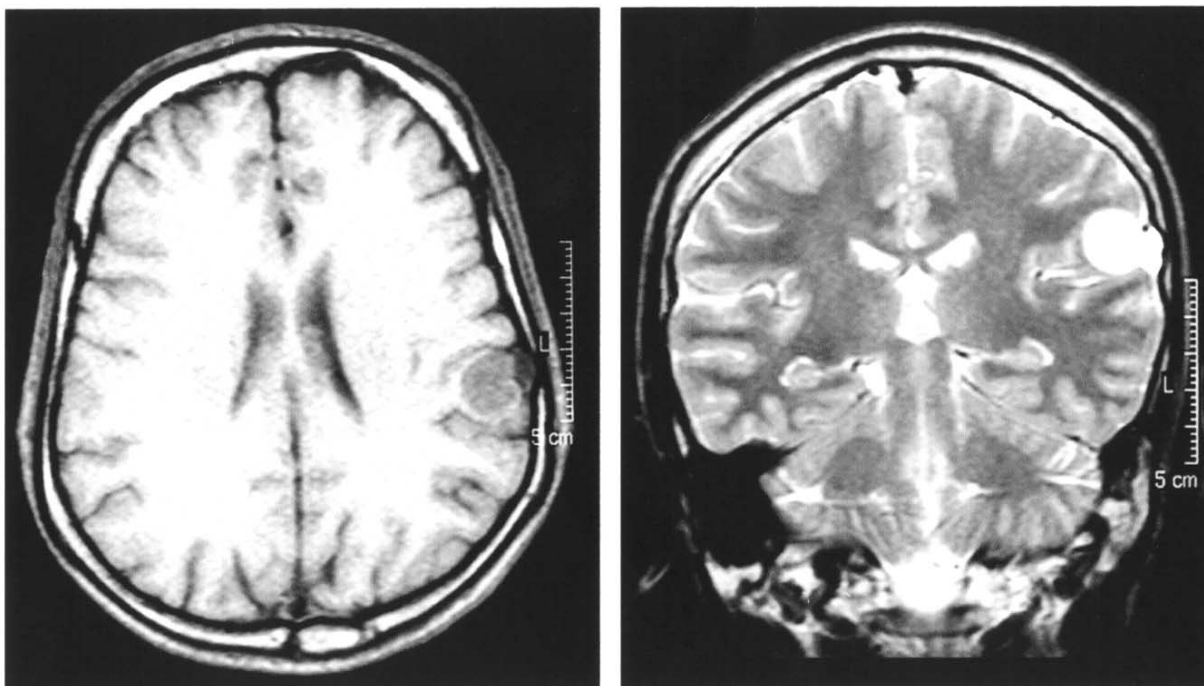


Fig. 1: MRI brain scan: T1 weighted axial section (TR: 500, TE: 15) and T2 weighted coronal section (TR: 2722, TE: 90). Left inferior parietal gyrus tumor (histology: DNET).

during sleep); (2) atypical absences with gradual onset and offset, loss of contact, psychomotor arrest and mild oro-alimentary automatisms; (3) generalized myoclonic seizures; (4) astatic episodes with falls, accompanying myoclonic or tonic attacks.

Diffuse, moderate cognitive dysfunction gradually developed, including short attention span, concentration deficit, language disturbances, lethargy and poor academic performance. Behavioural and personality disturbance with aggressiveness, disinhibition and poor social integration was also noted. A brain magnetic resonance imaging (MRI) scan, performed at the age of 15 years, disclosed a left inferior parietal gyrus space occupying lesion. Routine awake EEGs showed slow background rhythm with frequent, diffuse, slow spike-and-wave complexes. Diffuse 10 Hz fast discharges were also observed during sleep EEG recordings.

Medical therapy including carbamazepine, phenobarbital, valproate, phenytoin, barbitone, vigabatrin, clonazepam (either in monotherapy or in add-on schedules) proved unsatisfactory.

In September 1999 the patient was admitted to our centre, for evaluation for a possible surgical approach. At this time, despite taking lamotrigine 400 mg/day, clobazam 30 mg/day, felbamate 600 mg/day and topiramate 200 mg/day, seizures continued to occur daily.

