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Clinical case

Psychiatric comorbidity in temporal DNET and improvement after surgery

Comorbidités psychiatriques dans les DNET temporales et amélioration après chirurgie

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ABSTRACT

Background. – "Alien tissue" may be responsible for a higher frequency of psychiatric disorders in patients with temporal lobe epilepsy (TLE). Also, ganglioglioma and dysembryoplastic neuroepithelial tumors (DNET) could represent a risk-factor for the development of post-surgical psychoses. Classically, severe psychiatric disorders contra-indicate epilepsy surgery.
Objectives. – Assessment of inter-ictal psychiatric disorders in 10 consecutive patients with temporal DNET, before and after epilepsy surgery with a minimum of a 2-year follow-up evaluation.
Methods. – DNETs were confirmed on histological examination. Psychiatric disorders were classified according to the DSM-IV-TR.
Results. – Five patients presented inter-ictal psychiatric disorders with, according to the DSM-IV-TR, undifferentiated schizophrenia (one case), "borderline" personality (two cases), intermittent explosive disorder with slight mental retardation (one case), and personality disorders not otherwise specified but with some traits of dependent personality and with mythomania (one case). The condition of these five patients dramatically improved after surgery. No psychiatric behavior or "de novo" psychosis was observed after surgery in any of the patients.
Conclusion. – The prevalence of inter-ictal psychiatric disorders appears to be high in epileptic patients with a temporal lobe DNET primarily in relation to personality and behavioral problems with some degree of impulsivity and verbal aggressiveness. The improvements after surgery suggest that this therapy could be performed in these patients and severe psychiatric disorders do not contra-indicate this procedure.
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Mots clés :
DNET
Chirurgie de l'épilepsie
Troubles psychiatriques

RÉSUMÉ

Contexte. – Un « tissu alien » peut être responsable d'une fréquence plus élevée de troubles psychiatriques chez les patients atteints d'épilepsie temporale (TLE). Les gangliomes et les tumeurs neuro-épithéliale dysembryoplasiques (DNET) pourraient représenter un facteur de risque pour le développement de psychoses post-chirurgicales. Classiquement, les troubles psychiatriques graves contre-indiquent la chirurgie de l'épilepsie.
Objectifs. – Évaluation des troubles psychiatriques intercritiques chez 10 patients consécutifs avec DNET temporale avant et après chirurgie de l'épilepsie avec au minimum de 2 ans de suivi.
Méthodes. – Les DNET ont été confirmées à l'examen histologique. Les troubles psychiatriques ont été classés selon le DSM-IV-TR.

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Résultats. – Cinq patients souffraient de troubles psychiatriques intercritiques avec, selon le DSM-IV-TR, schizophrénie indifférenciée (un cas), personnalité « borderline » (deux cas), trouble explosif intermittent avec un léger retard mental (un cas) et trouble de la personnalité non spécifié, avec traits de la personnalité dépendante et mythomanie (un cas). L'état de ces cinq patients s'est considérablement amélioré après la chirurgie. Aucun comportement psychiatrique ou psychose « de novo » n'a été observée après l'intervention chirurgicale.
Conclusion. – La prévalence des troubles psychiatriques intercritiques semble élevée chez les patients épileptiques avec DNET temporale ; il s'agissait essentiellement des troubles de la personnalité et du comportement avec impulsivité et agressivité verbale. Les améliorations après chirurgie de l'épilepsie suggèrent que ces procédures peuvent être bénéfiques chez ces patients et les troubles psychiatriques graves ne doivent pas contre-indiquer la chirurgie.
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Dysembryoplastic neuroepithelial tumors (DNET) correspond to a benign mixed neuronal-glial brain tumor, which occurs during embryogenesis. Previously reported as low-grade gliomas or "hamartomas", they were first described in the eighties [1]. Epileptic seizures initially appear during childhood mostly before the age of 20. When accessible, these tumors can be surgically removed [1].

Epileptic patients with temporal lobe epilepsy may develop inter-ictal psychosis [2,3]. Seizures start in adolescence. Onset of epilepsy precedes the development of psychosis by an interval of several years (10–15 years) [4,5]. Drug-resistance, a history of status epilepticus, complex partial seizures, and several types of seizures appear as risk-factors for psychosis [6]. Taylor (1975) reported that "alien" tissue, such as small tumors, hamartomas, or focal dysplasia might be responsible for a higher frequency of psychiatric disorders in patients with temporal lobe epilepsy [7]. Ganglioma and DNET could represent a risk-factor for the development of post-surgical psychoses [8,9]. Usually, temporal lobectomy is contra-indicated in cases of severe inter-ictal psychiatric disorders because of a risk of decompensation. We decided to examine 10 consecutive drug-resistant epileptic patients with temporal DNET treated with surgery in order to determine the frequency and nature of inter-ictal psychiatric disorders and their evolution after surgical treatment.