A pre-surgical non-invasive diagnostic protocol was performed. The history of the attacks was reviewed and it seemed that a few focal signs had been present initially. These included ictal tonic mouth and head

deviation towards the right and post-ictal dysphasia.

Neurological examination revealed nystagmus, lethargy and mild diffuse cognitive dysfunction with poor attentional and concentrational capacity.

Neuropsychological assessment revealed a global IQ (WAIS) of 77 and deficits of verbal fluency, verbal naming, word comprehension and verbal memory with phonemic paraphasias (Aachen Aphasia Test).

A MRI scan (0.5 T magnet) showed a round, bilobated, well-circumscribed lesion which appeared hyperintense on T2 weighted images (WI) and hypointense on T1 WI, slightly enhanced on gadolinium, localized in the left inferior parietal gyrus (Fig. 1). A CT scan detected erosion of the bone of the adjacent calvarium. The neuroradiological findings were suggestive of a dysembryoplastic tumour.

Long term intensive video-EEG monitoring (Telefactor Corp, Conshohocken, PA) was carried out in accordance with international guidelines<sup>10</sup>. Forty-two hours of recording revealed monomorphic 7–8 Hz background activity intermingled with subcontinuous bilateral 2–2.5 Hz spike-and-wave complexes. Rare isolated left centro-temporo-parietal spikes and spike-and-waves (Fig. 2(a) and (b)), and left polyspike-and-wave complexes were also detected (Fig. 2(c)). Several subclinical seizures indicated a well-localized focal activity, involving T3–T5 and C3–P3 channels (Fig. 2(d)). Sleep recordings showed 10 Hz diffuse paroxysmal discharges (Fig. 2(e)) and subcontinuous 2–2.5 Hz spike-and-wave complexes.