1. Patients and methods

Subjects with DNET were identified from a database concerning patients from the medical and surgical units for epilepsy of Montpellier during 10 consecutive years. Only epileptic patients with temporal DNET operated on with a minimum of 2-year follow-up evaluation were considered. All patients had drug-resistant temporal lobe epilepsy. All patients had a first phase of non-invasive exploration including five days of non-stop EEG-video recording (10/20 system plus anterior–inferior temporal electrodes). During this recording, patients underwent neuropsychological tests and inter-ictal and ictal SPECT whenever possible. Four patients underwent an invasive phase with implantation of intra-cerebral electrodes (SEEG). DNET diagnosis was made both on the basis of clinical and radiological criteria and confirmed on histological examination (Figs. 1–5). Psychiatric assessment was performed by the same psychiatrist prior to and following surgery. Psychiatric disorders were classified according to the DSM-IV-TR [10], and the ICD-10 criteria (World Health Organization). Patients after surgery had follow-up appointments at 1, 3, 6, 12, 18 and 24 months, and every year thereafter. Seizure outcome was classified according to Engel's classification [11,12].

2. Results

Patients included 3 men and 7 women with an average age of 31.4 years at the time of surgery (range from 18–40 years). The tumor was located in the left temporal lobe in six cases, and in the right temporal lobe in the other four cases. Table 1 summarizes the clinical features and demographic characteristics of the population.

Five out of 10 patients presented psychiatric disorders before surgery including personality traits in 4 (80%). Psychiatric disorders were classified according to the DSM-IV-TR and the ICD-10 as follows: two cases with "borderline" personality (301.83; F60.31) (patient 1, 2), one case with intermittent explosive disorder and slight mental deficiency (312.34; F 63.89) (patient 3) and one case with personality disorders not otherwise specified but with some traits of dependent personality and with mythomania (301.9; F60.9) (patient 4). One patient was diagnosed having undifferentiated schizophrenia (295.90; F 20.3) (patient 5). For three patients, psychiatric disorders were severe enough to justify involuntary admittance to a psychiatric ward (patient 1, 2, 5). Table 2 summarizes the psychiatric disorders. All patients dramatically improved after surgery. Patients 1 and 2 were cured as they had been treated with neuroleptic drugs before surgery and these drugs were stopped after surgery. The patient with undifferentiated schizophrenia had an acute psychotic decompensation three months and 4 years after surgery requiring his admittance to a psychiatric ward. However, over the five years of follow-up after surgery, this patient's mental condition improved significantly as

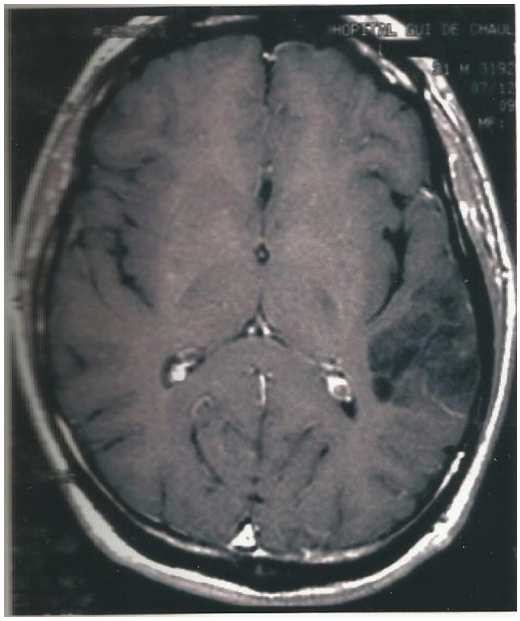

Fig. 1. Axial T1-weighted MRI sequence, hypointense left temporal aspect with heterogeneous polycystic appearance.
IRM séquence pondérée en T1, coupe axiale, aspect d'hyposignal temporal G d'allure polykystique hétérogène.

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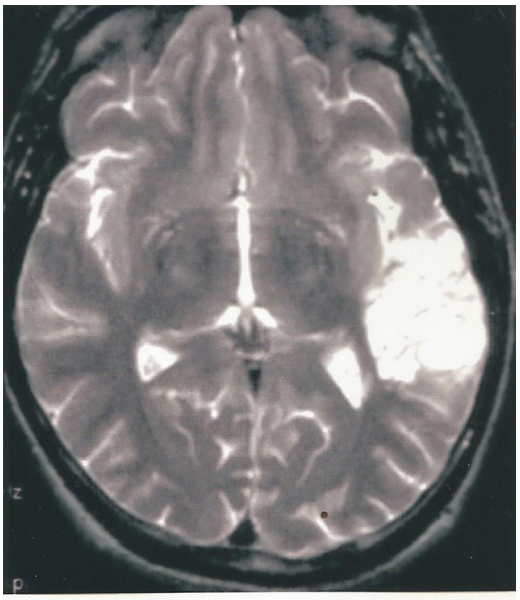

Fig. 2. Axial and coronal T2-weighted MRI sequence, hyperintense left temporal lesion.
IRM séquence pondérée en T2, coupe axiale et coronale, aspect d'hypersignal temporal G.

did his epilepsy. Before surgery, his seizures led to serious psychological disturbances. He was unable to deal with his auras that he found unbearable. The dramatic improvement of epilepsy led to a dramatic improvement of his mental condition. No psychiatric disorders including "de novo" psychosis was observed after surgery in any of the patients. Table 3 summarizes clinical, EEG features and treatments of patients with temporal DNET and psychiatric disorders.

3. Discussion

It is generally observed that psychological or psychiatric problems are more frequent among epileptic patients than in the general population. The nature of these disorders can be social isolation, anxiety, depression and personality disorders, partly in response to the permanent fear of a sudden seizure and to the chronic nature of epilepsy. Personality changes, behavioral disorders and cognitive disorders can be caused by multiple treatments. A patient with brain damage can be affected at the same time with mental deficiency, mental disorders and epilepsy. However, different psychiatric profiles have been reported according to the type of epilepsy: alternative psychosis in generalized epilepsy [13], schizophrenia-like disorders after several years of temporal lobe epilepsy [2,3], and personality and social adaptability disorders for juvenile myoclonic epilepsy [14]. In this population of patients with refractory epilepsy due to a temporal DNET, 50% presented psychiatric disorders before surgery. These disorders were severe enough to cause involuntary admission of three patients to a psychiatric ward. Except for the patient with undifferentiated schizophrenia, the others had psychiatric disorders related to personality and behavioral problems and except for the patient with some traits

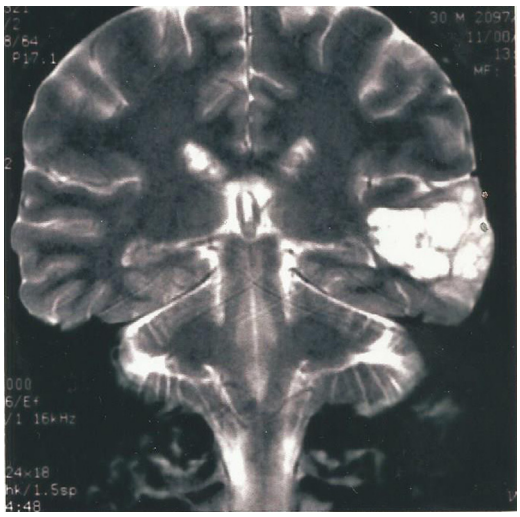

Fig. 4. Axial and coronal T2-weighted MRI sequence, hyperintense left temporal lesion.
IRM séquence pondérée en T2, coupe axiale et coronale, aspect d'hypersignal temporal G.

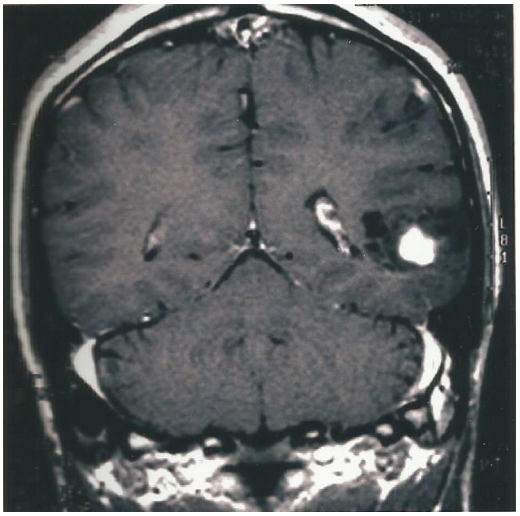

Fig. 3. Coronal T1-weighted MRI with gadolinium sequence, homogeneous nodular contrast enhancement.
IRM séquence pondérée en T1 avec gadolinium, coupe coronale, prise de contraste nodulaire homogène.