Twenty-five seizures were recorded and three

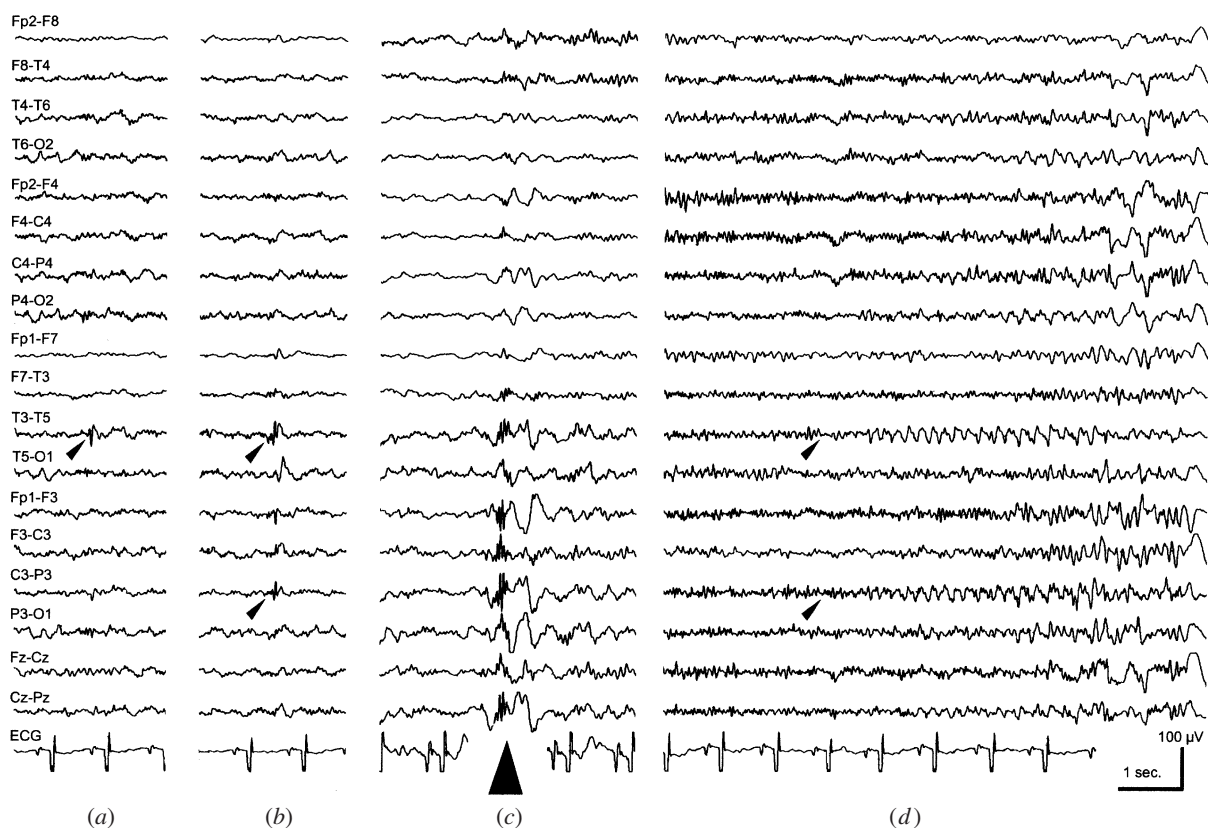


Fig. 2: (a) Isolated spike on T3–T5; (b) brief polyspikes complex on left centro-temporo-parietal regions; (c) left hemispheric polyspikes complex; (d) subclinical recruiting rhythmic theta activity well localized on T3–T5 and C3–P3 with mild contralateral diffusion.

electro-clinical patterns recognized: (1) atypical absences, associated with diffuse slow spike-and-wave complexes; (2) tonic axial seizures, associated with bilateral fast 15–18 Hz activity; (3) atonic seizures, corresponding to brief generalized EEG flattening followed by rapid rhythms.

In addition, several focal ictal clinical and EEG signs were identified. The former include subtle lateralizing motor signs (right lateral deviation of eyes, head and mouth, and right arm tonic posturing), which were recognized at the beginning of three episodes. Focal EEG abnormalities were constituted by left centro-temporo-parietal flattening followed by recruiting irregular spike-and-wave discharge (Fig. 3(a)) or left hemispheric polyspikes (Fig. 3(b)) preceding bilateral discharges. Moreover, focal spike-and-wave irregular discharges could be occasionally observed at the end of the diffuse ictal patterns (Fig. 3(c)).

A Wada test demonstrated left hemisphere dominance for language. The patient was scheduled for resective surgery, and in November 1999 resection of the left parietal lesion was performed without neurological sequelae. Post-operative MRI scanning confirmed the complete removal of the lesion that was histologically identified as a DNET.

In the early post-operative period and 1 month after surgery, two isolated tonic seizures occurred.

No subsequent seizures have been reported, and at the 14-month follow-up the patient was still seizure-free with awake and sleep EEG recordings entirely normal. Neuropsychological assessment also showed a dramatic improvement of cognitive functions.

## DISCUSSION

We have described an unusual case of drug resistant atypical LGS in whom imaging revealed a parietal lesion suggestive of DNET and whose focal electro-clinical signs were only detected by meticulous video-EEG monitoring. This is not the first time focal anatomical lesions in atypical LGS have been reported. The most common localization of focal pathology is to the frontal lobes<sup>5,6</sup>, but temporo-parietal areas can also be affected, although less commonly<sup>7</sup>. Other authors have found atypical LGS patients showing focal ictal clinical signs<sup>11</sup>, lateralizing EEG findings<sup>11</sup> or localized PET abnormalities<sup>12</sup>, indicating the wide spectrum of the syndrome. Moreover, Ohtahara *et al.*<sup>13</sup> suggested that a cortical mechanism of secondary bilateral synchrony may play an important role in the development of LGS.

In the case described here, although the clinical history and the EEGs were suggestive of generalized LGS, focal ictal electro-clinical signs detected by