Fig. 5. CT scan, calcifications of the left temporal pole.
TDM, calcifications du pôle temporal G.

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Table 1
Clinical characteristics of the 10 patients with temporal DNET.
Caractéristiques cliniques des 10 patients avec DNET temporale.

Patient	Sex	Laterality	Onset of epilepsy (years)	DNET localisation	Type of temporal lobe epilepsy	SEEG	Age at surgery (years)	Type of surgery	Surgical outcome (follow-up)
1	M	Right	13	Right pole and mid-temporal region	Mesiolateral	No	31	Amygdalo-hippocampectomy + anterior and lateral temporal lobectomy (DNET resection)	Engel 1a (8 years)
2	F	Right	26	Right temporal lobe	Mesiolateral	No	30	Amygdalo-hippocampectomy + anterior and lateral temporal lobectomy (DNET resection)	Engel 1d (7 years)
3	F	Left	4	Left medial temporal lobe	Mesial	No	40	Amygdalo-hippocampectomy + temporal lobectomy including the DNET	Engel 1a (5 years)
4	M	Right	7	Left lateral temporal lobe	Mesiolateral	Yes	33	Anterior temporal lobectomy + inferior part of the DNET. Hippocampus not removed	Engel 2b (8 years)
5	M	Right	14	Left lateral temporal lobe	Mesial	Yes	18	Anterior temporal lobectomy and DNET resection. Hippocampus not removed	Engel 2b (5 years)
6	F	Right	17	Right lateral temporal lobe	Mesiolateral	Yes	29	Amygdalo-hippocampectomy + temporal lobectomy including the DNET	Engel 1b (4 years)
7	F	Right	0.4	Right medial temporal lobe	Mesial	No	33	Amygdalo-hippocampectomy + anterior temporal lobectomy with DNET	Engel 1d (3 years)
8	F	Left	14	Left temporal lobe (medial and pole)	Mesial	No	31	Amygdalo-hippocampectomy + anterior temporal lobectomy with DNET	Engel 1a (6 years)
9	F	Right	18	Left temporal pole	Mesial	Yes	34	Anterior temporal lobectomy. DNET resection. Hippocampus not removed (Hippocampus functional and IQ = 140)	Engel 1d (7 years)
10	F	Right	13	Left medial temporal lobe	Mesial	No	35	Amygdalo-hippocampectomy + anterior temporal lobectomy with DNET	Engel 1a (2 years)

F: female; M: male; IQ: intelligence quotient.
F : femme ; H : homme ; IQ : quotient intellectuel.

Table 2
Psychiatric disorders in patients with temporal DNET.
Troubles psychiatriques chez les patients avec DNET temporale.

Patient	Onset of psychiatric disorders/epilepsy	Symptoms	Psychiatric admissions	Diagnosis	DSM-IV-TR ICD-10	Follow-up after surgery (years)	Outcome of psychiatric disorders
1	With onset of epilepsy (13 years)/13 years	Numerous suicide attempts (phlebotomy, electrocution, rifle). First suicide attempts at 13 years. Self-harming, violent. Chronic treatment with neuroleptics before surgery	Yes, many involuntary admissions	Borderline personality	301.83 F60.31	8	Cured of psychiatric disorders
2	Adolescence (18 years)/16 years	Verbal violence, frustration intolerance. One episode of agitation and aggressiveness leading to hospitalization in a psychiatric ward. Chronic treatment with neuroleptics before surgery	Yes, one involuntary admission	Borderline personality	301.83 F60.31	7	Cured of psychiatric disorders
3	Childhood (9 years)/1 years	Slight mental deficiency, frustration intolerance, emotional state with anger, anxiety. Some delusions of persecution. Chronic treatment with neuroleptics before surgery	No	Intermittent explosive disorder and slight mental retardation	312.34 F63.89	5	Dramatic improvement
4	Adolescence (16 years)/7 years	Immaturity, dependent personality, mythomania	No	NOS personality disorder	301.9 F60.9	8	Dramatic improvement
5	Adolescence (16 years)/14 years	Delusions of persecution, somatic delusions with hypochondria, auditory hallucinations, social isolation	Yes, involuntary and voluntary admissions	Undifferentiated schizophrenia	295.90 F20.3	5	Major improvement. On neuroleptic treatment.

NOS: Not otherwise specified.
NOS : non spécifié autrement.

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Table 3
Clinical, EEG features and treatments of patients with temporal DNET and psychiatric disorders.
Caractères cliniques, EEG, et traitements des patients avec DNET temporale et troubles psychiatriques.