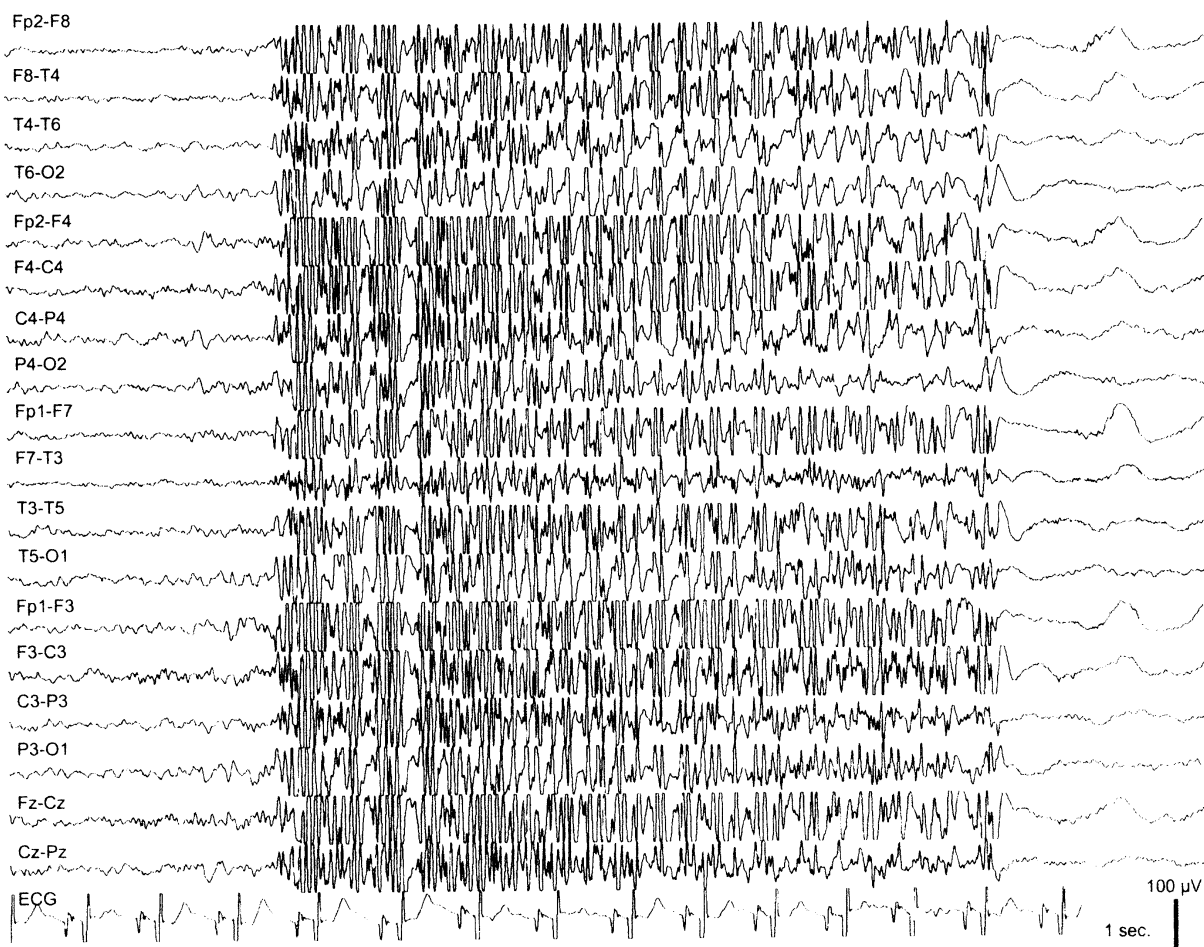


Fig. 2 continued: (e) EEG recording during sleep: 10 Hz diffuse paroxysmal discharge.

long-term video-EEG allowed to surmise a relationship between the left parietal tumour and the epileptogenic zone. The presence of severe language deficits together with a Wada test proven left hemisphere dominance supported this hypothesis. Taking these findings into account, the surgical resection of the DNET was planned. It was decided to avoid intracranial EEG investigations for several reasons: (1) the lesion was surrounded by unresectable cortical areas; (2) the onset of ictal discharges often occurs within DNETs, which are characterized by abnormal neuronal components<sup>14</sup>; and (3) the complete resection of DNETs has been reported to give excellent seizure control in patients with location related epilepsies<sup>15</sup>. In our LGS patient the removal of the parietal DNET was successfully performed and an excellent clinical and EEG outcome was achieved, confirming the important role of secondary bilateral synchrony in the pathophysiology of this case. In particular, the normalization of EEG may explain the dramatic improvement of the post-operative neuropsychological performance, according with the assumption that cognitive impairment found in some people with epilepsy may not only be considered as

a more or less static disability, due to drugs, cerebral pathology, etc., but may in part be a dynamic process related to the occurrence of seizures and/or subclinical epileptiform discharges<sup>16</sup>.