Patient	Clinical features	EEG	Pre-op treatment	Post-op treatment
1	Auditory aura, contact rupture, gestural automatisms; sometimes left gyration, rare generalization, post-ictal phase with temporo-spatial disorientation, hunger, ambulation	Right temporal focus	PHT, PB, CBZ, VPA, BZD (clonazepam, clobazam)	–
2	Impression of already lived, olfactive aura unpleasant smell, perfume, feeling of fear, children's song, contact rupture, trouble with word recall	Puffs of left temporal spikes or slow spikes, sometimes diffusing to contralateral regions with sensitivity to hyperventilation	PB, VPA, LMT, CBZ, TGB, GBP, GVG, BZD	–
3	Contact rupture, gestural automatisms, chewing	Left temporal spikes and spike-waves	VPA, PB, LMT, CBZ, PHT, TGB, VGV, TPM, BZD	–
4	Contact rupture, staring, stopping of the on-going activity, gestural automatisms, aphasia	Left temporal slow waves, discharges of left polyspikes, left spikes and slow spikes	PB, VGB, CBZ, LMT	VGB, CBZ, LMT
5	Feeling of fear, contact rupture, epigastric discomfort, disordered activity, incoherent words, jargon, mouth noises	Left anterior temporal focus with spread to medial temporal structures	CBZ, TPM	–

PB: phenobarbital; PHT: phenytoin; CBZ: carbamazepine; VPA: sodium valproate; BZD: benzodiazepine; LMT: lamotrigine; GVG: vigabatrin; TGB: tiagabine; TPM: topiramate; GBT: gabapentin.

of dependent personality, the most characteristic finding was the observation of some degree of impulsivity and verbal aggressiveness in the other 4 (80%). The figure of 50% of psychiatric disorders appears high. However, it is well known that severe drug-resistant epilepsy leads to a large amount (50%) of DSM abnormalities before surgery whatever the etiology. There is probably an overestimation as we are a tertiary referral center recruiting the most severe cases and, in this study, we chose to include only patients treated with surgery and DNET proved by histology. Patients whose condition was not severe enough to have surgery and those having only a suspicion of DNET on MRI were not included.

The recurrence of seizures, in particular from the temporal-limbic lobe (which controls emotions and affects) is thought to play a role in the genesis of psychiatric disorders in epileptic patients [3]. "Alien tissues" could also be one of the other specific factors in lesional epilepsy. In a series of 255 patients operated for drug-resistant temporal epilepsy, Taylor [7] compared patients presenting an "alien tissue" to those with hippocampal sclerosis. Pre-surgery psychosis was found respectively in 23% and 5% ($P = 0.05$). The so called "alien tissues" were generally discrete with no specific location in the temporal lobe.

Severe psychiatric disorders are often considered as a contra-indication for epilepsy surgery because it may be difficult to establish accurate pre-surgical assessment, to obtain an informed consent and for fear of worsening psychiatric disorders. But it is possible to improve the quality of life and reduce the drug load if seizures can be fully controlled after surgery. Reutens et al. [15] reported good results with operations on five cases of chronically psychotic patients. Recovery from epilepsy led to better management with psychotropic agents. Psychosis does not currently represent a contra-indication to surgical treatment [16]. This was the case of patient 5. In this schizophrenic patient, the hippocampus was not removed although it participated in the seizures (SEEG). We were afraid of the possibility of psychotic exacerbation if we removed it and also because in this right-handed patient the left hippocampus was functional (neuropsychological and Wada tests).

It is well established that surgery for epilepsy, particularly temporal lobe epilepsy, can cause psychiatric disorders, especially depressive states [17]. Psychotic disorders are the most severe psychiatric complications, which occur after temporal lobectomy. They represent either depressive or paranoid-like psychosis [18,19]. Taylor and Falconer [8] first reported psychotic disorders after surgical treatment for temporal lobe epilepsy due to a ganglioglioma. Andermann et al. [9] also reported that psychotic disorders could appear more frequently after resection of ganglioglioma than after any other lesion but also after resection of a DNET. They reported an 8-year-old girl with autistic features before surgery who became psychotic after a transient improvement in her behavior. A right temporal DNET was resected and she remained seizure-free over the years. In our series, the long follow-up after surgery (over 5 years) permitted us to be reassuring.

In conclusion, prevalence of inter-ictal psychiatric disorders appears to be high for patients with refractory temporal epilepsy that is symptomatic of a DNET. In almost all cases, the disorders disappeared after surgery. Thus, even severe psychiatric disorders do not represent a contra-indication for surgical treatment of temporal DNET-related epilepsy.

Disclosure of interest

The authors declare that they have no competing interest.

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