Previous reports detailing unsatisfactory results after lesionectomy in LGS<sup>6</sup> do not diminish the value of our observation, the favourable outcome of which could be dependent on the peculiar epileptogenic potential of dysembryoplastic tissue<sup>14</sup>. Our observation also stresses that in some atypical LGS cases, anatomo-electro-clinical correlations may achieve correct identification of the epileptogenic zone and allow 'curative' surgery.

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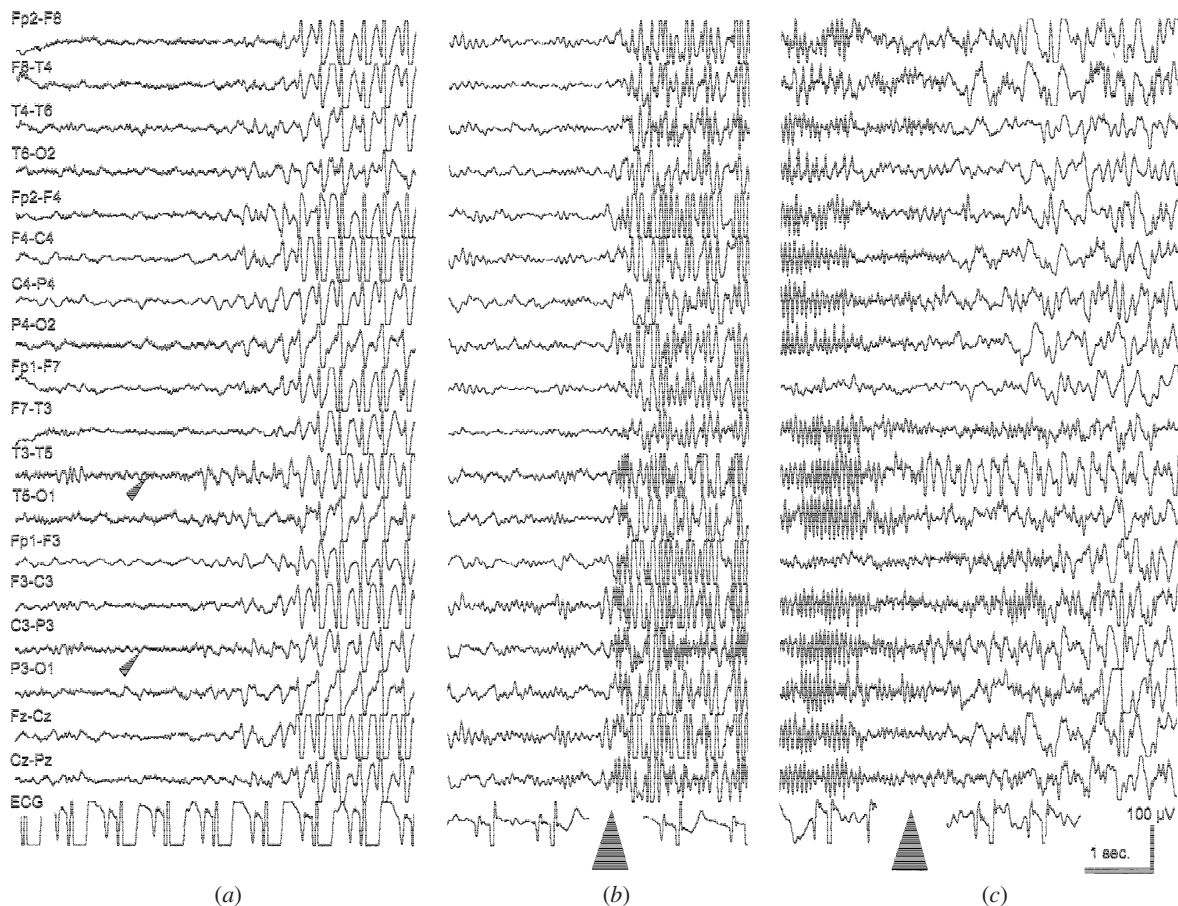


Fig. 3: (a) Flattening followed by recruiting irregular spike-wave complexes well-localized on T3–T5 and C3–P3 before diffuse spike-wave discharge; (b) brief burst of polyspikes on left centro-temporo-parietal regions at onset of diffuse tonic ictal pattern; (c) T3–T5 and C3–P3 spike-wave irregular discharge observed at the end of a tonic seizure.

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